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Clinical Benefit of Hospitalization for Older Adults with Unexplained Syncope: A Propensity-Matched Analysis.

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BCS and MAP designed the study. BCS obtained funding for this study. ANY and SEM were responsible for data collection and management. ES and REW provided statistical advice on study design and analyzed the data. MAP and BCS drafted the manuscript. All authors contributed substantially to manuscript revisions. BCS takes responsibility for the paper as a whole. BCS, ES, REW, ANY, and SEM had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final report for submission.

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Abstract

Objective: Many adults with syncope are hospitalized solely for observation and testing. We sought to determine whether hospitalization versus outpatient management for older adults with unexplained syncope was associated with a reduction in post-disposition serious adverse events at 30 days.

Methods: We performed a propensity score analysis using data from a prospective, observational study of older adults with unexplained syncope/near-syncope who presented to 11 emergency departments (ED) in the United States. We enrolled adults (≥60 years) who presented with syncope/near-syncope. We excluded patients with a serious diagnosis identified in the ED. Clinical and laboratory data was collected on all patients. The primary outcome was rate of post-ED serious adverse events at 30 days.

Results: We enrolled 2,492 older adults with syncope and no serious ED diagnosis from April, 2013 to September, 2016. Mean age was 73 years (SD: 8.9 years) and 51% were female. The incidence of serious adverse events within 30 days after the index visit was 7.4% for hospitalized patients and 3.19% for discharged patients representing an unadjusted difference of 4.2% (95% CI, 2.38 – 6.02%). After propensity score matching on risk of hospitalization, there was no statistically significant difference in serious adverse events at 30 days between the hospitalized group (4.89%) and the discharged group (2.82%) (risk difference = 2.07%, 95% CI, -0.24, 4.38%).

Conclusions: In our propensity matched sample of older adults with unexplained syncope, for those with similar clinical characteristics as the discharged cohort, hospitalization was not associated with improvement in 30-day serious adverse event rates.

Introduction

Background

There are over 1 million emergency department (ED) visits for syncope (transient loss of consciousness) in the United States (US) every year[1], resulting in $2.4 billion in annual hospital costs.[2] The wide range of potential etiologies, some benign and others life-threatening, make the clinical management of this entity challenging.[3]

Importance

Despite substantial research efforts to develop and validate accurate risk stratification tools[4–10], there remains considerable uncertainty regarding which patients with syncope can be safely discharged from the ED.[11] Over 30% of these visits result in hospitalization; for older adults (≥60 years) this proportion is over 50%.[12] While some of these hospitalizations are for specific therapeutic reasons (e.g., pacemaker insertion, anticoagulation for pulmonary embolism), older adults with unexplained syncope are often admitted to inpatient or observation units solely for observation or further testing.[13–15] Such hospitalizations for syncope patients without a serious diagnosis identified in the ED are costly and may be of little to no clinical benefit.[2,16–18]

Goals of This Investigation

To our knowledge, there are no data demonstrating the benefit of hospital-based evaluation for patients with syncope and an unremarkable ED evaluation.[11] Using propensity score matching, we sought to determine whether hospitalization versus outpatient management for older adults with unexplained syncope was associated with a reduction in post-ED serious adverse events at 30 days.

Methods

Study design and setting

We performed a secondary analysis of data from a multicenter, prospective, observational study of older adults who presented to an ED with syncope or near-syncope (ClinicalTrials.gov identifier NCT01802398). The institutional review boards at all enrolling sites approved the study and we obtained written, informed consent from all participating subjects or their representatives. The study was conducted at 11 academic EDs, all located in not-for-profit hospitals, across the US (eTable 1) from April 28, 2013 to September 21, 2016. Ten out of 11 of the EDs were teaching hospitals with a trauma center; ED volume ranged from 47,000 to 120,000 visits per year.

Selection of Participants

Patient inclusion criteria for eligibility were age ≥60 years and a complaint of syncope or near-syncope. We defined syncope as transient loss of consciousness, associated with postural loss of tone, with immediate, spontaneous, and complete recovery. We defined near-syncope as the sensation of impending loss of consciousness, without actual loss of consciousness. We excluded candidates if their symptoms were thought to be due to intoxication, seizure, stroke, head trauma, or hypoglycemia. Additional exclusion criteria

were the need for medical intervention to restore consciousness (e.g., defibrillation), new or worsening confusion, and inability to obtain informed consent from the patient or a legally authorized representative.

For this analysis, we also excluded all patients who had a serious diagnosis identified in the ED: death, significant cardiac arrhythmia, myocardial infarction, significant structural heart disease, stroke, pulmonary embolism, aortic dissection, hemorrhage or anemia requiring blood transfusion, acute pulmonary edema, pneumonia, sepsis, acute renal failure, intracranial bleed, or acute surgical illness (eTable 2). We identified serious diagnoses in one of two ways: 1) Directly by the treating physician during the ED visit using a pre-specified list of serious diagnoses presented in the data collection form, or 2) Via ED chart review by trained research assistants (RAs) who were blinded to the results of the 30-day follow-up telephone call. We used both methods to ensure that the final study cohort consisted of only patients that truly had no serious diagnosis identified in the ED.

