

## EM ADVANCES

## Acute myocardial infarction in patients with syncope

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## ABSTRACT

**Objective:** We sought to determine the incidence of acute myocardial infarction (AMI) in emergency department (ED) patients with syncope, the characteristics of these AMIs and how helpful the initial electrocardiogram (ECG) was in identifying these cases.

**Methods:** In a prospective cohort of consecutive patients with syncope, the initial ECG was found to be abnormal using a prespecified definition (any nonsinus rhythm or any new or age-indeterminate abnormalities). Patients were then followed up to identify an AMI diagnosed within 30 days of presentation.

**Results:** There were 1474 consecutive patient visits for syncope or near-syncope over a 45-month period spanning from Jul. 1, 2000, to Feb. 28, 2002, and Jul. 15, 2002, to Aug. 31, 2004, of which 46 (3.1%) were diagnosed with AMI. The majority of the AMI patients (42) had no ST segment elevation. The initial ECG was abnormal in 37 out of 46 cases. The diagnostic performance of the initial ECG was sensitivity 80% (95% confidence interval [CI] 67%–89%), specificity 64% (95% CI 61%–67%), negative predictive value 99% (95% CI 98%–100%), positive predictive value 7% (95% CI 6%–8%), positive likelihood ratio 2.2 (95% CI 1.6–2.5) and negative likelihood ratio 0.3 (95% CI 0.2–0.5).

**Conclusion:** The incidence of AMI in patients presenting with syncope is low. A normal ECG has a high negative predictive value, although its sensitivity is limited.

**Keywords:** syncope, myocardial infarction, electrocardiogram

## RÉSUMÉ

**Objectif :** Nous avons cherché à déterminer l'incidence d'infarctus aigu du myocarde (IAM) chez les patients se présentant à l'urgence avec une syncope, les caractéristiques de ces IAM et l'utilité de l'électrocardiogramme (ECG) initial pour diagnostiquer ces cas.

**Méthodes :** Dans une cohorte prospective de patients présentant une syncope vus consécutivement, l'ECG initial était anormal selon une définition préétablie (rythme non sinusal ou toute nouvelle anomalie, sans égard à l'âge). Les patients ont ensuite fait l'objet d'un suivi afin de déterminer s'ils avaient reçu un diagnostic d'IAM dans les 30 jours suivant leur visite à l'urgence.

**Résultats :** On a recensé 1474 visites de patients présentant une syncope ou des symptômes évocateurs d'une syncope vus consécutivement sur une période de 45 mois allant du 1 juillet 2000 au 28 février 2002, et du 15 juillet 2002 au 31 août 2004. Parmi ces patients, 46 (3,1 %) ont reçu un diagnostic d'IAM. Pour la majorité des patients avec un IAM (42), il n'y avait pas d'élévation du

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segment ST. Le premier ECG était anormal chez 37 de ces 46 patients. La performance diagnostique se présentait comme suit : sensibilité de 80 % [intervalle de confiance (IC) à 95 %, de 67 à 89 %]; spécificité de 64 % (IC à 95 %, de 61 à 67 %); valeur prédictive négative de 99 % (IC à 95 %, de 98 à 100 %); valeur prédictive positive de 7 % (IC à 95 %, de 6 à 8 %); rapport de vraisemblance positif de 2,2 (IC à 95 %, de 1,6 à 2,5); et rapport de vraisemblance négatif de 0,3 (IC à 95 %, de 0,2 à 0,5).

**Conclusion :** L'incidence d'IAM chez les patients présentant une syncope est faible. Un ECG normal a une valeur prédictive négative élevée, quoique sa sensibilité soit limitée.

