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Predictors of Short-Term (Seven-Day) Cardiac Outcomes After Emergency Department Visit for Syncope

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Syncope is a common reason for emergency department (ED) visits, and patients are often admitted to exclude syncope of cardiovascular origin. Population-based data on patterns and predictors of cardiac outcomes may improve decision-making. Our objective was to identify patterns and predictors of short-term cardiac outcomes in ED patients with syncope. Administrative data from an integrated health system of 11 Southern California EDs were used to identify cardiac outcomes after ED presentation for syncope from January 1, 2002, to December 31, 2005. Syncope and cause of death were identified by codes from the *International Classification of Disease, Ninth Revision*. Cardiac outcomes included cardiac death and hospitalization or procedure consistent with ischemic heart disease, valvular disease, or arrhythmia. Predictors of cardiac outcomes were identified through multivariate logistic regression. There were 35,330 adult subjects who accounted for 39,943 ED visits for syncope. Risk of cardiac outcome sharply decreased following the 7 days after syncope. A 7-day cardiac outcome occurred in 893 cases (3%). Positive predictors of 7-day cardiac outcomes included age ≥60 years, male gender, congestive heart failure, ischemic heart disease, cardiac arrhythmia, and valvular heart disease. Negative predictors included dementia, pacemaker, coronary revascularization, and cerebrovascular disease. There was an age-dependent relation between 7-day cardiac outcomes and arrhythmia and valvular disease, with younger patients (<60 years of age) having greater risk of an event compared to their same-age counterparts. In conclusion, ED decision-making should focus on risk of cardiac event in the first 7 days after syncope and special attention should be given to younger patients with cardiac co-morbidities. Published by Elsevier Inc. (Am J Cardiol 2010;105:82–86)

Emergency department (ED) evaluation of syncope may benefit from improved epidemiologic understanding of patterns and predictors of short-term cardiac events. Previous studies have examined risk factors at 1 year after an episode of syncope, a time frame not ideal for decision-making in the acute-care setting.[1–4] Recent cohort studies identifying predictors of short-term (7 to 30 days) events after syncope are relatively small (n = 444 to 791)[2,5–8] and reported prediction models have limited stability and generalizability.[9,10] In this retrospective cohort study, we describe patterns and predictors of short-term cardiac outcomes after ED visits for syncope. We studied a population-based, managed-care cohort receiving care from a regional, integrated health system. Cardiac outcomes included cardiac death and hospitalizations and procedures consistent with a diagnosis of arrhythmia, ischemic heart disease, and valvular heart disease.

Methods

Kaiser Permanente Southern California (Pasadena, California) is an integrated health system that provides comprehensive care to 3.1 million members throughout Southern California. Health care is delivered at 12 medical centers and >100 outpatient clinics. At the time of the study, 11 health system EDs were available to members. All members have similar health care benefits, including coverage of emergency services within and outside the health system. Electronic administrative databases track all health care encounters within the health system. A claims reimbursement system tracks health care provided at outside facilities. Detailed information on diagnoses and procedures are available regardless of setting. Laboratory, pharmacy, and other specialized databases provide information on clinical care. All members are assigned a unique medical record number that is used for data linkage.

Study subjects were members of Kaiser Permanente

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Table 1
Demographic characteristics of study subjects and association with a seven-day cardiac outcome

Characteristics	Cohort (n = 35,330)	Developed 7-d Cardiac Outcome (n = 893)	No 7-d Cardiac Outcome (n = 34,437)	p Value
Age (years), mean ± SD	60.1 ± 21	73.3 ± 13	59.8 ± 21	<0.0001
Women	19,751 (56%)	369 (41%)	19,382 (56%)	<0.0001
White	16,583 (47%)	582 (65%)	16,001 (46%)	<0.0001
Black	4,140 (12%)	104 (12%)	4,036 (12%)	<0.0001
Asian or Pacific Islander	1,590 (5%)	44 (5%)	1,546 (4%)	<0.0001
Hispanic	5,756 (16%)	112 (13%)	5,644 (16%)	<0.0001
Other, multiple, unknown	7,261 (21%)	51 (6%)	7,210 (21%)	<0.0001
Diabetes mellitus	7,425 (21%)	301 (34%)	7,124 (21%)	<0.0001
Hypertension	19,293 (55%)	711 (80%)	18,582 (54%)	<0.0001
Heart failure	4,709 (13%)	347 (39%)	4,362 (13%)	<0.0001
Arrhythmia	5,996 (17%)	512 (57%)	5,484 (16%)	<0.0001
Pacemaker or implantable cardioverter–defibrillator	1,538 (4%)	99 (11%)	1,439 (4%)	<0.0001
Valvular heart disease	3,051 (9%)	212 (24%)	2,839 (8%)	<0.0001
Percutaneous transluminal coronary angioplasty or coronary artery bypass graft surgery	1,622 (5%)	109 (12%)	1,513 (4%)	<0.0001
Myocardial infarction	2,386 (7%)	246 (28%)	2,140 (6%)	<0.0001
Cerebrovascular disease	3,124 (9%)	124 (14%)	3,000 (9%)	<0.0001
Seizure history	2,004 (6%)	65 (7%)	1,939 (6%)	0.0355
Dementia	2,373 (7%)	70 (8%)	2,303 (7%)	0.1748

