Low Diagnostic Yield of Electrocardiogram Testing in Younger Patients With Syncope

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Study objective: Routine ECG testing is recommended in the evaluation of syncope, although the value of such testing in young patients is unclear. For ECG testing, we assess the diagnostic yield (frequency that ECG identified the reason for syncope) and predictive accuracy for 14-day cardiac events after an episode of syncope as a function of age.

Methods: Adult patients with syncope or near-syncope were prospectively enrolled for 1 year at a single academic emergency department (ED). A 3-physician panel reviewed ED charts, hospital records, and telephone interview forms to identify predefined cardiac events. The primary outcome included all 14-day, predefined cardiac events including arrhythmia, myocardial ischemia, and structural heart disease.

Results: Of 592 eligible patients, 477 (81%) provided informed consent. Direct telephone contact or admission/outpatient records were successfully obtained for 461 (97%) patients, who comprised the analytic cohort. There were 44 (10%) patients who experienced a 14-day cardiac event. Overall diagnostic yield of ECG testing was 4% (95% confidence interval 2% to 6%). For patients younger than 40 years, ECG testing had a diagnostic yield of 0% (95% confidence interval 0% to 3%) and was associated with a 10% frequency of abnormal findings.

Conclusion: ECG testing in patients younger than 40 years did not reveal a cardiac cause of syncope and was associated with a significant frequency of abnormal ECG findings unrelated to syncope. Although our findings should be verified in larger studies, it may be reasonable to defer ECG testing in younger patients who have a presentation consistent with a benign cause of syncope. [Ann Emerg Med. 2008;51:240-246.]

INTRODUCTION

Background
Syncope, defined as a transient loss of consciousness, is a common emergency department (ED) presentation and accounts for 740,000 US ED visits per year. The ED evaluation of syncope is complicated by the many potential causes that include benign and life-threatening conditions, and a cause of syncope is not identified in more than 50% of patients despite extensive evaluation.

ECG testing has been advocated in almost all patients with syncope. Although the ECG reveals a cause of syncope in less than 5% of patients, ECG testing is noninvasive and may reveal other abnormalities that indicate risk for arrhythmia or cardiac ischemia. Several practice guidelines suggest routine ECG testing in the evaluation of syncope, although the American College of Emergency Physicians recommends ECG testing when medical history and physical examination do not reveal a diagnosis.

Importance
Physician ordering of an ECG appears to vary significantly by patient age. In an analysis of nationally representative ED
practice data of patients who presented with syncope, documentation of ECG testing increased from 33% in patients younger than 20 years to 83% in patients older than 80 years. However, the clinical value of ECG testing for syncope as a function of age is not well understood. It is possible that routine ECG testing in a younger, low-risk population can identify incidental abnormalities without improving diagnostic yield. Such findings may have the potential to trigger unnecessary health care use, including cardiology consultation and hospitalization.

Goals of This Investigation
Using data from a prospective cohort of ED patients with syncope, we describe the diagnostic yield and predictive accuracy of ECG testing as a function of age. We defined diagnostic yield as the frequency that the initial ED ECG identifies a presumed cardiac reason for syncope (eg, ventricular tachycardia). We defined predictive accuracy as the ability of any ECG abnormalities, including nondiagnostic findings, to identify patients at risk of a 14-day cardiac event (eg, ECG finding of sinus rhythm with left bundle branch block in a patient who later develops ventricular tachycardia). We a priori hypothesized that the diagnostic yield and predictive accuracy of ECG testing would be low and associated with a significant frequency of incidental findings in young patients.

MATERIALS AND METHODS
Study Design and Setting
This was a single-center, prospective, observational, cohort study that enrolled patients from April 18, 2005, to April 18, 2006.8 The study site is an urban, academic ED with an emergency medicine residency and an annual volume of 40,000 visits. The study site institutional review board approved the research protocol.

Selection of Participants
Adult patients with a complaint of syncope or near-syncope were eligible for enrollment. Syncope is defined as a sudden, transient loss of consciousness. Near-syncope is defined as a sensation of imminent loss of consciousness, without actual syncope. The treating resident or attending physician determined patient eligibility for study enrollment.

Exclusion criteria included loss of consciousness related to a witnessed seizure, loss of consciousness after head trauma, ongoing confusion (including baseline cognitive impairment or dementia), intoxication, age younger than 18 years, inability to speak English or Spanish, do not resuscitate or do not intubate status, and lack of follow-up contact information.