## Introduction

Syncope accounts for 1%–2% of all emergency department (ED) visits.<sup>1–3</sup> The causes of syncope are usually benign, but are occasionally significant and life-threatening. Cardiovascular causes are particularly concerning, with a mortality rate of 10% at 6 months, and are twice as likely to result in death compared with noncardiac causes.<sup>4</sup> Cardiac etiologies include arrhythmia, structural abnormalities and myocardial infarction. Unfortunately, a cause for syncope can only be identified in 50% of patients at the time of their ED visit, and, for those patients, it is often unclear if a cardiac condition caused their syncope.<sup>5</sup> As a result, many patients are admitted to rule out a cardiac cause, and US\$2 billion is spent on admissions to hospital for syncope each year in the United States.<sup>6</sup>

Much work has been done to risk-stratify patients with syncope. Martin and colleagues<sup>7</sup> assessed risk factors for ventricular arrhythmia and death for patients presenting to the ED with syncope. In an Italian study, Colivicchi and colleagues<sup>3</sup> derived the Osservatorio Epidemiologico sulla Sincope nel Lazio risk score for predicting 1-year mortality. Sarasin and coauthors<sup>8</sup> derived a risk prediction score to assess for arrhythmia in patients with unexplained syncope. More recently, the San Francisco Syncope Rule was prospectively derived and validated to predict short-term serious outcomes in patients presenting to the ED with syncope,<sup>1,2</sup> and was shown to be predictive of death up to 1 year after an ED visit.<sup>9</sup> In each of these studies, the presenting electrocardiogram (ECG) was consistently shown to be an important predictor of serious outcomes.<sup>1–3,7–9</sup> In these studies, the definition of an abnormal ECG was variable and the incidence of particular cardiac causes, such as acute myocardial infarction (AMI), was unclear.

The purpose of our study was to determine the frequency of AMI, the characteristics of these AMIs and the utility of the emergency physician's (EP's) interpretation of the initial ECG in a large cohort of ED patients with syncope.

## Methods

### *Study design and setting*

We conducted our prospective cohort study at a large university teaching hospital with 38 000 ED visits per year. The institution's committee on human research approved the study with a waiver of informed consent and waiver of the Health Insurance Portability & Accountability Act authorization for patient enrolment. We obtained verbal consent from all patients when they were contacted for follow-up.

### *Study population*

We included patients presenting with acute syncope or near-syncope as a reason for their ED visit. As an operational definition for the study, we defined "syncope" as a transient loss of consciousness with return to baseline neurologic function, and "near-syncope" as an acute event suggestive of syncope, but without loss of consciousness. We made no distinction between syncope and near-syncope in our study and were specifically interested in the subset of patients who were in the cohort and were considered to have an AMI as their primary outcome. We specifically excluded patients with loss of consciousness associated with trauma, and alcohol or drug use, and those deemed to have definitely experienced a seizure. Patients with an altered level of consciousness or persistent new neurologic deficits did not meet our operational definition of syncope and were also excluded.

### *Patient identification*

All physicians, student volunteers and house staff were made aware of the study. We also used an electronic tracking system based on the patients' presenting complaints (e.g., the patient is faint, light-headed, dizzy or syncopal, has syncope, or has passed out, fallen or collapsed) that identified potential patients to study personnel via text messaging immediately upon the patients' presentation in the ED.<sup>10</sup> The attending physician made the final decision to enroll the patient, depending on whether, in his or her opinion, syncope had occurred.

### Data collection

During the study, physicians were not required to obtain any tests, including an ECG, unless indicated. Emergency physicians interpreted all ECGs using a structured data form during the patient ED evaluation. At that time, all efforts were made to obtain a previous ECG using a readily available and searchable electronic hospital database, or by facsimile from other hospitals.

An ECG was considered to be abnormal if, when compared with a previous ECG, the rhythm was nonsinus (including paced or chronic atrial fibrillation) or if there were any new abnormalities (including any minimal changes such as a first-degree block, conduction delays or any morphologic changes to the QRS complex or ST segments). If there was no previous ECG available, any changes to the ECG were considered abnormal. The attending EP who cared for the patient on the initial visit classified the ECG as normal or abnormal.

### Primary outcome measure

We followed up with all patients in the cohort to determine whether they had been diagnosed with an AMI within 30 days of the ED presentation. The diagnosis and determination of AMI was made by the inpatient cardiologist based on his or her opinion of the patients' presentation, their ECG and their troponin level. Serum troponin I concentrations above 2.0 µg/L were generally considered to be positive (Abbott Laboratories, AxSYM microparticle enzyme immunoassay).