Proportions of subjects who developed cardiac outcomes of those with and those without a co-morbidity were compared using Fischer's exact test and a 2-sided hypothesis. Race/ethnicity were compared using chi-square test.

Southern California with ≥1 ED visit for syncope from January 1, 2002, to December 31, 2005. Subjects were restricted to an age ≥18 years due to the different nature of syncope in children.[11] ED visits within and external to the health system were included. A subject had to be a member of the health plan at the time of the ED visit; however, no minimum health plan enrollment period was required.

Syncope was identified by *International Classification of Disease, Ninth Revision* (ICD-9) code 780.2, "syncope and collapse," among all ED diagnoses of Kaiser and non-Kaiser facilities. Cases with multiple diagnoses in addition to syncope were included. To validate the accuracy of these codes, blinded physician chart review was performed on consecutive ED visits (n = 100) with and without a diagnosis code consistent with syncope. Compared to physician chart review, ICD-9 codes demonstrated a positive predictive value of 92% and a negative predictive value of 100%.

Demographic information on date of birth, age, gender, and race were obtained from administrative databases. Co-morbid conditions were used to classify risk in subanalyses. We obtained information on major co-morbid conditions related to syncope using data available from the health plan within the observation period and during the ED visit. Case-identification criteria for diabetes included a combination of inpatient and outpatient diagnosis and procedural codes, medications, and laboratory tests.[12] Identification of other co-morbidities was based solely on diagnosis and procedural codes. History of arrhythmia was based on ICD-9 codes signifying ventricular tachycardia, ventricular fibrillation/flutter, type II Mobitz heart block, anomalous atrioventricular excitation, paroxysmal atrial tachycardia, atrial flutter, atrial fibrillation, or sinoatrial node dysfunction. A subject was noted to have a history of syncope if there was an ED visit for syncope within 30 days preceding the index ED visit.

The primary outcome was a 7-day cardiac outcome occurring after an ED visit for syncope. Cardiac outcomes included cardiac death and hospitalizations or procedures consistent with an arrhythmia, ischemic heart disease, and valvular heart disease. Mortality and cause-of-death data were identified through linked California vital statistics files. A death was classified as cardiac in origin if the ICD-9 cause of death code indicated ischemic heart disease, arrhythmia, cardiac valve disease, or congestive heart failure.

We defined arrhythmic events as a hospitalization with primary discharge code consistent with arrhythmia or procedure codes consistent with insertion or revision of a cardiac pacemaker or an implantable cardioverter–defibrillator (AICD). Ischemic heart events included hospitalization with a primary discharge diagnosis of myocardial infarction or unstable angina or procedure codes consistent with coronary artery bypass graft surgery or percutaneous transluminal coronary angioplasty. We defined valvular heart events as hospitalization with a primary discharge diagnosis of valve disease or procedure codes consistent with valve replacement or revision.