An ED-based research assistant was available from 8 AM to 10 PM, 7 days a week. Research assistants identified all potentially eligible patients by reviewing the ED intake log and querying the charge nurse, attending physicians, and resident physicians as they were evaluating active ED patients. A research assistant explained the goals of the study to eligible patients and obtained written informed consent for enrollment. Retrospective internal quality checks, including medical record review and ED intake log review, demonstrated that 76% of potentially eligible patients were identified and screened. There were no differences in age and sex among potentially eligible patients who were screened and those who were not screened.

After assessing enrolled patients, the treating resident physician completed a structured data form, including history of cardiac comorbidities and ECG findings. Cardiac comorbidities included coronary artery disease, congestive heart failure, aortic stenosis, pulmonary heart disease, or arrhythmia (including ventricular arrhythmia, supraventricular rhythms including atrial fibrillation or flutter, bradycardia, sick sinus syndrome, or implanted pacemaker or defibrillator). Any ECG finding of nonsinus rhythm, left or right bundle branch block, left axis deviation, left or right ventricular hypertrophy, abnormal conduction interval excluding first-degree block, Q/ST/T changes consistent with acute or chronic ischemia, or sinus bradycardia less than 50 beats per minute was considered abnormal (see Appendix E1, available online at http://www.annemergmed.com). The treating physician also noted whether the ECG demonstrated nonspecific ST/T changes in the absence of other abnormalities. Information about age, sex, race, and ethnicity was obtained by research assistants from registration data. A research assistant verified completeness of data forms.

The clinical evaluation data forms were completed by emergency medicine residents with 2 to 4 years of experience. To assess the interrater reliability of ECG interpretation, the attending physician independently completed a second data form in a convenience sample of 230 patients. There was 84%
agreement on the presence of any ECG abnormality ($\kappa=0.6$) and 75% agreement on the presence of either ECG abnormalities or non-specific ST/T changes ($\kappa=0.5$).

For patients who did not receive ECG testing as part of routine care, a research assistant obtained patient permission to perform a study ECG. Study ECGs were immediately sealed and were not made available to treating physicians; they were interpreted later by a study investigator (B.C.S.), who was blinded to other aspects of the patient’s presentation.

A work group of emergency physicians, cardiologists, internists, and geriatricians identified syncope-related, cardiac conditions for which hospital admission may be beneficial, including sudden death, myocardial infarction, arrhythmias, and diagnosis of structural heart disease thought to be related to syncope. The work group identified 14 days as the relevant period for assessing the necessity for acute hospitalization after an episode of syncope.

We consulted with local electrophysiologists to define clinically significant arrhythmias. Arrhythmias included ventricular tachycardia more than 3 beats, sick sinus disease with alternating sinus bradycardia and tachycardia, sinus pause greater than 3 seconds, third-degree atrioventricular block, Mobitz II atrioventricular block, symptomatic supraventricular tachycardia (pulse rate >100 beats/min), symptomatic atrial flutter or fibrillation with rapid ventricular response (pulse rate >100 beats/min), symptomatic bradycardia (pulse rate <60 beats/min), and bradycardia with pulse rate less than 40 beats/min. "Symptomatic" refers to the simultaneous occurrence of dizziness, lightheadedness, hypotension (systolic blood pressure <90 mm Hg), or syncope with an arrhythmia on ECG monitoring. Structural heart disease included aortic outflow obstruction, cardiomyopathy, and heart transplant complications. Admitted patients who required an acute cardiac intervention during their stay were also considered to have a serious outcome. Acute cardiac interventions included pacemaker or defibrillator insertion, coronary angioplasty, and surgery for valvular heart disease.

Outcome Measures

Direct patient telephone follow-up was performed to identify hospital admissions or any serious clinical events that occurred outside the study site. We attempted to contact all patients at 14 days after index ED visit for a structured telephone interview by a research assistant. Transcribed summaries of all inpatient and outpatient visits at the study site hospital were available through a computer data system. Inpatient records and discharge summaries were obtained for all patients transferred from the study site ED to other hospitals for admission.

Two emergency physicians independently reviewed available ED documentation, inpatient records, and telephone interview forms for all enrolled patients. Records for all patients identified as potentially experiencing a serious outcome were then reviewed by a panel of 3 emergency physicians. All reviewing physicians were blinded to the structured data forms completed by treating physicians. The treating physician’s interpretation of the initial ED ECG was unavailable to the reviewing physicians. Occurrence and timing of cardiac events were determined through panel consensus and recorded on a structured data form.

For patients who experienced a cardiac outcome, the 3-physician panel re-reviewed ED records and ECGs to determine whether ECG testing was diagnostic for the cardiac event. For example, if the panel review identified a patient as experiencing ventricular tachycardia, an ED ECG demonstrating ventricular tachycardia would be considered diagnostic for the event. If, on the other hand, the initial ECG demonstrated sinus rhythm with left bundle branch block and the patient developed ventricular tachycardia later in the hospital stay, then the initial ED ECG would be considered nondiagnostic. The classification of ECGs as diagnostic or nondiagnostic was made by panel consensus.