Measurements

All patients underwent standardized history, physical examination, cardiac biomarker, and 12-lead electrocardiogram (ECG) testing. Trained RAs directly questioned patients about symptoms associated with the syncopal or near-syncopal episode. They prospectively collected data on the patient's past medical history, medications, and physical examination findings from treating providers. No standardized clinical protocols were implemented as part of our study, i.e. clinical management, other than ECG and biomarker testing, was left to the discretion of the ED and in-patient providers.

Research staff obtained blood samples for testing at a core laboratory (University of Rochester, Rochester, NY). Lab staff performed two assays using the Roche Elecsys platform: N-terminal pro B-type natriuretic peptide (NT-proBNP) and the 5th generation high-sensitivity cardiac troponin T (hs-TnT). We classified NT-proBNP as abnormal above a cutoff of 125 pg/ml. We classified hs-TnT as abnormal above the 99th percentile for a reference population (19 ng/L). Although hs-TnT was not approved by the US Food and Drug Administration (FDA) at the time of the study, we anticipated that this assay would receive approval and be integrated into future standard of care (FDA granted approval in January 2017). Core laboratory results for NT-proBNP and hs-TnT were unavailable at the time of the ED evaluation; however, the ED providers were free to order local BNP and conventional troponin testing. The disposition of the patients (admission vs. observation vs direct discharge) was at the discretion of the treating providers.

The post-ED disposition of the patient was prospectively collected by RAs and confirmed via electronic medical record review. The disposition was classified as one of the following: 1) Admitted to inpatient service, 2) Sent to observation, 3) Transferred to outside hospital, and 4) Discharged from the ED. We classified all patients who were admitted, observed, or transferred as "hospitalized".

Outcomes

Our primary outcome was the rate of serious adverse events identified after ED disposition within 30 days of the index ED visit, (including serious events occurring both during the

index hospitalization and after discharge). These included death due to any cause, significant cardiac arrhythmia, myocardial infarction, new diagnosis of structural heart disease, stroke, pulmonary embolism, aortic dissection, subarachnoid hemorrhage, cardiopulmonary resuscitation, internal hemorrhage or anemia requiring transfusion, recurrent syncope or fall resulting in major traumatic injury, or cardiac intervention. Significant cardiac arrhythmias included ventricular fibrillation, ventricular tachycardia, sick sinus disease, Mobitz II atrioventricular heart block, complete heart block, symptomatic supraventricular tachycardia, symptomatic bradycardia and pacemaker malfunction. These outcomes are consistent with standardized research reporting and clinical management guidelines.[11,19]

The occurrence of a serious adverse event was determined using data collected via a review of the electronic medical records conducted by research personnel at each study site, as well as telephone calls (performed by the central site) to enrolled patients at 30 days to identify out-of-hospital deaths, ED visits, and hospitalizations that occurred outside the study sites. Local research personnel performing chart review were blinded to the results of the telephone follow-up. If a patient or his or her authorized representative reported an ED or hospital visit that occurred outside of the study site, then we obtained and reviewed the medical charts associated with those visits. For patients who research staff was unable to contact at 30 days, we queried of the Social Security Death Index Master File in May 2018.

Analysis

We calculated descriptive statistics for the baseline characteristics of the patient cohort, stratified by disposition, before and after propensity score matching. We used chi-squared tests or t-tests to test associations between the categorical or continuous variables and ED disposition. To account for possible confounding variables for disposition, we used a propensity score analysis, using greedy nearest neighbor matching, to evaluate the association between hospitalization and risk of serious adverse events.[20] This approach balances measured patient characteristics between patients who were discharged and patients who were hospitalized at the cost of a reduced sample size. At each matching step we chose the hospitalized subject that had not yet been matched but was closest to the discharged subject. As this was a secondary analysis of data collected with the primary aim of deriving a syncope risk-stratification tool, the sample size and power calculations were driven by this primary analysis.

