4-1-2022

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Received: 18 November 2021 | Revised: 3 February 2022 | Accepted: 10 February 2022

DOI: 10.1002/emp2.12695

JACEP OPEN
JOURNAL OF THE AMERICAN COLLEGE OF EMERGENCY PHYSICIANS OPEN
A GLOBAL JOURNAL OF EMERGENCY MEDICINE
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ORIGINAL RESEARCH

Evidence-Based Emergency Medicine

Troponin is unrelated to outcomes in heart failure patients discharged from the emergency department

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Funding information
Patient-Centered Outcomes Research Institute, Grant/Award Number: AD-1409-21656

Abstract

Background: Prior data has demonstrated increased mortality in hospitalized patients with acute heart failure (AHF) and troponin elevation. No data has specifically examined the prognostic significance of troponin elevation in patients with AHF discharged after emergency department (ED) management.

Objective: Evaluate the relationship between troponin elevation and outcomes in patients with AHF who are treated and released from the ED.

Methods: This was a secondary analysis of the Get with the Guidelines to Reduce Disparities in AHF Patients Discharged from the ED (GUIDED-HF) trial, a randomized, controlled trial of ED patients with AHF who were discharged. Patients with elevated conventional troponin not due to acute coronary syndrome (ACS) were included. Our primary outcome was a composite endpoint: time to 30-day cardiovascular death and/or heart failure-related events.

Results: Of the 491 subjects included in the GUIDED-HF trial, 418 had troponin measured during the ED evaluation and 66 (16%) had troponin values above the 99th percentile. Median age was 63 years (interquartile range, 54-70), 62% (n = 261) were male, 63% (n = 265) were Black, and 16% (n = 67) experienced our primary outcome. There were no differences in our primary outcome between those with and without troponin elevation (12/66, 18.1% vs 55/352, 15.6%; $P = 0.60$). This effect was maintained regardless of assignment to usual care or the intervention arm. In multivariable regression analysis, there was no association between our primary outcome and elevated troponin (hazard ratio, 1.00; 95% confidence interval, 0.49–2.01, $P = 0.994$)

Conclusion: If confirmed in a larger cohort, these findings may facilitate safe ED discharge for a group of patients with AHF without ACS when an elevated troponin is the primary reason for admission.

KEYWORDS
acute heart failure, biological markers, emergency medicine, quality, readmission, transitional care, troponin

1 | INTRODUCTION

1.1 | Background

Acute heart failure (AHF) is a common disease presentation to the emergency department (ED), resulting in admission rates greater than 80%.[1,2] As the average age of our population rises, the number of ED visits will likely increase from the approximately 670,000 new cases seen annually in the United States.[3] AHF evaluation and treatment begins in the ED but rarely leads to a discharge home for the patient. Prior studies suggest patients with AHF who are treated and released from the ED may have worse outcomes than those who are admitted.[4,5] Thus, many patients are admitted for further testing, risk stratification, and continued medical care including blood pressure control and decongestive treatment.

1.2 | Importance

The initial ED evaluation for AHF includes measurement of cardiac troponin for diagnostic and prognostic purposes. An elevated troponin in patients with AHF is common and has been widely studied. The prevalence of troponin elevation depends on the assay, the type and severity of the HF, and presenting symptoms.[6] When using a conventional cardiac troponin T assay, 10.4% of a chronic HF population may have a detectable troponin, whereas the same population tested with a high sensitivity assay found 92% had a detectable troponin.[7,8] Given the variety of assays and AHF etiologies, the ED physician must frequently distinguish between an elevated cardiac troponin due to acute coronary syndrome (ACS) and those due to other physiologic processes.[9,10] The cause for an elevated cardiac troponin in AHF is twice as likely to be related to supply demand mismatch and poor diastolic

perfusion rather than plaque rupture.[8] However, an elevated troponin has been associated with an increased risk for mortality in patients with AHF and this clinical finding often biases the emergency physician toward hospital admission even when the remainder of the ED evaluation is reassuring.[11,12] Conversely, other studies suggest troponin may be of less prognostic significance when measured during the initial patient presentation.[13,14] These studies were inherently biased, however, because they evaluated the prognostic significance of troponin in patients who were already admitted to the hospital.

