Circulation

ORIGINAL RESEARCH ARTICLE

Duration of Electrocardiographic Monitoring of Emergency Department Patients With Syncope

BACKGROUND: The optimal duration of cardiac rhythm monitoring after emergency department (ED) presentation for syncope is poorly described. We sought to describe the incidence and time to arrhythmia occurrence to inform decisions regarding duration of monitoring based on ED risk stratification.

METHODS: We conducted a prospective cohort study with enrolled adult patients (≥16 years old) presenting within 24 hours of syncope at 6 EDs. We collected baseline characteristics, time of syncope and ED arrival, and the Canadian Syncope Risk Score (CSRS) risk category. We followed subjects for 30 days, and our adjudicated primary outcome was serious arrhythmic conditions (arrhythmias, interventions for arrhythmias, and unexplained death). After excluding patients with an obvious serious condition on ED presentation and those with missing CSRS predictors, we used Kaplan-Meier analysis to describe the time to serious arrhythmic outcomes.

RESULTS: A total of 5581 patients (mean age, 53.4 years; 54.5% females; 11.6% hospitalized) were available for analysis, including 346 (6.2%) for whom the 30-day follow-up was incomplete and who were censored at the last follow-up time. A total of 417 patients (7.5%) experienced serious outcomes, 207 of which (3.7%; 95% CI, 3.3%–4.2%) were arrhythmic (161 arrhythmias, 30 cardiac device implantations, 16 unexplained deaths). Overall, 4123 (73.9%) were classified as CSRS low risk, 1062 (19.0%) medium risk, and 396 (7.1%) high risk. The CSRS accurately stratified subjects as low risk (0.4% risk for 30-day arrhythmic outcome), medium risk (8.7% risk), and high risk (25.3% risk). One-half of arrhythmic outcomes were identified within 2 hours of ED arrival in low-risk patients and within 6 hours in medium- and high-risk patients, and the residual risk after these cut points were 0.2% for low-risk, 5.0% for medium-risk, and 18.1% for high-risk patients. Overall, 91.7% of arrhythmic outcomes among medium- and high-risk patients, including all ventricular arrhythmias, were identified within 15 days. None of the low-risk patients experienced ventricular arrhythmia or unexplained death, whereas 0.9% of medium-risk patients and 6.3% of high-risk patients experienced them (P<0.0001).

CONCLUSIONS: Serious underlying arrhythmia was often identified within the first 2 hours of ED arrival for CSRS low-risk patients and within 6 hours for CSRS medium- and high-risk patients. Outpatient cardiac rhythm monitoring for 15 days for selected medium-risk patients and all high-risk patients discharged from the hospital should also be considered.

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Clinical Perspective

What Is New?

- The optimal duration of emergency department (ED) and post-ED cardiac rhythm monitoring for arrhythmia among patients with syncope is unknown.
- Our results show that the overall arrhythmia risk and the risk after 2 hours of ED arrival for Canadian Syncope Risk Score low-risk patients is very low.
- Similarly, the overall risk and risk 6 hours after ED arrival for medium- and high-risk patients is moderate and high.
- No low-risk patient experienced ventricular arrhythmia or unexplained death.
- Most of the arrhythmias among non–low-risk patients occurred within 15 days of index syncope.

What Are the Clinical Implications?

- The results of our study support brief monitoring in the ED for 2 hours for Canadian Syncope Risk Score low-risk patients and for 6 hours for medium- and high-risk patients, followed by selective admission.
- Our results also support 15-day outpatient monitoring for medium-risk patients at a selected threshold and for all high-risk patients.
- The diagnostic yield of detecting an underlying arrhythmia is highest when cardiac monitoring devices are applied early after syncope, ideally at the index visit.

Syncope is defined as sudden transient loss of consciousness, followed by spontaneous complete recovery, caused by transient global hypoperfusion of the brain.[1] Syncope is a common emergency department (ED) presentation constituting 1% to 3% of ED visits and up to 1% of hospitalizations from the ED.[2] The most important objective of ED evaluation is to exclude a serious underlying condition such as arrhythmia, acute cardiac ischemia, pulmonary embolism, or internal hemorrhage.[3,4] Previous studies have estimated that one-third to one-half of these serious conditions, particularly arrhythmias, are missed during ED evaluation and become evident only after ED disposition.[5,6] This concern for occult serious conditions, particularly arrhythmias, contributes to prolonged ED monitoring, extended observation in syncope units, and unnecessary hospitalization.[3,7–9]

Several tools have been developed for risk stratification of ED patients with syncope, including the Canadian Syncope Risk Score (CSRS; Figure 1).[6,10] The CSRS was developed by prospectively enrolling a large cohort of patients presenting to a network of Canadian hospitals for syncope and following them for 30 days to identify serious outcomes (Figure I in the online-only Data Supplement). In addition to developing the risk score, the study also sought to identify where and when these serious adverse outcomes were first identified relative to the time of ED presentation. By prospectively collecting these data, we sought to inform management decisions regarding the length of ED cardiac rhythm monitoring and disposition, as well as the need for further monitoring using risk stratification at the end of the initial ED evaluation.

Therefore, the objective of this study was to describe the time to occurrence of serious arrhythmias relative to time of ED arrival based on the CSRS risk category. The ultimate goal was to provide guidance for decision making regarding the duration and location of cardiac rhythm monitoring.