Two expert physicians (a senior EP with additional expertise in ECG interpretation, and a senior cardiologist) independently reviewed the initial ECGs of AMI-positive patients. These physicians were blinded to clinical information, initial ECG interpretation by the EP and the final diagnosis. They compared the initial ECG with a previous ECG, if available, and rated it as normal or abnormal, using our study definition. The experts reviewed the same initial ECG as the EP. We measured agreement between the experts and the initial EP. The diagnostic test performance of the ECG is reported based on the initial EP's interpretation.

### Follow-up

A research nurse and an ED physician, who were both familiar with the protocol, coordinated the follow-up for all patients in the cohort. Chart review was the primary method of assessment, followed by contact with the primary physicians when data were not available. We also attempted to contact patients by telephone, or by structured questionnaire sent via regular mail when they could not be reached by telephone. Our follow-up inquiry was specific for all serious

outcomes in our study, including AMI. We were interested in any hospital admissions after the initial syncopal event. For patients subsequently admitted to other hospitals, we obtained patient consent to procure additional information assessing for the possibility of AMI. We also reviewed the Social Security Death Index to identify missing patients.<sup>11</sup>

### Data analysis

We determined the frequency of AMI for the whole cohort. We estimated the sensitivity and specificity of the initial ECG to predict these outcomes using exact binomial calculation, using only those patients who had an ECG performed at initial ED presentation. We compared agreement between the initial EP's ECG interpretation and the experts' using the kappa statistic.

### Results

There were 1474 visits for syncope or near-syncope during a 45-month period spanning from Jul. 1, 2000, to Feb. 28, 2002, and Jul. 15, 2002, to Aug. 31, 2004, representing 1% of the total ED visits. We successfully reached 95% of patients for follow-up, and no patient was admitted to an outside institution or was identified on the death registry. Of this cohort, 1393 (93.2%) underwent an ECG as part of their ED evaluation. Moreover, 46 patients from the entire cohort (3.1%, 95% CI 2.3%–4.1%) were diagnosed with AMI, 42 of which (91%) had no ST segment elevation. All 46 patients who were diagnosed with AMI were admitted to hospital from the ED. Approximately half of the patients had a positive troponin test while in the ED. Previous demographics of the entire cohort have been published<sup>9</sup> and are summarized in Table 1. The characteristics of the AMI patients are shown in Table 2.

The initial ECG interpretation was considered "abnormal" by the treating EP in 37 of these 46 AMI cases. The diagnostic test performance of the initial ECG for patients with and without AMI is presented in Table 3.

The blinded expert physicians had excellent agreement among themselves for classifying the initial ECG as normal versus abnormal (kappa 0.80, 95% CI 0.57–1.00). There was only fair agreement between the experts and the initial EP read (kappa 0.44, 95% CI 0.15–0.73). Experts and EPs each believed that 9 patients with AMI had a normal ECG on initial presentation, but did not agree on the same 9.

### Discussion

The possibility of a cardiac cause for syncope is an important concern. These patients have been associated with

significantly higher morbidity and mortality in multiple studies.<sup>4,5</sup> We specifically evaluated patients with syncope and AMI in this large cohort of consecutive patients with syncope. We found that AMI was rare in patients presenting with syncope. This small group of patients with AMI mostly had atypical presentations without ST segment elevation, including several with an apparently normal initial ECG. The negative predictive value of a normal ECG is high because of the low incidence of AMI in patients with syncope, yet a normal ECG is only moderately sensitive to rule out AMI. Overall, the likelihood ratio indicates that a normal ECG decreases the pretest probability of an AMI by 3-fold in this population.

**Table 1. Characteristics of consecutive emergency department visits for syncope**

Characteristic	No. (%) of patients,* n = 1474
Mean age, yr [95% CI]	62 [61–63]
Female	830 (56.3)
Admitted from ED	840 (57.0)
Known cause at follow-up	
Cardiac	166 (11.3)
Neurologic	41 (2.8)
Orthostasis	180 (12.2)
Vasovagal	304 (20.6)
Medications	72 (4.9)
Psychiatric	17 (1.2)
Unknown cause	694 (47.1)

CI = confidence interval; ED = emergency department.  
\*Unless otherwise indicated.