1.3 | Goals

We have previously reported the primary outcome of our randomized trial of a self-care intervention in patients with AHF who were discharged after ED management.[15] In this secondary analysis, we compare the 30- and 90-day outcomes of patients with AHF who were discharged from the ED with an elevated troponin to those who were discharged without an elevated troponin.

The Bottom Line

Prior data suggest that patients with acute heart failure and an elevated troponin have increased mortality and should be admitted. In this secondary analysis of 491 subjects enrolled in the GUIDED-HF trial, there was no difference in 30-day cardiovascular death or heart failure related events between those with and without elevated troponin (>99th percentile). These data suggest that some heart failure patients with an elevated troponin may be safely discharged from the emergency department.

2 | METHODS

2.1 | Study design and setting

We conducted a secondary analysis of patients with AHF who were discharged after ED management and enrolled in the randomized clinical trial Get with the Guidelines to Reduce Disparities in AHF Patients Discharged from the ED (GUIDED-HF). This trial evaluated usual care versus an intensive ED based self-care strategy. The rationale and design and primary results for the GUIDED-HF trial have been previously reported.[15,16]

2.2 | Selection of participants

Patients presenting to the ED with AHF who met the following criteria were approached for enrollment: prior history of AHF, systolic blood pressure (BP) >100 mm Hg, no evidence of ACS (based on clinical evaluation including history, physical exam, ECG, and troponin), and not on outpatient inotrope therapy. Patients remained eligible for enrollment in GUIDED-HF if they had an elevated cardiac troponin that the treating physician felt was not due to ACS. All eligible patients enrolled in GUIDED-HF were discharged either directly from the ED or after ED-based observation.

2.3 | Measurements

Follow-up telephone encounters were conducted for all patients at 30 and 90 days after discharge by research staff blinded to the intervention arm. Outcomes recorded included date of an unscheduled clinic visit for AHF with intravenous diuretics given, ED revisit, or hospital admission and whether it was related to AHF and cardiovascular (CV) or non-CV death. All events were adjudicated by a clinical event committee consisting of two emergency physicians and a cardiologist. The GUIDED-HF trial was approved by the institutional review board of each participating institution.

2.4 | Outcomes

The primary outcome for this secondary analysis was time to the first HF-related adverse events within 30 days of ED discharge based on the phone follow-up and chart review conducted by the study coordinator blinded to treatment arm. This included unscheduled HF clinic visits with intravenous diuretics given, ED return visits or hospital admissions for AHF, and CV-related death. We also evaluated the primary outcome measured over 90 days. Our safety outcome was time to the following events within 90 days of ED discharge: all-cause ED revisit that includes readmission for ACS, hospitalization, and all-cause death.

2.5 | Statistical analysis

All patients who had troponin measured in the ED were included for analysis. To help standardize troponin values because different assays were used, cardiac troponin was dichotomized and was considered elevated if it was above the 99th percentile site-specific upper reference limit (URL). Troponin results were available to the treating physician. All troponin assays used at the time of this study were based on conventional sensitivity assay platforms. The first troponin was used to classify participants. Data summaries are presented as medians with interquartile ranges (IQR), counts, and proportions, as appropriate. Wilcoxon rank-sum and Pearson χ^2 tests were used to compare continuous and categorical data between those with elevated and nonelevated troponin values, respectively. Kaplan–Meier (KM) plots together with log-rank tests were used to compare survival outcomes by troponin status. Cox proportional hazards models were used to assess the association of survival outcomes and troponin status in the overall cohort and within each treatment arm, adjusting for

treatment assignment, traditional measures of HF severity including age, sex, ejection fraction (moderate/severe vs normal), systolic BP, b-type natriuretic peptide level (BNP), estimated glomerular filtration rate (eGFR), and outpatient dose of diuretic. Proportional hazards assumptions were also checked using the residual-based method.[17] Significance was set a priori at $P < 0.05$. Missing data were imputed using predictive mean matching and 10 imputation replications. Adjusting variables with any missingness were imputed, including ejection fraction (moderate/severe vs normal), systolic BP, BNP, and eGFR. The predictive mean matching was based on the linear predictors and thus was used for categorical variables as well (eg, using multinomial model or logistic regression as the imputation model). We used *aregImpute* function in Hmisc R package, which by default uses a draw from a multinomial distribution with probabilities derived from distance weights for "matching," where the distance weights are calculated using the tricube function. Records with longer distance (based on linear predictors of the imputation model) from the target record will have smaller probabilities of being drawn. Therefore, there was not a fixed number of donors used for each target variable. We assumed missing at random for all variables with any missingness. We did not think any of those variables are likely not missing at random. We drew plots of imputed values against sequential imputation numbers separately for each missing observations and variable. We did not observe any systematic patterns that suggest the imputation might be problematic. All statistical analyses were conducted using R statistical software (version 3.5.2).