METHODS

Study Setting and Population

A prospective cohort study was conducted at 6 large EDs in Canada, and adult patients (≥16 years old) who presented within 24 hours of most recent syncope were potentially eligible. We excluded patients who did not meet the definition of syncope for the following reasons: prolonged loss of consciousness (>5 minutes), mental status changes from baseline, obvious witnessed seizure based on previous history or current clinical evaluation, or head trauma causing loss of consciousness.[11,12] We also excluded patients with major trauma requiring hospitalization and patients from whom it was not possible to obtain an accurate history (eg, language barrier, intoxication caused by alcohol or drugs). Because the study was observational with no patient interventions, the ethics committees at all study sites approved the study with the requirement of only verbal consent. The patient-level data will not be made available to other researchers; however, the analytical methods and statistical analysis codes can be provided on request.

Data Collection

The data were collected as part of a large multicenter study whose primary objective was to develop a risk-stratification tool for ED syncope.[13] One of the prespecified secondary objectives was to identify the optimal duration of cardiac rhythm monitoring, and the location of such monitoring based on the time and place the serious arrhythmia was identified. ED attending physicians and emergency medicine trainees at each study site were trained on the study protocol during a 1-hour didactic session. The training included assessment of standardized and explicitly defined variables from history and physical examination, as well as the diagnostic criteria for the type of syncope as per the European Society of Cardiology guidelines for arriving at the final ED diagnosis when no serious conditions were identified during the ED evaluation.[11] Emergency physicians were asked to enroll consecutive eligible patients at the time of the index visit. We collected patient demographics, time of syncope, the time and mode (eg, by ambulance) of ED arrival, event characteristics, medical history, and ED length of stay, management, and disposition. The treating emergency physician explicitly collected the 8 predictors in the CSRS risk tool (Figure 1). To allow calculation

Category	Points
Clinical evaluation	
Predisposition to vasovagal symptoms*	−1
History of heart disease†	1
Any systolic pressure reading < 90 or > 180 mm Hg‡	2
Investigations	
Elevated troponin level (> 99th percentile of normal population)	2
Abnormal QRS axis (< −30° or > 100°)	1
QRS duration > 130 ms	1
Corrected QT interval > 480 ms	2
Diagnosis in emergency department	
Vasovagal syncope	−2
Cardiac syncope	2
Total score (−3 to 11)	____

Total score	Estimated risk of serious adverse event,§ %	Risk category
−3	0.4	Very Low
−2	0.7	Very Low
−1	1.2	Low
0	1.9	Low
1	3.1	Medium
2	5.1	Medium
3	8.1	Medium
4	12.9	High
5	19.7	High
6	28.9	Very High
7	40.3	Very High
8	52.8	Very High
9	65.0	Very High
10	75.5	Very High
11	83.6	Very High

Figure 1. The Canadian Syncope Risk Score.
*Triggered by being in a warm crowded place, prolonged standing, fear, emotion, or pain. †Includes coronary or valvular heart disease, cardiomyopathy, congestive heart failure, and nonsinus rhythm (ECG evidence during index visit or documented history of ventricular or atrial arrhythmias, or device implantation). ‡Includes blood pressure values from triage until disposition from the emergency department. §Shrinkage-adjusted expected risk.

of the CSRS, the ECG or serum troponin level was imputed to be normal if not obtained. No other missing data imputation was performed. Subjects were classified based on the CSRS as low risk (total score of −3 to 0), medium risk (1–3), and high risk (≥4).[6] We collapsed the very low and low in the original tool to a single low-risk category and the high and very high as high-risk category for this study.

Serious Outcomes

Serious outcomes included the detection or occurrence of any of the following within 30 days of syncope (Figure I in the online-only Data Supplement): death, arrhythmia, myocardial infarction, serious structural heart disease, aortic dissection, pulmonary embolism, severe pulmonary hypertension, significant hemorrhage, subarachnoid hemorrhage, any other serious condition causing syncope, or procedural interventions for treatment of syncope. This list of serious outcomes, as well as a list of prespecified arrhythmias deemed to be serious, was selected as most clinically relevant by an international panel of experts as conditions that would need to be either detected or predicted during ED evaluation and in the short term.[14,15] We collected data on every serious outcome that occurred, including the phase of care (ie, before ED arrival, in the ED, as an inpatient, or after index visit discharge) and the time of its occurrence or detection. We then classified these serious outcomes as arrhythmic (ie, any serious arrhythmias, intervention to treat arrhythmias such as pacemaker/defibrillator insertion, or cardioversion, and any death of an unknown cause) or nonarrhythmic (ie, all other serious outcomes). For this study, the outcome of interest is only the arrhythmic serious outcomes. The occurrence of serious outcomes was assessed by a stepwise approach. First, a structured review of all available medical records related to the index ED visit, subsequent ED visits, hospitalizations, or death was undertaken, and an examination of the results of all investigations, including those performed in the outpatient setting, was conducted. Second, we undertook a scripted telephone follow-up immediately after 30 days. Third, we reviewed administrative health records for return visits, outpatient investigations, or hospitalizations at all local adult hospitals for patients in Ontario, and within citywide regional or provincial administrative health databases for patients in Alberta. Both provinces have universal health insurance, and all hospital-based health services are reliably captured in the health databases. Finally, for Ontario patients unable to be reached by telephone and not known to be alive and well at 30 days, we searched the provincial coroner's office for a reported death; by Ontario law, the coroner is notified of sudden and unexpected deaths. Deaths among Alberta patients are updated in hospital electronic records quarterly. If no definite information was available regarding serious outcomes with the above approaches, then the patient was designated as incomplete for 30-day follow-up. An adjudication committee comprising 2 physicians blinded to all study data independently adjudicated all serious outcomes and the time and place of their initial occurrence or detection. Disagreements were resolved by a third physician. Serious outcomes that occurred or were detected before ED arrival were excluded for this time-to-event analysis.