Analyses were conducted to identify the risk of a cardiac outcome after an ED visit for syncope. For subjects with multiple ED visits for syncope, counts over time were determined using the first visit within the study period. The association of co-morbidities and a cardiac outcome at 7 days was examined by Fischer's exact test. Hazard functions were prepared for age groups to examine the absolute probability of an event as a function of time after syncope. Risk by age was examined for ages 18 to 39, 40 to 59, 60 to 79, and ≥80 years. Cause of death was examined using ICD-9 and ICD-10 codes from death certificates. Reliability of ICD grouping to identify cardiac death was assessed by physician chart review (blinded to ICD cause of death code)

Table 2
Cardiac events at seven days

Outcome Type	No. (%)*
Total cardiac events	893
Cardiac death	135 (15%)
Arrhythmia	
Hospital admission	560 (63%)
Device placement	269 (30%)
Ischemic heart disease	
Hospital admission	231 (26%)
Revascularization	117 (13%)
Valvular heart disease	
Hospital admission	27 (3%)
Valve procedure	27 (3%)

All patients with cardiac outcomes were hospitalized. Some subjects had >1 cardiac event at 7 days.
* Percentage of total cardiac events.

of 60 inpatient deaths occurring after syncope (kappa = 0.7).

Hazard plots were examined for 7, 30, 180, and 365 days and suggested that excess cardiac risk was concentrated in the first 7 days after syncope, the time frame used for subsequent risk modeling. Logistic regression results were used to help guide subgroup analysis of hazard functions, such as the risk relation between age groups and having a cardiac co-morbidity. Multiple ED visits by the same subject were controlled for in regression analyses. Coefficient SEs were adjusted for subject correlation (i.e., clustering) using robust variance estimates. Predictors of 7-day cardiac outcomes were identified through multivariate logistic regression. Univariate analyses suggested a step increase in risk at 60 years of age, and subsequent models dichotomized age at this threshold. Interactions were tested between age and cardiac co-morbidities. The final model used statistically (i.e., $p < 0.05$) and clinically significant covariates and interactions to identify the predictors of a 7-day cardiac outcome.

Sensitivity analyses were conducted to evaluate the robustness of our model. Additional models were constructed with the same predictors and distinct outcomes of cardiac death, atherosclerotic event, or arrhythmic event. The 3 models were qualitatively similar to the combined-outcomes model. Valvular events were not modeled because of too few events to perform reliable modeling. Our model also evaluated 30-day combined cardiac outcomes. The predictors in this modified model were also very similar in their significance and direction of effect. To improve interpretability of our findings, we present only results of the combined 7-day cardiac events model.

All analyses were conducted at Kaiser Permanente Southern California's department of research using SAS 9.1 (SAS Institute, Cary, North Carolina). The study protocol was reviewed and approved by the institutional review board of Kaiser Permanente Southern California and the University of California, Los Angeles.

Results

Over the 4-year observation period, there were 35,330 subjects who accounted for 39,943 ED visits for syncope.

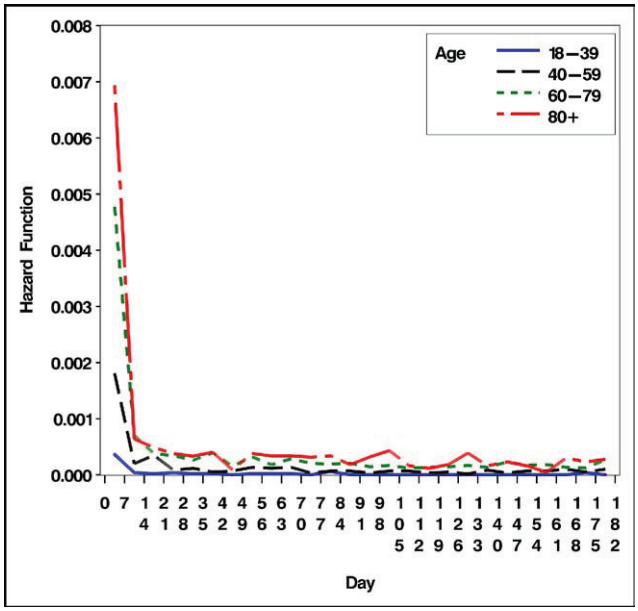

Figure 1. Hazard of cardiac outcome to 180 days according to different age groups. Rate of a cardiac outcome at 7-day intervals given the survival to the end of the interval *(y axis)* and day from the first syncope ED visit to a cardiac outcome *(x axis)* are displayed.