3 | RESULTS

3.1 | Baseline characteristics

There were 491 patients enrolled at 15 sites. Of these, 12 withdrew consent and 61 did not have a troponin measured, leaving 418 patients who fulfilled all study criteria (Figure 1). Within this cohort, 66 (16%) patients had an elevated troponin and 352 (84%) did not. These two cohorts were similar with respect to age, sex, and race (Table 1). There were significant differences ($P < 0.05$) in prior EF, initial creatinine value, initial systolic BP, ED measures of natriuretic peptides, ACE inhibitor use in the ED, and history of MI (Table 1).

3.2 | Primary outcome at 30 days

The primary outcome occurred in 16% ($n = 67$) of patients (Table 2). One CV-related death was reported in the nonelevated troponin group. Compared to those with nonelevated troponin values, subjects with an elevated troponin did not have an increased proportion of events in our primary outcome (12/66, 18.1% vs 55/352, 15.6%; $P = 0.60$). This difference was similar regardless of assignment to the intervention or usual care arm (Table 2). From the KM plot, the probability of being event-free within 30 days also did not differ by troponin status (Figure 2).

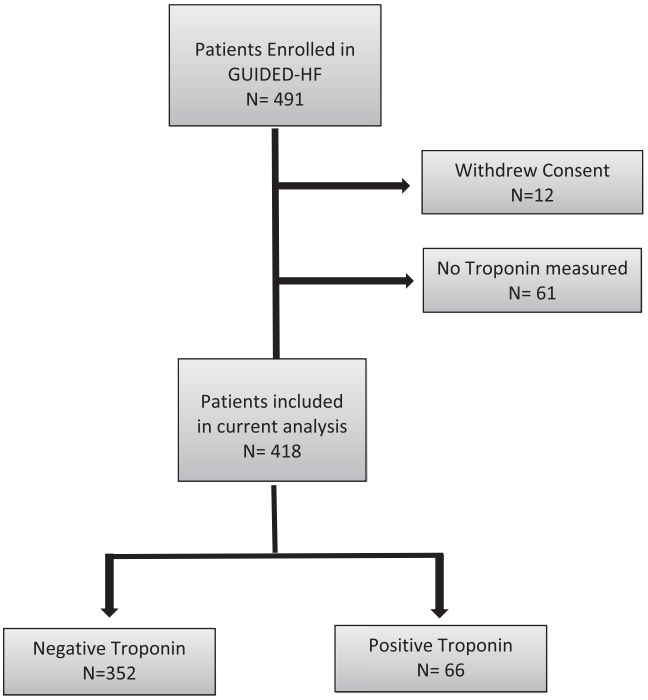

FIGURE 1 Consort diagram

After adjusting for known measures of HF severity, relative to patients with a nonelevated troponin, an elevated troponin was not associated with our primary outcome (adjusted hazard ratio [aHR], 1.00; 95% confidence interval [CI], 0.49–2.01; $P = 0.99$). The aHR in intervention (aHR, 0.50; 95% CI, 0.10–2.64; $P = 0.42$) and usual care arms (aHR, 1.41; 95% CI, 0.59–3.42; $P = 0.44$) both found no significant differences in our primary outcome in those with and without troponin elevation (Table 3).