Statistical Analysis

We used mean, range, and SD or median and interquartile range as appropriate for continuous variables and frequency with proportion for categorical variables for descriptive analysis. We compared proportions using χ^2 or Fisher exact test as appropriate. We report the time interval between the occurrence of the last syncopal event and arrival at the ED. Kaplan-Meier curves were constructed to identify the time to any serious outcome and arrhythmic outcome occurrence relative to the time of ED arrival. When only the date but not the time for serious outcome was recorded in the medical record, the time of noon was used for the interval calculation if >24 hours had elapsed after the index ED visit. We compared the proportion of patients who experienced any serious outcome

and arrhythmic outcomes among the 3 CSRS risk categories and report *P* values using a log-rank test. Visual inspection of the Kaplan-Meier curves, estimated survival functions, and frequency distributions of arrhythmic outcomes over time within each of the CSRS categories was used to determine recommendations for duration of ED and post-ED monitoring. Patients with no 30-day follow-up information were censored at the time of last follow-up. We report the number of patients at risk, number of arrhythmic outcomes, and survival (arrhythmia free) estimates with 95% CIs before and after the recommended cut points for the 3 CSRS risk categories. We adjusted the Kaplan-Meier variance estimation for clustering using Taylor series approximation.[16,17] Because there was no hypothesis being tested and this study was embedded within a larger study, an a priori sample size calculation was not performed. We used SAS (version 9.4) for data analysis.

RESULTS

We enrolled 5719 patients with syncope at the study hospitals from September 2010 to March 2015 (Figure 2), representing 78.9% of all potentially eligible patients based on manual review of all ED visits by research personnel.

The 1526 patients who were potentially eligible but not enrolled were similar in age and sex (mean age, 55.4 years; SD, 22.9 years; 53.1% females) to the enrolled patients. Among those enrolled, 121 patients (2.1%) presented to the ED with an obvious serious condition causing syncope, and 17 patients (0.3%) with missing CSRS predictors were excluded, which left 5581 patients available for this analysis. The 121 patients who presented to the ED with an obvious serious condition included 70 patients with arrhythmias and 51 patients with nonarrhythmic serious conditions (Table I in the online-only Data Supplement). Of these, 1042 patients (18.7%) were referred to a consulting service in the ED, and 650 (11.6%) were hospitalized during the index visit. The characteristics of the study patients are detailed in Table 1.

The median time to ED arrival after the syncopal episode was 1.1 hours (interquartile range, 0.7–1.9 hours; time of syncope not recorded in 1507 patients; Figure II in the online-only Data Supplement). Patients who did not have an ECG performed or troponin levels measured were younger, with low prevalence of comorbidities, and the vast majority were deemed low risk as per the CSRS tool (Tables II and III in the online-only Data Supplement).

A total of 417 patients (7.5%; 95% CI, 6.8%–8.2%) experienced serious outcomes (including 40 patients who died; Table IV in the online-only Data Supplement) within 30 days of the index ED visit, 207 of which (3.7%; 95% CI 3.3, 4.2%) were arrhythmic outcomes (Table 2). In our study, 161 patients experienced arrhythmias (19 patients with ventricular arrhythmias), 16 had unexplained death (out of 40 deaths), and 30 had device insertions (26 pacemakers and 4 implantable cardioverter-defibrillators) with no documented arrhythmia in the medical records. Of the 161 patients who experienced arrhythmias, 63 had a pacemaker inserted, 8 had an implantable cardioverter-defibrillator inserted, 5 underwent cardioversion, 3 patients had ablation, 1 patient underwent dialysis to correct hyperkalemia, and the remaining patients had medical management for