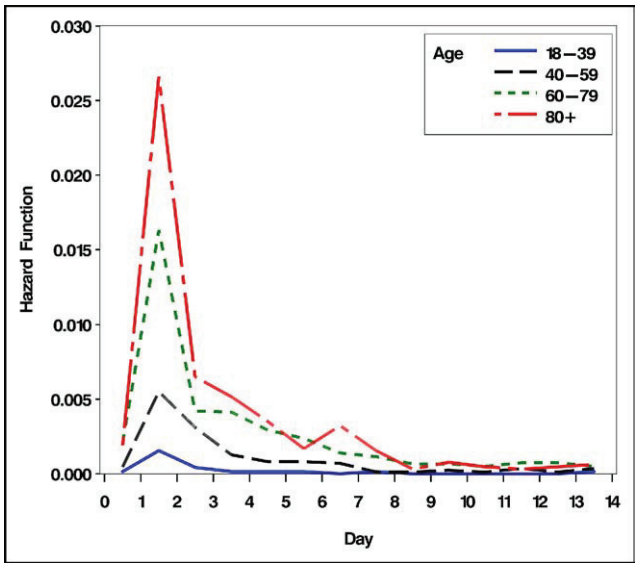

Figure 2. Hazard of cardiac outcome to 14 days. Rate of a cardiac outcome at 1-day time intervals given the survival to the end of the interval *(y axis)* and day from the first syncope ED visit to a cardiac outcome *(x axis)* are shown.

There were 893 7-day cardiac outcomes, representing an event rate of 2.5% (Table 1). Ninety percent of subjects had 1 visit for syncope; the number of syncope visits was 1 to 12 per subject. Table 2 lists types of cardiac events at 7 days. Of the 893 subjects who had a cardiac event, most outcomes were caused by arrhythmias (63%). There were several subjects who had multiple categories of cardiac outcomes.

Figures 1 and 2 illustrate the absolute probability of cardiac event after ED visit for syncope. There is a marked

Table 3
Multivariate logistic regression for seven-day cardiac outcome

Explanatory Variables	Coefficient	OR (95% CI)	p Value
Male gender	0.396	1.49 (1.30–1.70)	<0.0001
Age ≥60 years*	1.3324	3.79 (2.89–4.96)	<0.0001
Asian/Pacific Islander†	0.1517	1.16 (0.86–1.58)	0.3087
Black†	−0.0467	0.95 (0.78–1.17)	0.6449
Hispanic†	−0.0385	0.96 (0.78–1.19)	0.7071
Other†	−0.7841	0.46 (0.34–0.61)	<0.001
Syncope, recent	0.1525	0.16 (0.89–1.52)	0.2373
Diabetes mellitus	−0.0216	0.98 (0.85–1.13)	0.7665
Heart failure	0.6668	1.95 (1.10–3.46)	0.0063
Pacemaker/AICD	−0.4213	0.66 (0.53–0.81)	<0.0001
Coronary artery bypass graft surgery/percutaneous transluminal coronary angioplasty	−0.2643	0.77 (0.61–0.97)	0.0161
Seizure	0.1339	1.14 (0.89–1.46)	0.2652
Dementia	−0.4342	0.65 (0.51–0.82)	<0.0001
Hypertension	0.0972	1.10 (0.91–1.34)	0.2895
Cerebrovascular disease	−0.3228	0.72 (0.60–0.88)	0.0006
Ischemic heart disease	1.308	3.70 (2.12–6.45)	<0.0001
Valve disease‡			
Age 18–59 years		2.14 (1.21–3.77)	0.0085
Age ≥60 years		1.15 (0.97–1.37)	0.1161
Arrhythmia‡			
Age 18–59 years		7.27 (4.43–11.94)	<0.0001
Age ≥60 years		3.17 (2.68–3.76)	<0.0001

This model also adjusts for interactions of age with congestive heart failure and age with ischemic heart disease. These are not shown due to nonsignificance.

* Reference group: 18 to 59 years of age.

† Reference group: white.

‡ Significant interaction terms for age by co-morbidity. OR for presence versus absence of a co-morbidity in the same age group.

increase in risk within the first 3 days, with return to baseline risk across all age groups following the first 7 days.