BNP (per 50 units) was associated with our primary outcome at 30 days in the overall cohort (aHR, 1.02; 95% CI, 1.00–1.04; $P = 0.01$), with little difference between the intervention (aHR, 1.02; 95% CI, 1.00–1.05; $P = 0.07$) and usual care arms (aHR, 1.02; 95% CI, 1.00–1.05; $P = 0.06$). Estimated GFR (per 1 unit) was shown to have no association with the primary outcome in the overall cohort (aHR, 0.99; 95% CI, 0.98–1.00; $P = 0.23$) or the intervention arm (aHR, 1.00; 95% CI, 0.98–1.02; $P = 1.00$) but did have an association in the usual care arm (aHR, 0.98; 95% CI, 0.97–1.00; $P = 0.03$). Outpatient diuretic dose in furosemide equivalents (per 20 mg) was not associated with the primary outcome in the overall cohort (aHR, 0.94; 95% CI, 0.85–1.03; $P = 0.19$) or the intervention arm (aHR, 1.02; 95% CI, 0.90–1.14; $P = 0.79$) but was associated with the primary outcome in the usual care arm (aHR, 0.81; 95% CI, 0.68–0.97; $P = 0.02$) (Table 3).

3.3 | Primary outcome and safety outcomes at 90 days

The primary outcome at 90 days occurred in 35% (n = 147) of patients. Subjects with an elevated troponin had a trend toward an increase in

TABLE 1 Baseline characteristics

	No.	Combined (N = 418)	Non-elevated Tn (N = 352)	Elevated Tn (N = 66)	*P*
Gender at birth	418				0.44
Male		62% (261)	62% (217)	67% (44)	
Female		38% (157)	38% (135)	33% (22)	
Race	418				0.118
American Indian/Alaska Native		0% (1)	0% (1)	0% (0)	
Asian		0% (0)	0% (0)	0% (0)	
Black/African American		63% (265)	61% (215)	76% (50)	
Hawaiian/Pacific Islander		0% (2)	0% (1)	2% (1)	
White non-Hispanic		33% (136)	34% (121)	23% (15)	
White Hispanic		2% (8)	2% (8)	0% (0)	
Multi-racial		0% (0)	0% (0)	0% (0)	
Other		0% (0)	0% (0)	0% (0)	
Declined to disclose		1% (6)	2% (6)	0% (0)	
Age at consent	418	62.94 (54.18, 70.01)	63.09 (53.8, 69.95)	61.82 (55.71, 71.43)	0.929
Prior ejection fraction	394				0.003
Normal (>X%)		40% (159)	44% (144)	24% (15)	
Moderate/severe (≤Y%)		60% (235)	56% (187)	76% (48)	
Prior ejection fraction missing indicator	418	6% (24)	6% (21)	5% (3)	0.649
Initial BUN value (mg/dL)	416	19 (14, 27)	18 (14, 26)	21 (15, 29)	0.099
Initial BUN value missing indicator	418	0% (2)	1% (2)	0% (0)	0.539
Initial creatinine value (mg/dL)	416	1.15 (0.9275, 1.44)	1.13 (0.9, 1.4)	1.275 (1.042, 1.722)	0.004
Initial creatinine value missing indicator	418	0% (2)	1% (2)	0% (0)	0.539
Initial systolic blood pressure (mm Hg)	417	143 (126, 165)	141 (124, 163)	153.5 (136.8, 183.5)	<0.001
Initial systolic blood pressure missing indicator	418	0% (1)	0% (1)	0% (0)	0.665
Initial BNP value (pg/mL)	194	521.5 (179.8, 1180)	461 (155, 995)	1048 (495, 1500)	0.003
Initial BNP value missing indicator	418	54% (224)	53% (187)	56% (37)	0.661
Initial NT-proBNP value (pg/mL)	209	1140 (324, 3500)	898 (297.8, 3081)	2998 (1152, 6870)	<0.001
Initial NT-proBNP value missing indicator	418	50% (209)	51% (178)	47% (31)	0.592
Initial troponin I (ng/mL)	398	0.025 (0.012, 0.04)	0.02 (0.012, 0.03)	0.06 (0.05, 0.09)	<0.001
Initial troponin T (ng/mL)	20	0.01 (0.01, 0.0325)	0.01 (0.01, 0.03)	0.14 (0.085, 0.27)	0.016
Beta blocker in the ED	406	9% (38)	9% (30)	13% (8)	0.322
Beta blocker in the ED missing indicator	418	3% (12)	3% (9)	5% (3)	0.375
ACEi in the ED	418	11% (44)	9% (31)	20% (13)	0.008
Diuretic in the ED	418	89% (371)	89% (314)	86% (57)	0.503
ACEi at discharge	413	43% (179)	43% (150)	45% (29)	0.821
ACEi at discharge missing indicator	418	1% (5)	1% (4)	2% (1)	0.795
ARB at discharge	409	20% (81)	20% (70)	17% (11)	0.567
ARB at discharge missing indicator	418	2% (9)	2% (7)	3% (2)	0.593
Beta blocker at discharge	415	76% (314)	76% (265)	75% (49)	0.955
Beta blocker at discharge missing indicator	418	1% (3)	1% (2)	2% (1)	0.403