We estimated the propensity scores for each individual using a logistic regression model where the outcome was whether the patient was discharged or not. We used 43 prospectively collected covariates to predict whether patients were discharged: age, gender, race, dyspnea, chest discomfort, hypotension, abnormal ECG, emergency physician risk assessment, NT-proBNP values, hs-TnT values, physical exam findings, medications, and whether patients had a history of baseline cognitive impairment or dementia, premature (<50 years) sudden death in siblings or parents, past history of stroke, heart failure, ejection fraction <40%, peripheral vascular disease, implanted permanent pacemaker/defibrillator, coronary artery disease, structural heart disease, arrhythmia, seizure disorder, diabetes requiring medication, hypertension, chronic renal insufficiency, or cancer requiring current active treatment (eTable 3). We determined physician risk assessment via the treating attending emergency

physician's estimate of the "probability that the patient will experience 30-day cardiac death or serious cardiac event." We matched each patient in the discharged group with an individual in the hospitalized group with the closest propensity score, resulting in pairs of observations that had similar propensity scores; the pairing was not used in further analysis. We compared the risk of 30-day post-ED disposition serious adverse events, as well as mortality alone, after the index visit in discharged and hospitalized patients, before and after propensity score matching.

As a sensitivity analysis, we used a Poisson regression model to compare the rates of 30-day post-ED serious adverse events (including mortality), as well as mortality alone, in both groups. The Poisson regression takes into account the amount of time that patients were at risk for serious adverse events, i.e. hospitalized patients had fewer post-discharge days out of the hospital at 30 days. One hundred one patients with missing length of stay data were excluded from the analysis. For patients that had a serious adverse event, time at risk was the number of days until the serious adverse event since ED disposition.

As an additional sensitivity analysis, we repeated the above analyses using a more restricted primary outcome, i.e., serious adverse events that occurred after the ED evaluation *excluding* those that occurred during the index hospitalization, also after propensity score matching. This sensitivity analysis was performed since our initial primary outcome, which included events which occurred during the index hospitalization, may have biased against the hospitalized cohort by increasing the number of adverse events detected in hospitalized patients. Mitigating such a detection bias is important since in-hospital monitoring may be more likely to detect certain conditions, e.g. cardiac arrhythmias. In the sensitivity analysis using a Poisson regression and this more restricted primary outcome, for discharged patients that did not have a serious adverse event, time at risk was the number of days since discharge at 30 days. For hospitalized patients, it was 30 days minus days in hospital. Statistical analyses were performed in R version 3.5.0.[21]

Results

Characteristics of study subjects

Of 6,930 eligible patients who presented during the 3.5 year study period, 3,686 consented for enrollment. Of those, 105 were withdrawn or lost to follow-up leaving 3,581 in the base cohort (Figure 1: Study flow chart). A total of 1,054 (29.4%) patients had serious diagnoses identified in the ED and were excluded from further analysis. Some patients were not enrolled due to the ED provider not having sufficient time to cooperate with the RA: "provider request"; others were excluded if the site-PI reviewed the chart and identified the presence of an exclusion criteria (e.g. a diagnosis of seizure) that was not initially detected by the RA in the ED: "PI withdrawal". A list of these diagnoses and their frequencies are provided in eTable 2. Our final study cohort consisted of 2,492 older adults with a mean age of 72.6 (SD: 8.9) years, 50.8% female. The vast majority of patients in the study cohort (n=2,482, 99.6%) were successfully reached by phone, with the remainder (n=10) requiring chart review and/or death index query. Table 1 describes the baseline characteristics of the study cohort before and after propensity score matching. Before matching, hospitalized patents were significantly older, had a greater prevalence of heart disease, and a greater rate

of elevated cardiac biomarkers than the discharged patients. These and other baseline characteristics were balanced after matching.

Main Results

Of the 2,492 patients in our final cohort, 1,866 (74.9%) were hospitalized. Of those hospitalized, the majority, 1,129 (60.5% of 1,866) were observed, 732 (39.2%) were admitted to the hospital, and 5 (0.3%) were transferred. The mean length of stay for the hospitalized cohort was 53.9 hours (SD=75.5) compared to 5.5 hours (SD=3.6) in the discharged patients. Overall, 158 (6.34%, 95% CI, 5.38 – 7.30%) had a serious adverse event within 30 days, including 17 (0.68%, 95% CI, 0.36 – 1.01%) who died. Of the patients who were lost to follow up, 7 were found to have died within 30 days based on query of the Social Security Death Index. The mean length of time elapsed before detection of any serious adverse event was 7.5 days in the hospitalized cohort and 13.8 days in the discharged cohort.

Table 2 describes the frequency of each serious adverse event by disposition. The most common serious outcome was serious cardiac arrhythmia (n=58/158, 36.7%), of which symptomatic supraventricular tachycardia was the most frequent (n=22/158, 13.9%). In the unadjusted analysis, the risk of post-discharge serious events at 30 days was higher among hospitalized patients (n=138/1,866, 7.4%, 95% CI, 6.21 – 8.58%) as compared to discharged patients (n=20/626, 3.19%, 95% CI, 1.82 – 4.57%), representing an unadjusted risk difference of −4.2% (95% CI, −2.38 – −6.02%).