Primary Data Analysis

We analyzed age by 20-year intervals (18 to 39; 40 to 59; 60 to 79; ≥80 years) that included similar numbers of patients. We performed descriptive and univariate analyses using contingency tables and Fisher’s exact test for categorical data. The ECG diagnostic yield is presented as a function of age.

We determined the predictive accuracy of ECG findings by calculating the sensitivity, specificity, negative predictive value, and positive predictive value of ECG abnormalities, including nondiagnostic findings, to identify patients with 14-day cardiac events. "True positive" classification included diagnostic ECGs, as well as abnormal ECGs that did not reveal a cause of syncope in patients who experienced a cardiac event. For example, a patient with an ECG finding of left bundle branch block who later developed ventricular tachycardia on monitoring would be classified as a "true positive." For the purpose of calculating test characteristics, an abnormal ECG finding was classified as a "false positive" if it occurred in a patient who did not have a 14-day cardiac event. For example, an ECG finding of left bundle branch block in a patient who did not experience the primary outcome would be considered a "false positive." In the primary analysis, we used ECG interpretations by the treating resident physicians.

In a sensitivity analysis, we assessed the effects of including nonspecific ST/T findings on ECG predictive accuracy. Finally, we assessed whether ECG predictive accuracy was dependent on the clinical experience of the treating physician (resident versus attending).

The study sample size was powered to externally validate a previously published clinical decision rule; this report is a planned secondary analysis of the study data.

Data management and statistical analyses were conducted using SAS software, version 9.1 (SAS Institute, Inc., Cary, NC). Tests characteristics and associated 95% confidence intervals (CIs) were calculated using a publicly available SAS macro.
RESULTS

Of the 709 patients who were screened during the study period, 592 (83%) were eligible, and 477 (81%) provided informed consent to participate. Of the 117 ineligible patients, reasons for exclusion included witnessed seizure (12%), head trauma (12%), alcohol intoxication (9%), age younger than 18 years (21%), inability to speak English or Spanish (12%), and do not resuscitate or do not intubate status (4%); some patients met more than 1 exclusion criterion. We found no important differences in age, sex, race, or ethnicity between eligible patients who provided or declined informed consent. Direct telephone follow-up was obtained for 436 (91%) patients. Of the remaining patients, 25 (6%) had available inpatient or outpatient data available for at least 2 weeks after the date of enrollment, and 16 (3%) had no available follow-up information. Patients without any available follow-up information were younger and more likely to be of nonwhite race compared with patients with follow-up information. The final analytic cohort included 461 patients who had available follow-up information.

Study sample characteristics are presented in Table 1. Frequency of cardiac comorbidities, cardiac events, and abnormal ECGs increased as a function of age. The overall cardiac event rate was 10%. Of the total cohort, 7% of patients did not receive an ECG as part of routine care and refused a study ECG, although all patients older than 60 years received ECG testing. All patients who experienced a 14-day cardiac event received ECG testing. ECG testing was diagnostic for a cardiac reason for syncope in 4% of all patients, but the ECG did not identify any cardiac causes of syncope in patients younger than 40 years.

Table 2 presents the predictive accuracy of ECG testing. Specificity decreased with advancing age, and the point estimate for positive predictive value was lowest in the youngest age interval. CIs for estimates of sensitivity were wide because of the low prevalence of events. Specificity, positive predictive value, and negative predictive value varied minimally when we included the presence of nonspecific, ST/T changes on ECG testing. There were no important differences in ECG test characteristics when interpreted by a resident or attending physician.

Description and frequency of “false-positive” ECG abnormalities are presented in Table 3. There were 13 (10%) false-positive ECG findings in the youngest age group; 2 patients were admitted to the hospital for concern of Brugada’s syndrome, and 1 patient received outpatient cardiology evaluation for a shortened PR interval. All 3 of these patients were thought to have vasovagal syncope by consulting cardiologists and discharged home without antiarrhythmic medication or further cardiac testing. None of these patients were thought to have Brugada’s syndrome or an accessory pathway by the consulting cardiologists.

LIMITATIONS

We performed a prospective, cohort study designed to minimize selection bias through high rates of screening (76%), enrollment (81%), and follow-up (97%), and the observed frequency of short-term, cardiac events is similar to that of other recently reported ED cohorts. However, our study has several potential limitations.