(Continues)

TABLE 1 (Continued)

	No.	Combined (N = 418)	Non-elevated Tn (N = 352)	Elevated Tn (N = 66)	*P*
Diuretic at discharge	418	89% (373)	90% (316)	86% (57)	0.412
Diuretic dose at discharge (Lasix-equivalents)	418	40 (20, 80)	40 (20, 80)	40 (20, 80)	0.23
Hx Diabetes	418	46% (192)	46% (162)	45% (30)	0.932
Hx COPD	418				0.099
Yes		34% (144)	36% (128)	24% (16)	
No		65% (270)	62% (220)	76% (50)	
Unknown		1% (4)	1% (4)	0% (0)	
Hx MI	418				0.015
Yes		31% (128)	28% (98)	45% (30)	
No		68% (285)	71% (250)	53% (35)	
Unknown		1% (5)	1% (4)	2% (1)	
Hx CKD	417				0.37
Yes		27% (112)	26% (90)	33% (22)	
No		73% (303)	74% (259)	67% (44)	
Unknown		0% (2)	1% (2)	0% (0)	
Hx CKD missing indicator	418	0% (1)	0% (1)	0% (0)	0.665
Hx Hypertension	418	93% (390)	93% (327)	95% (63)	0.446
Prior ejection fraction	391				0.006
Not reported		2% (9)	2% (7)	3% (2)	
Normal		39% (152)	42% (138)	22% (14)	
Moderate		30% (116)	27% (90)	41% (26)	
Severe		29% (113)	28% (93)	32% (20)	
Unknown		0% (1)	0% (0)	2% (1)	
Hx EF missing indicator	418	6% (27)	7% (24)	5% (3)	0.491

Abbreviations: ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BNP, B-type natriuretic peptide; BUN, blood urea nitrogen; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; NT-proBNP, N-terminal prohormone b-type natriuretic peptide; Tn, troponin.

TABLE 2 Event rates of the primary outcome[a] at 30 days and their components for overall and stratified by Tn and intervention arms

	Overall				Intervention Arm				Usual Care Arm			
	No (N = 352)	Yes (N = 66)	Combined (N = 418)	*P*	No (N = 176)	Yes (N = 28)	Combined (N = 204)	*P*	No (N = 176)	Yes (N = 38)	Combined (N = 214)	*P*
Primary outcome (30 days)	16% (55)	18% (12)	16% (67)	0.603	14% (25)	14% (4)	14% (29)	0.991	17% (30)	21% (8)	18% (38)	0.558
HF clinic visit	0% (1)	2% (1)	0% (2)	0.184	1% (1)	0% (0)	0% (1)	0.689	0% (0)	3% (1)	0% (1)	0.031
ED revisit for HF	15% (49)	17% (11)	15% (60)	0.649	13% (22)	14% (4)	13% (26)	0.827	17% (27)	19% (7)	17% (34)	0.755
Hospital admission for HF	13% (44)	12% (8)	13% (52)	0.856	12% (21)	11% (3)	12% (24)	0.821	14% (23)	14% (5)	14% (28)	0.925
CVD	0% (1)	0% (0)	0% (1)	0.665	0% (0)	0% (0)	0% (0)		1% (1)	0% (0)	0% (1)	0.641

Abbreviations: CVD, cardiovascular death; ED, emergency department; HF, heart failure; IV, intravenous; No, nonelevated Tn; Tn, troponin; Yes, elevated Tn.
[a]Unscheduled clinic visit with IV diuretic, HF-related ED visit or hospitalization, or CVD.