Propensity Score Analysis

Propensity score matching resulted in a sample size of 1,064, with 532 patients each in the discharged and hospitalized groups. eTable 3 describes the propensity score model for predicting patient discharge. All covariates were balanced in the two cohorts after matching (Table 1), with overlapping propensity score distributions after matching (eFigure 1). After propensity score matching, there was no significant difference in the risk of post-ED serious adverse events at 30 days between the hospitalized (4.89%, 95% CI, 3.06 – 6.72%) and discharged (2.82%, 95% CI, 1.41 – 4.23%) cohorts (risk difference = 2.07%, 95% CI, −0.24 – 4.38%) (Table 3). Our sensitivity analysis using a Poisson regression model after propensity score matching gave similar results. The rate of post-ED adverse events per 30 days was 2.86% (95% CI, 1.73– 4.75%) in the directly discharged group and 5.1% (95% CI, 3.47 – 7.49%) in the hospitalized group (rate ratio: 0.56, 95% CI, 0.30, 1.06). Our analysis using risk of 30-day mortality post-ED visit produced similar results, i.e. no statistically significant mortality difference between the hospitalized (0.75%, 95% CI, 0.21 – 1.91%) and discharged (0.56%, 95% CI, 0.12 – 1.64%) cohorts (risk difference = −0.19%, 95% CI, −1.16 − 0.78%). Our Poisson regression model using the propensity score-matched cohorts to compare 30-day mortality rates gave similar results (Table 3). Our sensitivity analysis using a more restricted primary outcome, which excluded serious adverse events occurring during the index hospitalization to account for detection bias, returned similar results, i.e. we found no significant difference in mortality or serious adverse events at 30 days using both risk difference and Poisson regression (eTable 4).

Limitations

Our study is subject to certain limitations. Due to its observational nature, unmeasured confounders may be a source of bias. We attempted to mitigate this limitation by using propensity score matching and by including an overall physician risk estimation of adverse cardiac outcomes at 30 days prospectively collected at the time of enrollment. As this was an observational study, standardized protocols were not used to guide the clinical care that patients received in the ED or in the hospital, and thus variation across sites may have occurred. As we only enrolled patients ≥60 years, our findings may not necessarily be valid in younger syncope patients. However, it is this age category that is most often admitted for observation or further testing, and, thus, is associated with the greatest resource utilization. Since 47% of eligible patients declined to participate, sampling bias may have occurred. Our sample size was limited by the size of the dataset that was collected for the primary analysis and thus the possibility of a Type II error remains. Our propensity score matching was only able to match 532 of the 1,886 hospitalized patients, which further reduced our sample size and statistical power. Nonetheless, this is the largest prospectively collected cohort of US syncope patients collected to date. Although our follow-up rate at 30 days was generally high, it is possible that certain patients who were lost to follow-up (n=95) suffered serious adverse events. We mitigated this limitation be querying the Social Security Death Index.

Discussion

Our results, using propensity score-matching, suggest that among older adults presenting with syncope or near-syncope and no serious diagnosis found in the ED, hospitalization is not associated with a significant reduction in serious adverse events at 30 days. These findings were consistent across our sensitivity analyses, using a Poisson regression model and using a narrower primary outcome that excluded inhospital adverse events, both of which demonstrated no difference in adverse events or mortality at 30 days. We conducted two differing analyses, one including in-hospital serious events in our primary outcome, and one excluding them. This was done to mitigate the potential detection bias which could have increased the number of serious events found in the hospitalized group simply by virtue of these patients being monitoring more closely in the hospital than as out-patients. Our secondary analysis, excluding the in-hospital serious events, has the potential to biases our results towards the null hypothesis by censoring the initial high-risk period post-ED visit. While neither of these analyses is perfect, both provide useful complimentary information. Overall, these findings challenge the current clinical care paradigm of frequent hospitalization for older adults for unexplained syncope/near-syncope, solely for the purpose of additional monitoring or further testing beyond that conducted in the ED.

Previous studies have demonstrated the wide variability in admission rates across hospitals for syncope in North America, ranging from 12% to over 80%.[8,22] Multiple studies have questioned the diagnostic yield of admission for syncope, demonstrating a lack of identifiable cause in over one third of admissions.[1,17,23] Given the substantial costs and potential iatrogenic harms associated with hospitalization[2,18], efforts to promote out-patient management may improve the value and safety of syncope care.[24] Although there was a non-significant trend towards reduction in post-discharge serious adverse events in the

hospitalized group (1.5%), given the substantial costs (over $2.4 billion annually) associated with hospitalization[2], this may constitute low-value care. Median hospital charges for syncope admission are on the rise,[25] and costs for syncope patients are positively correlated with increased length of stay.[26]

Our results failed to show a significant clinical benefit of hospitalization for ED patients with unexplained syncope who were matched to similar patients in the discharged cohort. This finding suggests that among older adults with unexplained syncope, who are not otherwise deemed high risk, hospitalization should not be the default pathway. Rather, a frank discussion of the reasonable disposition options, and their corresponding risks and benefits, should be had -- an approach known as shared decision-making.[28]. Alternative clinical pathways using ambulatory cardiac monitors[29,30] or specialized out-patient syncope units[31] could represent a less disruptive, more patient-centered, and more cost-effective approach to managing unexplained syncope after initial ED evaluation.