We enrolled patients with syncope and near-syncope because the diagnostic evaluation is similar for both of these conditions.

sun et al
ECG Testing in Patients With Syncope

Table 1. Demographic characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Patients (n=461)</th>
<th>18-39 (n=133)</th>
<th>40-59 (n=105)</th>
<th>60-79 (n=114)</th>
<th>≥80 (n=109)</th>
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</thead>
<tbody>
<tr>
<td><strong>Age Group, y</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Any cardiac history*</td>
<td>139 (30)</td>
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<tr>
<td>Male*</td>
<td>204 (44)</td>
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<tr>
<td>Hispanic*</td>
<td>43 (9)</td>
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<tr>
<td>Nonwhite</td>
<td>101 (22)</td>
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<tr>
<td>Chief complaint of syncope**</td>
<td>160 (65)</td>
<td></td>
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<tr>
<td>Any 14-day cardiac events*</td>
<td>44 (10)</td>
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<tr>
<td>Arrhythmia</td>
<td>33 (7)</td>
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<tr>
<td>Myocardial ischemia</td>
<td>2 (1)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Aortic outflow obstruction</td>
<td>5 (1)</td>
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<tr>
<td>Cardiomyopathy</td>
<td>2 (1)</td>
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<td>Heart transplant complication</td>
<td>2 (1)</td>
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<tr>
<td>Missing ECG*</td>
<td>31 (7)</td>
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<td>Study ECG*</td>
<td>40 (9)</td>
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<td>Abnormal ECG*</td>
<td>127 (28)</td>
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<td>Nonnormal ECG*</td>
<td>165 (36)</td>
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<tr>
<td>Diagnosis made by ECG*</td>
<td>17 (4)</td>
<td></td>
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<tr>
<td>95% CIs</td>
<td>2-6</td>
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</tbody>
</table>

All data are No. (%) except where indicated.

*Difference by age group: P<.01 on χ² testing.

**Versus chief complaint of near syncope.

*ECG not ordered by treating physicians; ECG was obtained for study purposes only.

*See Materials and Methods: nonnormal ECG includes all abnormal ECGs, as well as ECGs that include nonspecific ST/T-wave changes.

Volume 51, No. 3 : March 2008
Annals of Emergency Medicine 243
It is possible that event rates and ECG test characteristics differ between patients with syncope and those with near syncope. In post hoc analysis, however, we found no qualitative change in our findings when patients were analyzed by presenting complaint of syncope versus near syncope.

We successfully screened 76% of potentially eligible patients during study hours. Most of the potentially eligible patients who were not screened were missed because of research assistant unavailability (eg, multiple patients requiring screening at the same time or gaps in research assistant coverage schedule). Although we did not find a difference in age and sex between potentially eligible patients who were screened and those who were not, this may be a source of selection bias.

Despite our study protocol, some enrolled patients who did not receive ECG testing as part of routine care refused to have a study ECG performed. Because all patients with a cardiac event received ECG testing, missing ECG data likely result in an underestimate of the frequency of false-positive results.

The interrater reliability of ECG interpretation was modest between resident and attending physicians. However, our results were not affected when we compared resident and attending ECG interpretations, and our reported interrater reliability of ECG interpretation is similar to findings from a recent ED-based syncope study (K=0.68).10

The classification of ECGs as diagnostic or nondiagnostic was performed by a 3-physician panel that had access to patient...
medical records and initial ECGs. ECG review unblinded to age may be source of bias. However, there was high degree of agreement among the 3 reviewers (89% unanimous judgment on first review) about whether the initial ECG was diagnostic for the cause of syncope, suggesting that the risk of bias is low.

Our composite outcome included arrhythmia, myocardial infarction, and structural heart disease. Structural heart disease includes preexisting conditions and may be conceptually distinct from discrete events such as arrhythmias and myocardial infarction. In a post hoc analysis, we found no qualitative changes in our findings when we excluded patients who were thought to have structural heart disease as the cause of syncope.

In our data collection forms, we considered sinus bradycardia less than 50 beats/min to be abnormal. In the outcomes adjudication phase of the study, however, we defined clinically significant bradycardia to include symptomatic bradycardia or a pulse rate less than 40 beats/min regardless of symptoms based on input from local electrophysiologists. We performed a post hoc analysis to harmonize these definitions by reclassifying isolated sinus rhythm of 40 beats/min and greater as a normal ECG finding. We found a nonsignificant trend toward reduced ECG sensitivity in patients older than 40 years, and there were no qualitative changes in ECG specificity. Thus, the way we defined "bradycardia" is unlikely to affect our overall findings of low ECG diagnostic yield and predictive accuracy in younger patients.