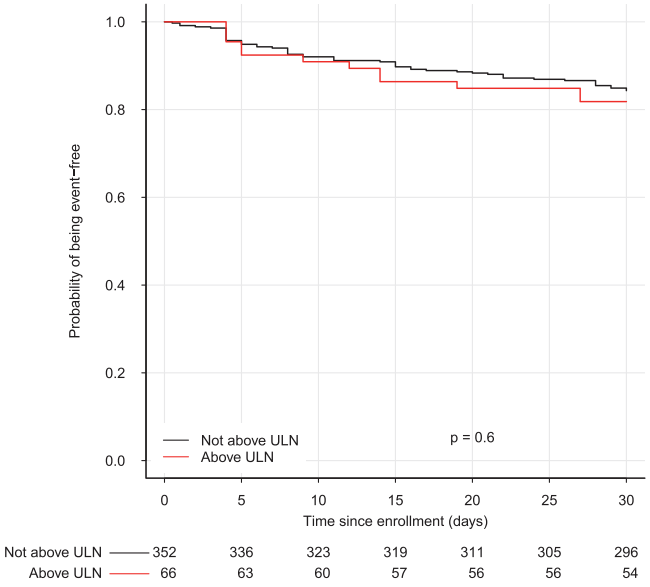

FIGURE 2 Kaplan–Meier curve: primary outcome at 30 days. The upper limit of normal (ULN) was defined as the local laboratory's 99th percentile value for cardiac troponin

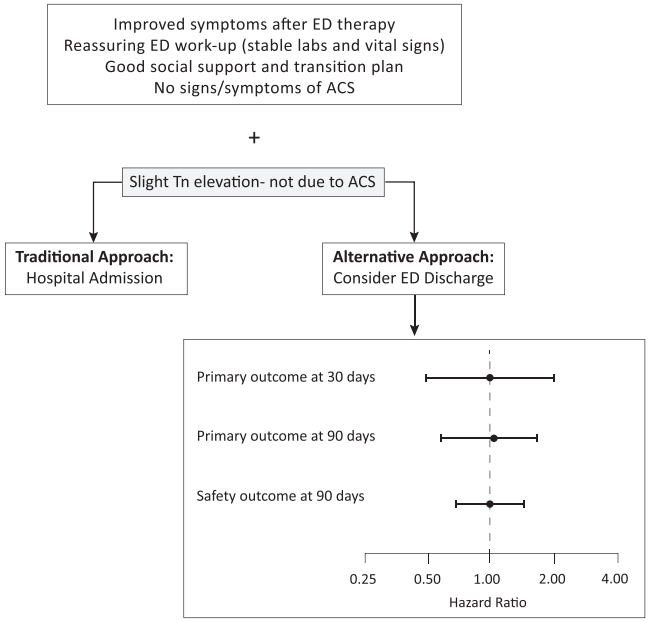

FIGURE 3 GUIDED-HF study with 30 and 90-day primary outcomes and 30-day safety outcome

events (30/66, 45.5%) compared to those with nonelevated troponin values (117/352, 33.2%; $P = 0.06$) due to differences in ED revisits and hospital admission for AHF. After adjusting for potential confounding variables there were no differences in the overall cohort or by treatment arm. An elevated troponin was not associated with 90-day HF-related adverse events in the overall cohort (aHR, 1.03; 95% CI, 0.63–1.69; $P = 0.90$), the intervention arm (aHR, 1.00; 95% CI, 0.46–2.15; $P = 1.00$), or usual care arm (aHR, 1.22; 95% CI, 0.66–2.26; $P = 0.52$) (Figure 3 and Supporting Information Table S1).

The 90-day safety outcome occurred in 58.4% (n = 244) of patients. Compared to those with nonelevated troponin values, subjects with an elevated troponin did not have an increased proportion of events (205/352, 58.2% vs 39/66, 59.1%; $P = 0.90$). After adjusting for known measures of HF severity, the results for the 90-day safety outcome did not differ significantly between those with and without an elevated troponin. An elevated troponin was not associated with the safety outcome in the overall cohort (aHR, 0.99; 95% CI, 0.69–1.42; $P = 0.97$), the intervention arm (aHR, 0.91; 95% CI, 0.50–1.64; $P = 0.74$), or usual care arm (aHR, 1.14; 95% CI, 0.70–1.86; $P = 0.59$) (Supporting Information Table S2).