One possible interpretation of these findings is that if a serious diagnosis is not found during the initial ED evaluation, and the patient is not considered high risk based on clinical variables, then the diagnostic benefit of an additional 24 to 48 hours of in-patient monitoring is likely to be very limited. The mean elapsed time before occurrence of a serious outcomes was greater than 48 hours in both the hospitalized and discharged cohorts. Notably, the most common cardiac arrhythmia in the hospitalized group was symptomatic supraventricular tachycardia, which typically does not pose a serious risk to patients even if subject to delayed diagnosis. In contrast, more malignant arrhythmias, such as ventricular tachycardia/ fibrillation and second-degree heart block, were rarely diagnosed post-discharge, even in the hospitalized group (Table 2).

Our unadjusted results, demonstrating a greater rate of serious adverse events in the hospitalized cohort, suggest that clinicians are adept at identifying, and appropriately hospitalizing, certain higher risk patients with syncope. However, it seems that a significant proportion of those hospitalized patients may actually be appropriate for out-patient management, as demonstrated by the low rate of adverse events in our matched sample.

Previous research aimed at increasing the value of syncope care has focused on the use of observation pathways[14,32] including two randomized controlled trials of observation syncope protocols.[33,34] These studies have demonstrated the safety and value of such an approach. However, no previous studies have compared hospitalization versus direct discharge in ED syncope patients with a negative initial evaluation. The 2017 American Heart Association/ American College of Cardiology/ Heart Rhythm Society syncope guidelines state that it “may be reasonable to manage selected patients with suspected cardiac syncope in the outpatient setting in the absence of serious medical conditions”, but that “hospital-based evaluation of syncope of unclear cause…has not demonstrated an improvement in patient-relevant outcomes.” Our study attempted to address this very question and, using propensity score matching, found no improvement in 30-day adverse event rates. To definitively answer this question, future research in the form of a well-designed, multicenter randomized trial comparing in-patient versus out-patient management for this cohort of patients would need to be performed.

In summary, in our propensity-matched sample of older adults with syncope/near-syncope and no serious diagnosis found on ED evaluation and similar clinical characteristics as the discharged cohort, hospitalization did not appear to be associated with a reduction in serious adverse events or mortality at 30 days post-ED visit. Shifting care from the in-patient to the out-patient setting for this cohort may be a more sensible approach to ED syncope care for patients who are not otherwise high risk. Future randomized trials evaluating these alternative clinical management strategies would be needed to confirm our findings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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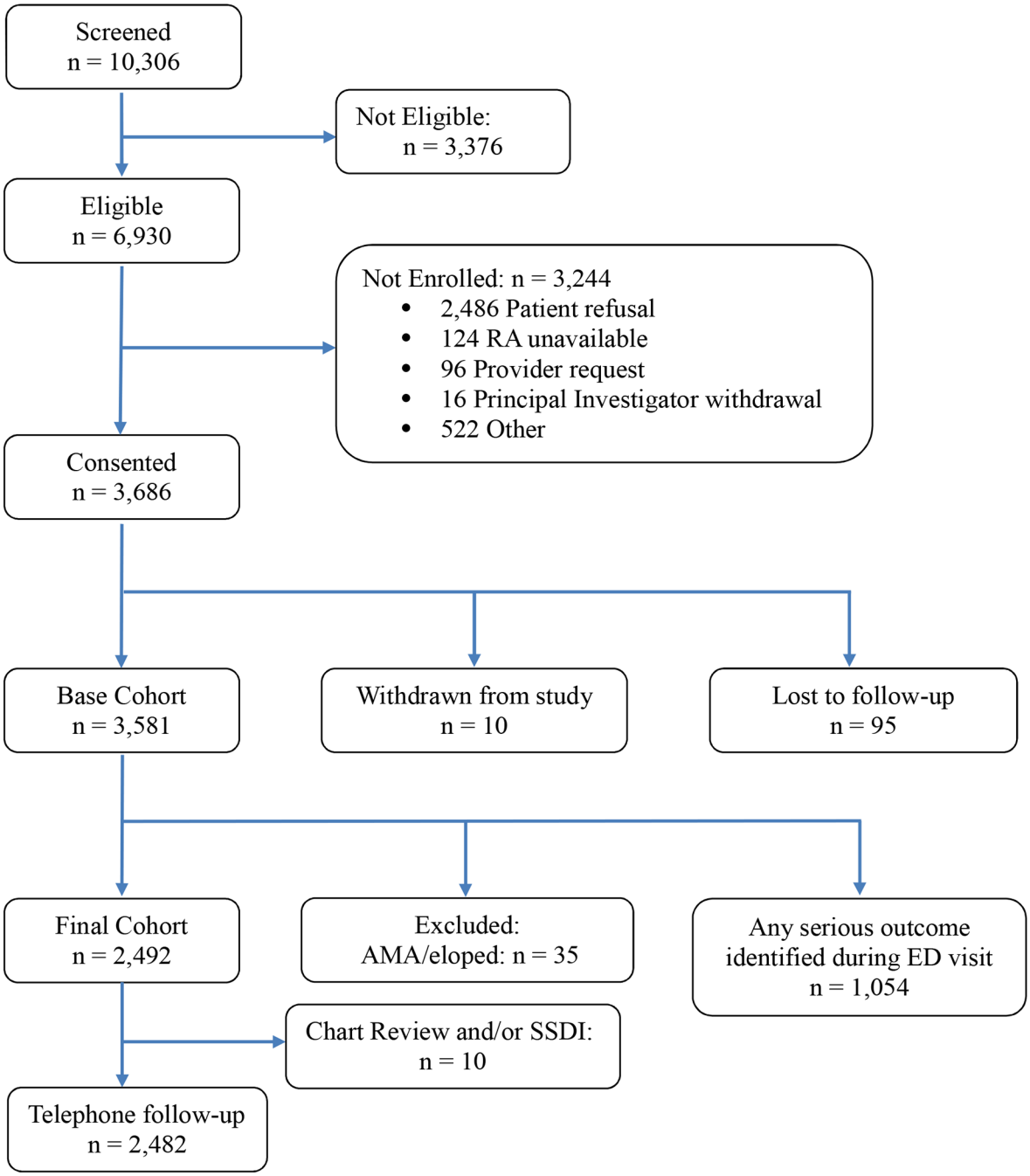