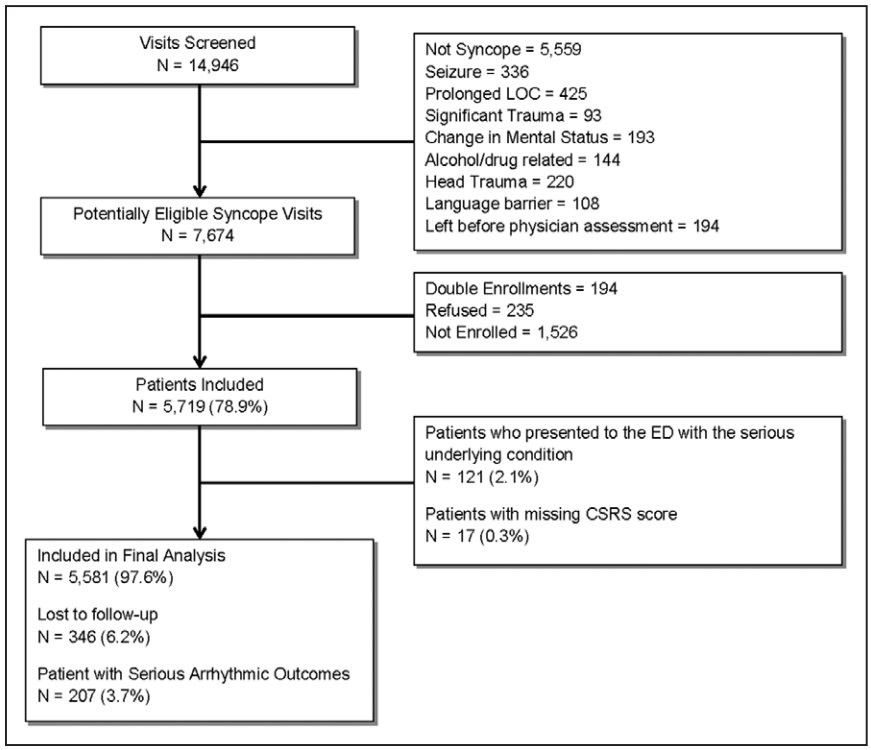


Figure 2. Patient flow.
CSRS indicates Canadian Syncope Risk Score; ED, emergency department; and LOC, loss of consciousness.

Table 1. Baseline Characteristics (n=5581)

Characteristics	
Age, y	
Mean (SD)	53.4 (23.0)
Range	16–102
Female	3042 (54.5)
Arrival by ambulance	3644 (65.3)
Medical history	
Coronary artery disease	650 (11.6)
Valvular heart disease	193 (3.5)
Congestive heart failure	178 (3.2)
Hypertension	1741 (31.2)
Diabetes mellitus	563 (10.1)
Cardiomyopathy	64 (1.1)
Syncope	606 (10.9)
Emergency department management	
ECG performed	5320 (95.3)
Blood tests performed	4753 (85.2)
CT head performed	1115 (20.0)
ED length of stay, median (IQR), h	4 (3–7)
Referred to consultant in ED	1042 (18.7)
Hospitalized	650 (11.6)
30-day serious outcomes	
Patients with serious outcomes	417 (7.5)
Patients with serious arrhythmic outcomes	207 (3.7)
Place of serious arrhythmic outcome identification	
During index ED evaluation	100 (1.8)
During index visit hospitalization	60 (1.1)
After the index visit*	47 (0.9)

Values are n (%) unless otherwise indicated. CT indicates computed tomography scan; ED, emergency department; and IQR, interquartile range.
*N=5235; 346 patients who were lost to 30-day follow-up were excluded.

their arrhythmias. Of the 5235 patients with 30-day follow-up, 47 (0.9%) had a serious arrhythmic outcome identified after index visit hospital discharge, including 30 patients with arrhythmias and 5 with cardiac device insertion. Of these 35 patients, 19 experienced recurrent syncope; 10 had prodromal symptoms such as dizziness, palpitations, or presyncope; and 1 experienced an implantable cardioverter-defibrillator shock secondary to ventricular arrhythmia. We were unable to complete the 30-day telephone follow-up for 346 patients (6.2%), but on review of the provincial health database and coroner's records, no death records were identified for these patients. In general, these patients with incomplete 30-day follow-up were younger with fewer comorbidities and were far less likely to have seen a consultant or to have been hospitalized after the index ED visit (Table V in the online-only Data Supplement).

In the study cohort, 4123 patients (73.9%) were classified as low risk, 1062 (19.0%) as medium risk, and 396 (7.1%) as high risk based on the CSRS. The proportion of patients who had any serious outcome or an arrhythmic outcome increased significantly with the CSRS risk (log-rank $P<0.0001$), with a higher proportion occurring closer to the index syncopal episode (Figure 3). We found that 2 hours for low-risk patients and 6 hours for medium- and high-risk patients were the optimal cut points for ED monitoring.

The patients at risk, observed arrhythmic outcomes, and arrhythmia-free survival estimates with 95% CI before and after the recommended cut points are detailed in Figure 3. Among low-risk patients, 15 (0.4%) experienced arrhythmic outcomes, 6 of which were identified within 2 hours of ED arrival. The types of arrhythmic outcomes among the 15 low-risk patients were as follows: 6 patients with sinus node dysfunction, 2 patients with high-degree atrioventricular block, 4 patients with new/uncontrolled atrial fibrillation, 2 patients with supraventricular tachycardia, and 1 patient with pacemaker insertion. The overall number of arrhythmic outcomes was 92 (8.7%) among medium-risk patients, with 45 identified within 6 hours of ED arrival, and 100 (25.3%) among high-risk patients, with 47 identified within 6 hours of ED arrival. The proportion of patients who experienced arrhythmic outcomes after the cut points based on complete 30-day follow-up data was 0.2% of low-risk patients after 2 hours of ED arrival and 5.0% of medium-risk patients and 18.1% of high-risk patients after 6 hours of ED arrival. Overall, 41 patients (9.8%) with serious outcomes had no time available and had it imputed as noon time. When the 417 study patients who experienced any serious outcome including nonarrhythmic events are considered, just over half (232, or 55.6%; Figure III in the online-only Data Supplement) were identified within 6 hours of ED arrival.