4 | LIMITATIONS

Although we report the first prospective evaluation of patients discharged from the ED with an elevated troponin, there are limitations

TABLE 3 Cox regression results for the primary outcome[a] at 30 days for overall and stratified by Tn and intervention arms

	Overall			Intervention			Usual care		
Covariate	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
Elevated troponin (ref = normal troponin)	1.00	0.49, 2.01	0.99	0.50	0.10, 2.64	0.42	1.41	0.59, 3.42	0.44
Intervention (ref = usual care)	0.72	0.43, 1.20	0.20						
Age (per 5 y)	1.05	0.95, 1.17	0.33	1.17	0.99, 1.38	0.06	0.95	0.82, 1.11	0.54
Female (ref = male)	0.92	0.54, 1.57	0.77	0.78	0.34, 1.77	0.55	0.85	0.43, 1.71	0.66
Moderate/severe prior EF (ref = normal)	0.70	0.39, 1.26	0.24	0.66	0.27, 1.64	0.37	0.58	0.25, 1.33	0.20
eGFR (per 1 unit)	0.99	0.98, 1.00	0.23	1.00	0.98, 1.02	1.00	0.98	0.97, 1.00	0.03
ED dystolic BP (per 5 units)	0.97	0.92, 1.02	0.18	1.00	0.92, 1.07	0.93	0.93	0.87, 1.01	0.07
BNP (per 50 units)	1.02	1.00, 1.04	0.01	1.02	1.00, 1.05	0.07	1.02	1.00, 1.05	0.06
Outpatient diuretic lasix-equivalents dose (per 20 mg)	0.94	0.85, 1.03	0.19	1.02	0.90, 1.14	0.79	0.81	0.68, 0.97	0.02

Abbreviations: BP, blood pressure; BNP, B-type natriuretic peptide; CI, confidence interval; ED, emergency department; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HR, hazard ratio; Tn, troponin.

[a]Unscheduled clinic visit with IV diuretic, HF-related ED visit or hospitalization, or CVD.

to consider. This is a specific population of patients with AHF deemed safe for discharge and were considered unlikely to have ACS by the treating physician. Therefore, our cohort cannot be generalized to all patients presenting with AHF in the ED. Although all troponin values were conventional sensitivity, the troponin assay used varied at each site, reflecting the pragmatic and multicenter nature of GUIDED-HF. Although the analysis treated troponin as a dichotomous variable above the site-specific 99th percentile, assessment of outcomes related to different assays, or treating troponin as a continuous variable, may also be of interest. The authors acknowledge higher troponin elevations are more likely to be associated with ACS and those patients were less likely to be included in the GUIDED-HF trial because of the previously described inclusion and exclusion criteria. We also acknowledge clinicians may have used several means to determine whether an isolated troponin elevation was due to ACS, including comparing troponin elevations to values from prior visits and measuring changes in troponin during the index ED visit. The degree to which this led to confirmation bias is unknown because the determination of ACS was left to the treating physician and not adjudicated.

High-sensitivity (hs) troponin was cleared for use in the United States toward the end of subject recruitment in GUIDED-HF and there has been much interest regarding the prognostic value of detectable levels that do not exceed the 99th percentile. A recent study of hs-troponin in AHF shows similar findings to those in our study, but further study of hs-troponin in AHF subjects is necessary.[2] The lack of serial troponin quantification is an additional limitation, particularly in determining whether troponin concentrations increase over time and may be suggestive of acute coronary syndrome rather than AHF. Subjects were not enrolled in GUIDED-HF if the clinical picture suggested ACS was a cause of presenting symptoms, and this clinical picture often includes serial troponin (Tn) evaluation in the ED. Finally, our sample size was relatively small and replication of our results in a larger cohort of ED patients with elevated troponin values would be informative.