**Table 2. Characteristics of syncope patients with acute myocardial infarction\***

Characteristic	No. (%) of patients,† n = 46
Mean age, yr [range]	75.4 [19–90]
Male	29 (63.0)
Lone syncope	10 (21.7)
Chest pain	8 (17.4)
Shortness of breath	14 (30.4)
History of congestive heart failure	8 (17.4)
History of coronary artery disease	25 (54.3)
ST segment elevation	4 (9.0)
Positive troponin in ED, (troponin > 2.0 µg/L)	23 (50.0)
Average peak troponin, µg/L [range]	15.1 [1.1 to > 50]
Troponin peak > 50 µg/L	7 (15.2)
Cardiac catheterization	23 (50.0)
Death within 30 d	7 (15.2)

ED = emergency department.  
\*The numbers in this table are the absolute numbers and percentages of demographic and symptom variables in patients with acute myocardial infarction who presented with syncope.  
†Unless otherwise indicated.

Previous work has been done in patients presenting with syncope for which an AMI was subsequently identified as the cause.<sup>1,2,12–15</sup> The proportion of syncope patients with AMI was between 0.2% and 4.0%, and the proportion in this study was 3.1%. The inclusion criteria and the definition of AMI varied among these studies, but the frequency of AMI was consistently low. Specific initial ECG abnormalities suggestive of ischemia were also variable, and it is unclear whether patients with normal ECGs underwent additional testing. We could find no convincing data to support further investigation of asymptomatic syncope patients with a normal ECG.

We compared expert opinion over-reads of each ECG with the initial reads of the bedside EP and found that agreement was only fair. This lack of agreement may be because of skill level, but may also reflect the influence of clinical information, including patient history, that was only available to the treating physician.

We developed and validated our definition of an abnormal ECG in our multiphase study to risk-stratify patients.<sup>12</sup> The definition is practical and explicit. However, it remains somewhat subjective given the only fair agreement between the initial interpretation and expert review. This could be an important source of variability when others try to apply the San Francisco Syncope Rule. Although an abnormal ECG predicted the majority of adverse outcomes in both the derivation and validation cohorts of the San Francisco Syncope Rule, variation in physician agreement may affect external performance of the decision rule. That said, several studies and guidelines provide a 1-paragraph definition of an abnormal ECG.<sup>3,7</sup> These complex definitions are variable and contain numerous subjective elements. There are no data demonstrating that these definitions can be easily remembered or accurately applied by physicians for risk stratification.<sup>16,17</sup>

**Table 3. Electrocardiogram test characteristics for patients presenting with syncope determined to have acute myocardial infarction**

ECG interpretation	AMI	No AMI
Abnormal	37	485
Normal	9	862
Abnormal ECG predicting AMI	%*	[95% CI]
Sensitivity	80	[67–89]
Specificity	64	[61–67]
Negative predictive value	99	[98–100]
Positive predictive value	7	[6–8]
Positive likelihood ratio	2.20	[1.60–2.50]
Negative likelihood ratio	0.31	[0.16–0.51]

AMI = acute myocardial infarction; CI = confidence interval;  
ECG = electrocardiogram.  
\*Unless otherwise indicated.

### Limitations

Our study was a subgroup analysis examining the predictive ability of the initial ECG to identify syncope patients with AMI. The diagnosis of AMI was determined by the inpatient cardiology service, and was determined by history/ECG, troponin elevation or both. Thus for many of the admitted patients, it was unclear at the time of their ED evaluation whether AMI was present. Our prespecified operational definition of an abnormal ECG was broad and inclusive to avoid missing any potential serious outcomes with syncope patients. Many subtle ECG changes, such as first-degree atrioventricular block and nonspecific ST-T wave changes may not suggest AMI. Further assessment looking at specific ECG characteristics may better define high-risk syncope patients with AMI.

### Conclusion

Acute myocardial infarction was rare in this large cohort of patients presenting to the ED for syncope. Among those who were ultimately diagnosed with AMI, the majority of patients had a nondiagnostic ECG, including some with an apparently normal ECG. Despite the importance of the initial ECG interpretation for risk stratification, there is only fair agreement between physicians reading these ECGs. Nevertheless, the likelihood of AMI in syncope patients with normal ECGs is extremely low.

**Competing interests:** None declared.

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