In our study, 13.1% of medium- and high-risk patients experienced arrhythmic outcomes within 30 days of the index ED visit. On the basis of the distribution of arrhythmic outcomes (Figure 4), almost all (91.7%, or 176 of the 192 outcomes) of the arrhythmic outcomes experienced by medium- and high-risk patients were identified within 15 days of the index syncope. In a sensitivity analysis, approximately half of the serious arrhythmic outcomes occurred within 6 hours of ED arrival regardless of the CSRS cut point selected to distinguish medium- and high-risk patients (Table 3).

In the study cohort, 35 patients (0.6%, all medium or high risk) had ventricular arrhythmia or died of an unknown cause within 30 days of the index ED visit (Figure 5). All ventricular arrhythmias were identified within 15 days of the index syncope presentation. The proportion of high-risk patients (6.3%) who experienced ventricular arrhythmia or unexplained death was significantly higher than for the medium-risk patients (0.9%; $P<0.001$).

Table 2. 30-Day Serious Arrhythmic Outcomes Among ED Patients With Syncope

Serious Arrhythmic Outcomes	All Arrhythmic Outcomes (N=207; 3.7%)	Identified During the Index Visit		Identified After the Index Visit (n=47; 0.9%)*
		ED Evaluation (n=100; 1.8%)	In Hospital (n=60; 1.1%)	
Death of unknown cause	16 (0.3)	1 (0.0)	3 (0.1)	12 (0.2)
Arrhythmia	161 (2.9)†	99 (1.8)	32 (0.6)	30 (0.6)
Sinus node dysfunction	61 (1.1)	38 (0.7)	12 (0.2)	11 (0.2)
New or uncontrolled atrial fibrillation	43 (0.8)	33 (0.6)	1 (0.0)	9 (0.2)
High-grade atrioventricular block	30 (0.5)	18 (0.3)	7 (0.1)	5 (0.1)
Ventricular arrhythmia	19 (0.3)	4 (0.1)	11 (0.2)	4 (0.1)
Supraventricular tachycardia	8 (0.1)	6 (0.1)	1 (0.0)	1 (0.0)
Interventions for arrhythmia: pacemaker/ICD insertion	30 (0.5)	0 (0)	25 (0.4)	5 (0.1)

Values are n (%). ED indicates emergency department; and ICD, implantable cardioverter-defibrillator.

*N=5235; 346 patients who were lost to 30-day follow-up were excluded.

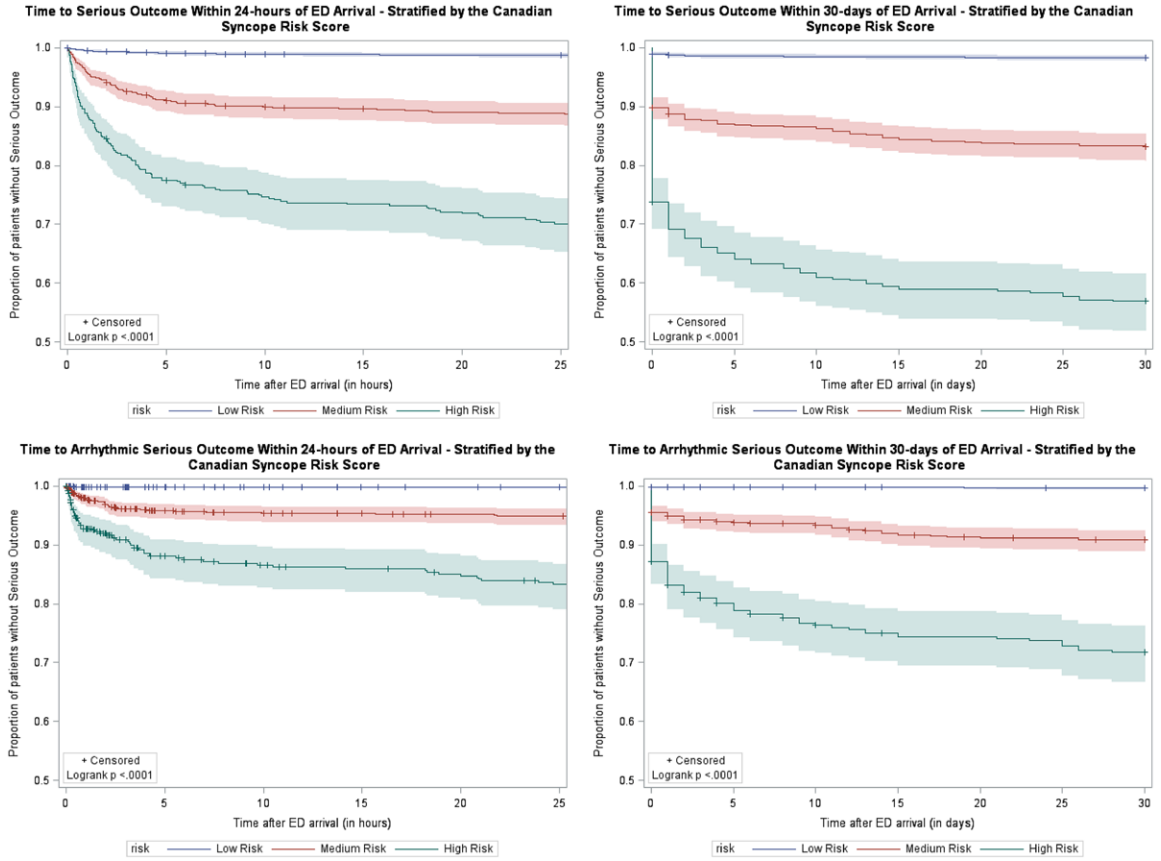
†Patients who had both an arrhythmia and a rhythm device implanted were counted as having the arrhythmia. Of the 161 patients who experienced arrhythmias, 63 had a pacemaker inserted, 8 had an ICD inserted, 5 underwent cardioversions, 3 had ablation, 1 underwent dialysis to correct hyperkalemia, and the remaining had medical management for their arrhythmias.