Figure 1:
Study Flow Chart
RA: Research Assistant; AMA: Against Medical Advice; ED: Emergency Department; SSDI: Social Security Death Index

Table 1.

Baseline Characteristics of Syncope Patients by Disposition

	No. (%)					
	Before Propensity Score Matching			After Propensity Score Matching		
Characteristic	Hospitalized (n=1866)	Discharged (n=626)	Standardized Differences	Hospitalized (n=532)	Discharged (n=532)	Staandardized Differences
Demographics						
Age, mean (SD)	73.1 (8.9)	71.1 (8.9)	22.1	70.6 (8.6)	71.4 (8.9)	9.2
Age			22.8			12.0
60 to <70	790 (42.3)	323 (51.6)		289 (54.3)	268 (50.4)	
70 to <80	593 (31.8)	185 (29.6)		158 (29.7)	161 (30.3)	
80 to <90	408 (21.9)	90 (14.4)		58 (10.9)	78 (14.7)	
90+	75 (4.0)	28 (4.5)		27 (5.1)	25 (4.7)	
Gender			10.8			1.1
Female	922 (49.4)	343 (54.8)		276 (51.9)	279 (52.4)	
Male	944 (50.6)	283 (45.2)		256 (48.1)	253 (47.6)	
Race			2.4			1.1
White or Caucasian	1541 (83.0)	513 (82.9)		453 (85.2)	447 (84.0)	
Black or African American	259 (13.9)	84 (13.6)		66 (12.4)	66 (12.4)	
Asian	24 (1.3)	7 (1.1)		7 (1.3)	7 (1.3)	
Other	33 (1.8)	15 (2.4)		6 (1.1)	12 (2.3)	
History of						
Congestive heart failure	219 (11.7)	35 (5.6)	22.0	29 (5.5)	31 (5.8)	1.6
Coronary artery disease	535 (28.7)	111 (17.7)	26.2	102 (19.2)	99 (18.6)	1.4
Arrhythmia	355 (19.0)	101 (16.1)	7.7	86 (16.2)	90 (16.9)	2.0
Any of CHF, CAD, or Arrhythmia	812 (43.5)	183 (29.2)	30.0	170 (32.0)	162 (30.5)	3.3
Dyspnea	353 (18.9)	112 (18.2)	2.7	83 (15.6)	86 (16.2)	1.5
Chest discomfort	160 (8.6)	37 (5.9)	10.3	33 (6.2)	31 (5.8)	1.6
Hypotension	166 (8.9)	32 (5.1)	14.9	29 (5.5)	30 (5.6)	0.8
Abnormal ECG	979 (53.0)	280 (46.1)	13.8	214 (40.2)	245 (46.1)	11.8
Heart Rate			2.4			1.1
<60 bpm	250 (13.5)	85 (13.8)		74 (13.9)	75 (14.1)	
60–100 bpm	1,492 (80.6)	498 (80.8)		433 (81.4)	431 (81.0)	
>100 bpm	109 (5.9)	33 (5.4)		25 (4.7)	26 (4.9)	
MD Risk Assessment, mean (SD)	8.7 (11.5)	4.2 (7.8)	45.8	4.9 (7.3)	4.3 (8.0)	8.0
Cardiac Biomarkers						
NT-proBNP						
BNP >125 pg/ml	1,128 (63.5)	305 (51.5) 602.0	24.4	260 (48.9)	277 (52.1)	6.4
BNP, mean (SD)	796.5 (2,323.3)	(2,709.1)	7.6	659.2 (2,443.3)	639.4 (2,849.9)	0.8
Hs-Troponin T						
Troponin >19 ng/L	476 (27.5)	104 (18.2)	22.4	98 (18.4)	100 (18.8)	1.0