Logistic regression identified demographic characteristics and co-morbidities that are most strongly associated with a cardiac outcome after an ED visit for syncope. Table 3 presents results for a 7-day cardiac outcome with adjustment for interaction terms between age and the co-morbidities of congestive heart failure, arrhythmia, valvular disease, and myocardial infarction. Cardiac outcomes were significantly positively associated with age ≥60 years (odds ratio [OR] 3.8, 95% confidence interval [CI] 2.9 to 5.0), male gender (OR 1.5, 95% CI 1.3 to 1.7), congestive heart failure (OR 2.0, 95% CI 1.1 to 3.5), and ischemic heart disease (OR 3.7, 95% CI 2.1 to 6.5). We noted significant negative interactions between age and arrhythmia and between age and valvular heart disease. When compared to the same-age group, we found that the risk of developing a cardiac outcome is greater for those who are younger (18 to 60 years) with an arrhythmia compared to their older (≥60 years) counterparts. For patients with a history of valvular disease, the age-stratified ORs were significant in the positive direction for younger patients only. Factors that appeared protective against cardiac outcomes include cardiac revascularization, pacemaker or AICD, cerebrovascular disease, and dementia.

Discussion

This large retrospective cohort study using clinically obtained data reveals 3 novel insights into patterns and predictors of short-term cardiac events and mortality after an ED visit for syncope. First, there is a marked risk of a cardiac outcome within the first 3 days of an ED visit, and risk returns to baseline after the first 7 days. Second, positive predictors of cardiac outcomes within 7 days of an ED visit include male gender, age ≥60 years, and cardiac co-morbidity. A history of a pacemaker, AICD, or a cardiac revascularization procedure appears to be protective. Third, we found a negative interaction effect between age and arrhythmia and between age and valvular heart disease. This finding suggests that compared to older patients, younger patients with arrhythmias or valvular heart disease have a greater, age-stratified OR of developing a cardiac outcome. This is the first description of the predictors of short-term cardiac outcomes after syncope in a large cohort of patients. Previous studies have shown that cardiac causes of syncope are common and can result in increased short-term mortality, but these studies are limited by cohort size.[7,13–15]

Our data demonstrate that most cardiac events and mortality occur in the first 3 days of the ED visit, suggesting that when decisions are made regarding disposition, physicians should take into account that the highest risk occurs in the first 3 days. We also found that after the first 3 days until 7 days after the ED visit, patients are at increased risk of developing a cardiac outcome, suggesting that patients discharged home after a negative evaluation should be closely monitored as outpatients.

We observed an event rate of 2.5%, a rate lower than what has been previously noted of 8% to 11%.[7,9,10,16] This could be due to the younger age of our cohort and to the better health status of managed-care patients. In addition, previous studies evaluating serious events in 7 days were conducted in academic centers that could have sicker patients.[7,9,10,16]

We identified multivariate predictors of 7-day cardiac outcomes after syncope. Our findings of male gender and age-related risk have been confirmed by other studies.[2,4,5,7,8,15] Previous studies have also found cardiac co-morbidity to be associated with an increased risk of morbidity and mortality.[1,2,4,8,13] What is most compelling and novel in our findings is the considerable age-dependent risk associated with arrhythmia and to a lesser extent with valvular disease. We found that the relative age-stratified risk for arrhythmia was much greater for younger patients (18 to 59 years, OR 7.3, 95% CI 4.4 to 11.9) compared to older patients (≥60 years, OR 3.2, 95% CI 2.7 to 3.8) and to a lesser extent for valvular disease. These findings suggest that younger patients with arrhythmia or valvular disease who develop syncope may be at increased risk of a cardiac event. When evaluating young patients with syncope, special attention must be given to those signs concerning for an arrhythmia or valvular disease.

We found that the risk of developing a cardiac outcome was lower in patients with cardiac revascularization, pacemaker or AICD, cerebrovascular disease, and dementia. Presumably, an intervention provides benefit by protecting against potentially fatal arrhythmias or coronary ischemia.

Cerebrovascular disease may indicate increased risk for a neurologic rather than a cardiac cause of syncope. The lower cardiac risk associated with dementia may be attributed to poor recall ability resulting in difficulty distinguishing syncope from other conditions such as generalized weakness, seizure, or an unwitnessed fall.

Our study has some limitations. The demographic characteristics of this managed-care population are similar to the surrounding population in Southern California. However, compared to syncope ED visits in a nationally representative sample,[17] our study cohort has a larger proportion of younger, nonwhite patients, and Hispanics. Care processes in this integrated health system may be different from other settings.[7,9,10] Therefore, the generalizability of our findings will need to be assessed in other settings. In addition, we collected co-morbidity information from existing administrative data, which limited our ability to assess clinically important elements such as symptoms and examination findings.[2,4,7,8,15,18] Addition of such data could potentially improve the ability to predict short-term cardiac death and events.

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