DISCUSSION

In this prospective multicenter study, most arrhythmic outcomes were identified immediately after the index syncopal episode. The risk of subsequent arrhythmias within 30 days increased substantially according to the CSRS risk category. Overall, very few patients (0.6%), and no CSRS low-risk patients, had ventricular arrhythmia or died of an unknown cause within 30 days. Among patients with syncope who did not have an obvious serious condition identified on arrival, approximately half of the arrhythmic outcomes were identified within a relatively brief interval of ED arrival: the first 2 hours in CSRS low-risk patients and 6 hours in medium- and high-risk patients. The residual risk of arrhythmic outcomes beyond 2 hours of observation is very low (0.2%) among low-risk CSRS patients. Among medium- and high-risk patients, the risk of arrhythmia after 6 hours of ED observation was 4.4%, and most of the remaining arrhythmic events were identified within 15 days of the index visit. Such monitoring intervals appear to us to be clinically sensible and to represent an appropriate balance between excessive testing versus diagnostic yield, although we recognize that clinicians in different healthcare jurisdictions may select different thresholds, based in part on perceived costs of falsely positive or negative testing.

When examining outcomes in a heterogenous condition such as syncope, it is important to consider the spectrum of disease severity. In our study, 0.7% died overall, and 0.6% of subjects died of an unknown cause or experienced ventricular arrhythmia within 30 days of the index ED visit. This prevalence is in line with the 1.6% overall 30-day mortality reported in a meta-analysis by Solbiati et al[18] and the 0.3% 30-day ventricular arrhythmia rate reported in the validation phase of the San Francisco Syncope Rule.[5] Del Rosso et al[19] reported a 1.4% risk of ventricular arrhythmias among patients with syncope at 2-year follow-up. Previous studies have reported that the proportion of patients with serious outcomes within 30 days of index syncope has been consistently around 10% and the proportion of patients experiencing arrhythmic serious outcomes around 5%.[9,10,20–23] Hospitalization rates, on the other hand, vary widely between studies and likely reflect substantial differences between healthcare systems rather than disease severity per se. We have previously published the reasons for hospitalization among ED syncope patients with no serious conditions identified during index ED evaluation and found that 46.5% of all hospitalizations were for suspected arrhythmias and for the purpose of cardiac monitoring.[24] A lower threshold for hospital admission from the ED for suspected arrhythmias and cardiac monitoring would, of course, increase the admission rate without necessarily increasing the absolute number of serious arrhythmic events identified.[9,25,26]

In our study, 3 of 4 patients were classified as low risk as per the CSRS. These patients rarely experience serious arrhythmic outcomes, especially after 2 hours of ED monitoring. None experienced an unexplained death or ventricular arrhythmia within 30 days. Hence, we believe these low-risk patients can be potentially discharged within 2 hours without further testing if no underlying conditions are suspected after initial clinical evaluation. Among the medium- and high-risk patients, approximately half of the serious arrhythmic conditions were identified within 6 hours of arrival, which suggests a reasonable decision point for ED discharge, continued observation, or consultation for admission. Notably, an important proportion (7.5%) of medium- and high-risk patients experienced arrhythmic outcomes after 6 hours, although most arrhythmias were nonventricular. These findings suggest that selected medium-risk pa-



Canadian Syncope Risk Score – Low Risk Patients				
Hours	**0**	**2***	**720†**	**Total**
Number at risk	4,123	4,117	4,108‡	4,123
Arrhythmic outcome	0	6	9	15
Event free estimates (95% CI)	100%	99.9% (99.8% – 99.9%)	99.6% (99.4% – 99.8%)	

Canadian Syncope Risk Score – Medium Risk Patients				
Hours	**0**	**6***	**720†**	**Total**
Number at risk	1,062	1,017	970‡	1,062
Arrhythmic outcome	0	45	47	92
Event free estimates (95% CI)	100%	95.7% (93.3% – 98.1%)	90.7% (86.8% – 94.7%)	

Canadian Syncope Risk Score – High Risk Patients				
Hours	**0**	**6***	**720†**	**Total**
Number at risk	396	349	296‡	396
Arrhythmic outcome	0	47	53	100
Event free estimates (95% CI)	100%	87.6% (82.1% – 93.1%)	71.2% (65.5% – 76.9%)	

Figure 3. Time to serious outcome and arrhythmia in the first 24 hours and within 30 days of emergency department arrival after syncope, stratified by the Canadian Syncope Risk Score.