	No. (%)					
	Before Propensity Score Matching			After Propensity Score Matching		
Characteristic	Hospitalized (n=1866)	Discharged (n=626)	Standardized Differences	Hospitalized (n=532)	Discharged (n=532)	Staandardized Differences
Troponin, mean (SD)	21.3 (60.1)	14.8 (26.6)	14.0	17.0 (38.2)	15.1 (27.4)	5.7

SD: Standard Deviation; CHF; Congestive Heart Failure; CAD: Coronary Artery Disease; ECG: Electrocardiogram; MD: Medical Doctor; NT-proBNP: N-Terminal pro-Brain Natrieutic Peptide; Hs: High-sensitivity.

Table 2.

Adverse Events Identified After Emergency Department Stay, Stratified by Disposition

Adverse Event[†]	Overall Cohort (n=2492) N (%)	Hospitalized (n=1866) N (%)	Admitted[*] (n=732) N (%)	Observed (n=1129) N (%)	Hospitalized: Identified During Index Hospital Visit N (%)	Hospitalized: Identified After Index Hospital Visit N (%)	Discharged (n=626) N (%)	% Difference[**] (95% CI)
Any 30-day serious event	158 (6.3)	138 (7.4)	79 (10.8)	59 (5.2)	98 (5.3)	46 (2.5)	20 (3.2)	4.2 (2.4,6.0)
30-day death	17 (0.7)	14 (0.8)	10 (1.4)	4 (0.4)	1 (0.1)	13 (0.7)	3 (0.5)	0.3 (−0.4,0.9)
Serious Cardiac Arrhythmias								
Any cardiac arrhythmia	58 (2.3)	54 (2.9)	31 (4.2)	23 (2.0)	44 (2.4)	14 (0.8)	4 (0.6)	2.3 (1.3,3.2)
Ventricular fibrillation	3 (0.1)	3 (0.2)	2 (0.3)	1 (0.1)	2 (0.1)	1 (0.1)	0 (0.0)	0.2 (0.0,0.3)
Ventricular tachycardia (>30 secs)	6 (0.2)	6 (0.3)	2 (0.3)	4 (0.4)	6 (0.3)	1 (0.1)	0 (0.0)	0.3 (0.1,0.6)
Symptomatic ventricular tachycardia (<30 secs)	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	−0.2 (−0.5,0.2)
Sick sinus disease with alternating sinus bradycardia and tachycardia	10 (0.4)	10 (0.5)	6 (0.8)	4 (0.4)	8 (0.4)	2 (0.1)	0 (0.0)	0.5 (0.2,0.9)
Sinus pause >3 seconds	2 (0.1)	2 (0.1)	1 (0.1)	1 (0.1)	2 (0.1)	0 (0.0)	0 (0.0)	0.1 (0.0,0.3)
Mobitz II atrioventricular heart block	4 (0.2)	4 (0.2)	4 (0.5)	0 (0.0)	3 (0.2)	2 (0.1)	0 (0.0)	0.2 (0.0,0.4)
Complete heart block	2 (0.1)	2 (0.1)	2 (0.3)	0 (0.0)	2 (0.1)	0 (0.0)	0 (0.0)	0.1 (0.0,0.3)
Symptomatic supraventricular tachycardia	22 (0.9)	21 (1.1)	10 (1.4)	11 (1.0)	16 (0.9)	6 (0.3)	1 (0.2)	1.0 (0.4,1.5)
Symptomatic bradycardia	8 (0.3)	6 (0.3)	4 (0.5)	2 (0.2)	5 (0.3)	2 (0.1)	2 (0.3)	0.0 (−0.5,0.5)
Pacemaker or ICD malfunction with cardiac causes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.0 (0.0,0.0)
Cardiac Intervention								
Any cardiac intervention	49 (2.0)	44 (2.4)	25 (3.4)	19 (1.7)	36 (1.9)	14 (0.8)	5 (0.8)	1.6 (0.6, 2.5)
Pacemaker	23 (0.9)	22 (1.2)	14 (1.9)	8 (0.7)	17 (0.9)	7 (0.4)	1 (0.2)	1.0 (0.4, 1.6)
AICD	6 (0.2)	6 (0.3)	2 (0.3)	4 (0.4)	5 (0.3)	3 (0.2)	0 (0.0)	0.3 (0.1, 0.6)
CABG	5 (0.2)	3 (0.2)	1 (0.1)	2 (0.2)	3 (0.2)	0 (0.0)	2 (0.3)	−0.2 (−0.6, 0.3)
PTCA	8 (0.3)	7 (0.4)	5 (0.7)	2 (0.2)	5 (0.3)	2 (0.1)	1 (0.2)	0.2 (−0.2, 0.6)
Other	7 (0.3)	6 (0.3)	3 (0.4)	3 (0.3)	6 (0.3)	2 (0.1)	1 (0.2)	0.2 (−0.2, 0.6)
Other Serious Outcomes								
Myocardial infarction	11 (0.4)	10 (0.5)	5 (0.7)	5 (0.4)	8 (0.4)	4 (0.2)	1 (0.2)	0.4 (−0.1,0.8)