The total number of cardiac events was low, and therefore CIs around test characteristic estimates were relatively wide. Our study provides preliminary findings that should be verified in larger patient cohorts.

Finally, our study was performed at a single academic center and may not be generalizable to other institutions.

**DISCUSSION**

Although routine ECG testing has been recommended for the evaluation of syncope, in our study cohort it had low diagnostic yield and predictive accuracy in younger patients. Furthermore, ECG testing was associated with a 10% frequency of incidental findings unrelated to syncope in patients younger than 40 years. Our findings of low predictive accuracy did not change when we considered nonspecific, ST/T-wave findings in addition to other predefined ECG abnormalities. Although our primary analysis relied on ECG interpretation by resident physicians, sensitivity analysis using attending physician ECG interpretation did not affect our results. To the best of our knowledge, this is the first study to report ECG test characteristics in syncope as a function of age.

In our cohort, the majority of patients younger than 40 years did not have a history of cardiac illness and were thought by the treating physicians to have a vasovagal cause for their presentation. The 2 patients in this age group who experienced a cardiac event had known, preexisting cardiac problems, and ECG testing was not diagnostic in either patient. One patient with known idiopathic ventricular arrhythmia had an initial ED ECG with nonspecific ST/T changes and was diagnosed with ventricular tachycardia on interrogation of his implanted defibrillator. The other patient with known idiopathic cardiomyopathy was noted to have an electronic pacemaker rhythm on his ED ECG; the admitting medical team attributed the patient's syncopal episode to a cardiac ejection fraction of 20%.

In this low-risk age group, a nondiagnostic ECG abnormality is likely to represent an incidental finding that is not predictive of a 14-day cardiac event. The low frequency of 14-day cardiac events in this age group results in a low positive predictive value and a significant number of false-positive findings. These false-positive findings may lead to additional evaluation, including cardiology consultation and hospitalization, and of 133 patients younger than 40 years in our study received additional cardiology evaluation triggered by abnormal ECG findings. Therefore, it may be reasonable to defer ECG testing in young patients without cardiac comorbidity and who have a medical history and physical examination result consistent with a benign cause of syncope.

ECG specificity decreased with advancing age, and this finding reflects an increasing ratio of ECG abnormalities to acute, syncope-related cardiac events as a function of age. The high prevalence of ECG abnormalities in older patients is likely due to chronic comorbidities, including coronary artery disease, cardiac valve disorders, and hypertension, whereas the incidence of acute cardiac events in syncope is relatively low even in higher-risk groups such as the elderly. However, the ECG did identify an arrhythmic cause of syncope in approximately 5% of patients older than 40 years. Routine ECG testing may therefore be necessary in these higher-risk age groups, despite the increase in incidental, abnormal findings.

In conclusion, we found that ECG testing for syncope had low diagnostic yield and was associated with a 10% frequency of incidental abnormalities unrelated to syncope in patients younger than 40 years. It may be reasonable to defer ECG testing in younger patients without cardiac problems and who have a presentation consistent with a benign case of syncope, although our findings should be verified in larger, multisite studies.

Supervising editor: Allan B. Wolfson, MD

Author contributions: BCS, JRH, WRM, and CMM conceived the study. BCS and CMM obtained funding for this study. BCS, GZS, and GZG were responsible for data collection and outcomes review, and BCS supervised the overall data collection process. BCS performed the data analysis and drafted the article. All authors contributed substantially to article revisions. BCS takes responsibility for the paper as a whole.

Funding and support: By Annals policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article, that may create any potential conflict of interest. See the Manuscript Submission Agreement in this issue for examples of specific conflicts covered by this statement. This study was...
supported by the UCLA Robert Wood Johnson Clinical Scholars Program (050721). Dr. Sun is supported by a UCLA National Institute of Aging K12 Award (K12AG001004) and an American Geriatrics Society Dennis Jahnigen Career Development Award. Dr. Mangione was also partially supported by the UCLA Center for Health Improvement in Minority Elders/Resource Centers for Minority Aging Research, NIH/NIA (AG 02-004).


GZ Gabayan originally submitted this article under the name Gelarah Zargaraff.

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APPENDIX E1

ECG abstraction form.

ECG Interpretation:
☐ Normal: includes sinus tachycardia, first-degree block, sinus bradycardia >50, premature atrial contractions
☐ Abnormal: includes nonsinus rhythms, bundle branch block, left axis deviation
☐ LVH/RVH
☐ Abnormal conduction intervals excluding first-degree block
☐ Q/ST/T changes consistent with acute or chronic ischemia
☐ Other—describe: _______________________

☐ Isolated, nonspecific ST/T abnormalities