ED indicates emergency department. *At the end of the indicated hour. †The 95% CI for survival estimates calculated based on last event occurrence out of the 720 hours (30-day follow-up): 592 hours for low-risk, 626 hours for medium-risk, and 663 hours for high-risk patients. ‡Of the 346 patients with incomplete 30-day follow-up, 308 were low risk, 35 were medium risk, and 3 were high risk. Hence, the proportions of patients who experienced arrhythmic outcomes after the cut points based on complete 30-day follow-up were 0.2% of low-risk patients, 5.0% of medium-risk patients, 18.1% of high-risk patients, and 7.5% for the combined medium- and high-risk categories (non–low-risk).

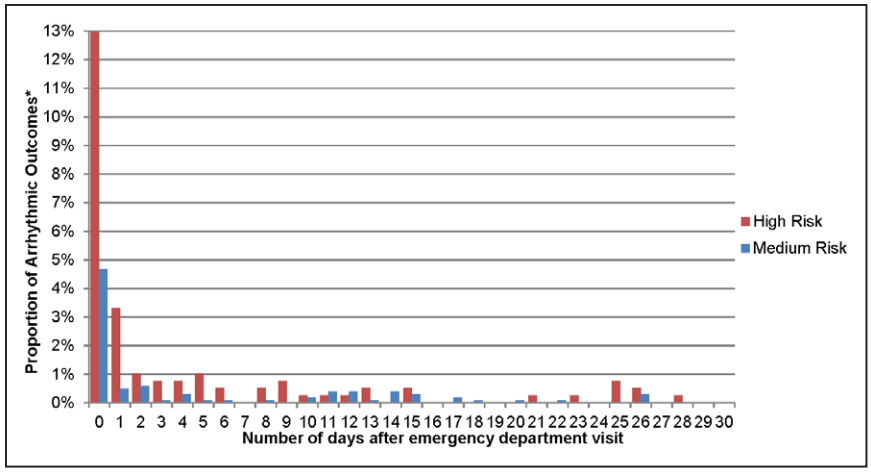


Figure 4. Time of occurrence of arrhythmic outcomes among medium- and high-risk patients.
*Proportion of medium and high-risk patients, stratified using the Canadian Syncope Risk Score with arrhythmic outcomes within 30 days of arrival at the emergency department.

tients (19.0% in our cohort) not suspected of having an evolving nonarrhythmic serious condition (eg, sepsis, or pulmonary embolism), or after appropriate workup, can be discharged home after 6 hours, potentially with consideration given to applying cardiac rhythm monitoring devices. The residual risk of arrhythmias after 6 hours of ED evaluation is even higher among high-risk patients, especially in the first few days, which suggests that brief hospitalization can be considered. Although an important number of patients experience ventricular arrhythmias and unexplained deaths within the first few days after the index syncope, these devastating serious outcomes continue to occur over the 30-day follow-up period. Further studies on medium- and high-risk patients to identify those at risk for ventricular arrhythmia or sudden unexplained death and those who will benefit from hospitalization are clearly needed.

Our study results show that among patients with moderate- and high-risk CSRS scores, the vast majority of the arrhythmic serious conditions occurred within 15 days of the index syncope. The threshold score for outpatient cardiac rhythm monitoring versus hospitalization will depend on the physician-patient preference, local practice environment, and perhaps medicolegal considerations. It is also likely that a longer duration of outpatient cardiac rhythm monitoring will increase both the yield and the false-positive rate of monitoring. Our suggestion for 15-day monitoring needs to be balanced against the incremental value, patient comfort, and cost implications. Further research is needed in this area.

Not surprisingly, the likelihood of arrhythmia detection is highest immediately after syncope, and this likelihood decreases over time. Moreover, given the crowding in the ED, with newly arrived patients often competing with boarded inpatients for monitored beds, the ability to initiate external rhythm monitoring at ED discharge offers an alternative option to hospitalization for the sole purpose of cardiac monitoring. In most centers, these devices are applied several days later through an outpatient facility. Our data suggest that the yield for such monitoring decreases substantially with each passing day. Locati et al[27] recently reported similar results in their prospective observational study of 395 patients with unexplained syncope or sustained palpitations; diagnostic yield of a 4-week external ECG monitor was higher if applied early (0–15 days) versus after 15 days.

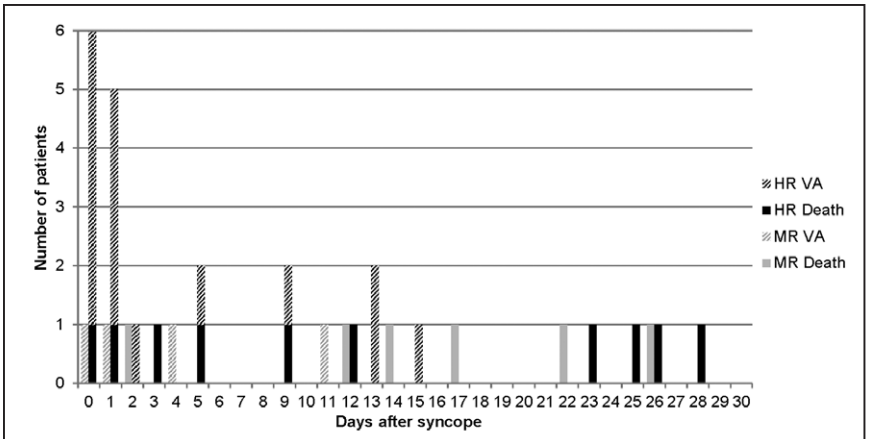
We believe our results are robust because they are based on a large cohort of patients recruited at multiple sites. In our study, a high proportion of eligible patients were enrolled, with very few lost to follow-up.