Adverse Event[†]	Overall Cohort (n=2492) N (%)	Hospitalized (n=1866) N (%)	Admitted[*] (n=732) N (%)	Observed (n=1129) N (%)	Hospitalized: Identified During Index Hospital Visit N (%)	Hospitalized: Identified After Index Hospital Visit N (%)	Discharged (n=626) N (%)	% Difference[**] (95% CI)
New diagnosis of structural heart disease	20 (0.8)	19 (1.0)	7 (1.0)	12 (1.1)	17 (0.9)	3 (0.2)	1 (0.2)	0.9 (0.3, 1.4)
Stroke	12 (0.5)	9 (0.5)	6 (0.8)	3 (0.3)	5 (0.3)	4 (0.2)	3 (0.5)	0.0 (−0.6, 0.6)
Pulmonary embolism	5 (0.2)	4 (0.2)	2 (0.3)	2 (0.2)	4 (0.2)	0 (0.0)	1 (0.2)	0.1 (−0.3, 0.4)
Aortic dissection	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.0 (0.0, 0.0)
Subarachnoid hemorrhage	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.0 (0.0, 0.0)
Cardiopulmonary resuscitation	3 (0.1)	3 (0.2)	1 (0.1)	2 (0.2)	1 (0.1)	2 (0.1)	0 (0.0)	0.2 (0.0, 0.3)
Internal hemorrhage/anemia	25 (1.0)	22 (1.2)	18 (2.5)	4 (0.4)	17 (0.9)	6 (0.3)	3 (0.5)	0.7 (0.0, 1.4)
Recurrent syncope/fall resulting in major injury	7 (0.3)	4 (0.2)	1 (0.1)	3 (0.3)	0 (0.0)	4 (0.2)	3 (0.5)	−0.3 (−0.8, 0.3)

AICD: Automated Implantable Cardioverter-Defibrillator; CABG: Coronary Artery Bypass Graft; PTCA: Percutaneous Transluminal Coronary Angioplasty; ICD: Implantable Cardioverter-Defibrillator;

[†] Includes patients with previous history of such events, with the exception of structural heart disease.

[*] Includes transferred patients.

[**] Difference and 95% CI for comparing occurrence of events between hospitalized and discharged patients.

Table 3:

Post-Emergency Department[≠] serious adverse events at 30-days before and after propensity score matching

	No. (%)					
	Before Propensity Score Matching			After Propensity Score Matching		
Outcome	Hospitalized (n=1866)	Discharged (n=626)	Risk Difference* (95% CI)	Hospitalized (n=532)	Discharged (n=532)	Risk Difference* (95% CI)
30-day serious adverse events	138 (7.40)	20 (3.19)	4.20 (2.38, 6.02)	26 (4.89)	15 (2.82)	2.07 (−0.24, 4.38)
30-day all-cause mortality	14 (0.75)	3 (0.48)	−0.27 (−0.94, 0.40)	4 (0.75)	3 (0.56)	−0.19 (−1.16, 0.78)
Poisson Regression						
			Rate Ratio**			Rate Ratio**
Outcome	%	%	(95% CI)	%	%	(95% CI)
Events per 30 days	7.86	3.25	0.41 (0.26, 0.66)	5.10	2.86	0.56 (0.30, 1.06)
30-day mortality rate	0.75	0.48	0.64 (0.18, 2.22)	0.76	0.57	0.75 (0.17, 3.34)

[≠] Post-Emergency Department events include events that occurred during the index hospitalization.

* Risk difference defined as percent risk for hospitalized patients minus percent risk for discharged patients.

** Rate ratios comparing discharged to hospitalized rates presented for Poisson regression instead of risk difference.