Our study does have some limitations. Approximately one-fifth of potentially eligible patients were

Table 3. Proportion of Patients With Arrhythmic Outcomes After 6 Hours of ED Monitoring for Select CSRS Thresholds

CSRS Threshold Scores*	N	Arrhythmic Outcomes Within 6 h of ED Arrival	Arrhythmic Outcomes After 6 h of ED Monitoring†	Total Arrhythmic Outcomes Within 30 d
≥1	397	5 (1.3)	17 (4.3)	22 (5.5)
≥2	384	22 (5.7)	13 (3.6)	35 (9.1)
≥3	281	18 (6.4)	17 (6.5)	35 (12.5)
≥4	144	13 (9.0)	10 (7.6)	23 (16)
≥5	130	11 (8.5)	19 (16.0)	30 (23.1)

Values are n (%). CSRS indicates Canadian Syncope Risk Score; and ED, emergency department.
*The proportion of patients with serious arrhythmic outcomes reported is for that value of the threshold risk score or higher.
†Proportions calculated based on the number of patients at risk at the end of 6 hours (after removing from the denominator all patients who already experienced arrhythmia within the 6 hours).



Proportion of Canadian Syncope Risk Score Medium and High-Risk Patients with Unexplained Death or Ventricular Arrhythmia

	Medium Risk Patients N=1,062	High Risk Patients N=396	p-value
Ventricular Arrhythmia	4 (0.4%)	15 (3.8%)	<0.0001
Death due to unknown cause	6 (0.6%)	10 (2.5%)	0.0021

Figure 5. Time of unexplained death and occurrence of ventricular arrhythmias among the study patients.
None of the low-risk patients experienced ventricular arrhythmia or unexplained death. HR indicates high risk; MR, medium risk; and VA, ventricular arrhythmia.

not enrolled. The proportion missed but truly eligible is likely overestimated, because inclusion/exclusion could not always be ascertained from the medical record, and therefore, uncertain cases were coded as missed. We are not aware of any systemic reasons for nonenrollment but can speculate that lower patient acuity led to shorter ED length of stay and lesser opportunity for subject identification, as well as competing priorities for the emergency physician with other, sicker patients in the ED. The basic characteristics (age and sex) of these patients were similar to those who were enrolled. In our study, approximately one-fourth of patients did not have the time of syncope recorded. Hence, we calculated the time to serious outcome occurrence from the time of ED arrival, which was objectively recorded, and used it as "time zero" in our analysis. In our study, 261 patients (4.7%) did not have an ECG performed. It is likely that physicians believed these were low-risk patients because they were younger, with low prevalence of comorbidities, and did not order an ECG for these patients (Table II in the online-only Data Supplement).

Our study centers are located in urban areas, and the majority of our patients arrived at the ED immediately after their syncope. Longer prehospital intervals might result in missed transient arrhythmias immediately after syncope. Approximately 6% of the patients did not complete the 30-day telephone follow-up, although these patients appeared to be at lower risk and hence unlikely to experience nonlethal serious arrhythmic outcomes. We did confirm that none of these patients were known to have died within 30 days of the index ED. The small proportion with missing predictors and lost to follow-up are unlikely to bias the results of our study. The CSRS tool includes the powerful predictors of ED diagnosis of vasovagal syncope or cardiac syncope based on the treating ED physician's impression. The degree of skill and experience of the emergency physicians participating in our study represents a diverse yet national standard. Moreover, the CSRS is intended to be applied at the end of the initial ED assessment and therefore should incorporate the diagnostic impression of the front-line clinician. We have previously shown that these predictors are both reliable and accurate.[28] We do assume an appropriate clinical evaluation consistent with the European Society of Cardiology guidelines and advocate for ongoing education to optimize diagnostic accuracy reliability. However, we have not tested the accuracy of these predictors outside of tertiary care academic Canadian hospitals. Finally, the decision to initiate outpatient cardiac rhythm monitoring was left to the treating physician, and the time interval to the application of such monitoring was variable. The interval to detection of arrhythmia would likely have been shorter with more standardized use of outpatient monitoring and the application of such monitors during the index visit. In our study, there was a subgroup of 30 patients (0.5%) who had pacemaker/implantable cardioverter-defibrillator insertion within 30 days without documented arrhythmias. A few reasons for this lack of information are that device insertion was confirmed by telephone follow-up, with no medical records available for review, or an arrhythmia was not documented or captured on a rhythm strip, or the device was inserted at the discretion of the treating electrophysiologist.

CONCLUSIONS

In this large multicenter, prospective study, among ED patients presenting with syncope who did not have an obvious serious condition identified on arrival, underlying arrhythmia was most often identified in the first 2 hours for CSRS low-risk patients and in the first 6 hours for

CSRS medium- and high-risk patients. A short course of hospitalization may be appropriate for high-risk patients. Outpatient 15-day cardiac rhythm monitoring of patients at a chosen CSRS threshold for medium-risk patients and all high-risk patients discharged from the hospital should also be considered. Such a strategy appears to represent an appropriate trade-off between diagnostic yield for arrhythmia and health resource utilization and will lead to improved detection of underlying important arrhythmias.

ARTICLE INFORMATION

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