5 | DISCUSSION

This secondary analysis is the first prospective study to evaluate the prognostic significance of an elevated troponin in patients with AHF discharged after ED-based management. We report several important findings. First, 66 patients with troponins above the 99th percentile were discharged from the ED. Importantly, they did not have increases in CV-related or non–CV-related events compared to those with nonelevated troponin values over 30 days. Second, the overall event rate in those discharged from the ED is lower than first reported,[4] is similar to recent reports in a large healthcare system in the United States,[18] and was similar in the intervention and usual care arms. Third, traditional risk factors for adverse events in HF inpatients and stable outpatients, such as renal function and natriuretic peptides, were also associated with HF adverse events in our cohort of patients discharged from the ED.

In the ASCEND-HF trial, a conventional troponin was undetectable in only 22% of subjects and elevated above the 99th percentile in 50% of subjects. These patients were not discharged from the ED like our cohort, but troponin elevations in the ED were associated with longer in-hospital length of stay, more episodes of worsening HF in the hospital, and higher in-hospital mortality. These associations were not sustained when the patients were followed for 30 and 180 days after hospital admission.[19] A recent secondary analysis of the same ASCEND-HF database found 2% of patients who were admitted for AHF had sudden cardiac death (SCD) after hospital discharge. In a multivariable model, elevated in-hospital troponin was not associated with SCD, Ventricular Tachycardia (VT)/Ventricular Fibrillation (VF), or resuscitated SCD after discharge through day 30.[20]

Prior studies suggest over 80% of patients who present to the ED with AHF are admitted. Many of the AHF risk stratification tools incorporate troponin as a predictor and all recommend those patients with an elevated troponin should be admitted to the hospital.[21–25] Thus, the cohort we studied with an elevated troponin most often is admitted to the hospital. Most of these tools incorporate a major adverse cardiac event outcome but the duration of follow-up often varies. However, the context of the troponin elevation and whether it can be modified with treatment, other than for ACS, is unclear. When evaluating the prognostic significance of an elevated Tn in our cohort, where ACS was excluded, there were no appreciable difference in the 30-day primary outcome. Although we identified a trend toward significance in our unadjusted of the primary outcome at 90 days ($P = 0.06$), this difference was no longer present in our adjusted model (see Supporting Information Tables S1 and S2). ED revisit and HF clinic visits appear to contribute most to this trend rather than 90-day CV mortality or HF hospitalizations. The cause of troponin elevation is important to consider as we aim to identify patients with modifiable risk where a hospital admission or close outpatient follow-up after ED discharge could impact near-term events. Those with a troponin elevation related to ACS may need further evaluation and treatment requiring hospitalization. Patients with slight troponin elevations not due to ACS may be a different population than those included in large inpatient cohorts like ASCEND-HF where troponin elevation was associated with ACS and unfavorable outcomes, particularly in the hospital.[19] Importantly, troponin is just one component of the overall risk-stratification process and its interpretation is often dichotomous (elevated or not elevated) in the ED setting. When used as a continuous variable, the magnitude of elevation often drives decision-making. The median cTnI value in those with elevated troponin was 0.06 ng/mL with an IQR of 0.05-0.09 ng/mL, a range most clinicians would describe as a "low level" elevation. The magnitude of the elevation may have influenced the clinician's decision to not suspect ACS. Disposition decision-making may need to be revisited and account for all modifiable risk factors including amount of congestion, patient engagement, and a safe transition plan to the outpatient setting.

Although our investigation suggests troponin may not be associated with an increased risk of adverse events in ED patients who are otherwise suitable for discharge after ED-based management, other traditional markers of increased risk were associated with increased CV mortality and adverse events in our population including eGFR and BNP. Across the spectrum of HF subtypes, CKD and worsening renal

function has been associated with all-cause mortality and CV-related adverse events during hospitalization, shortly after discharge (30-day and 90-day) and long-term follow-up (1 and 5 years).[26] BNP similarly demonstrates the ability to predict short- and long-term mortality and CV-related adverse events.[27]

Patients discharged after ED-based management had a low overall 30-day event rate in this secondary analysis of GUIDED-HF. An elevated conventional troponin was not associated with 30-day adverse outcomes. If confirmed in a larger cohort, these findings may facilitate safe ED discharge for a select group of patients with AHF when an elevated troponin is the primary reason for admission.

ACKNOWLEDGMENT

This work was supported through a Patient-Centered Outcomes Research Institute (PCORI) Award (AD-1409-21656).

AUTHOR CONTRIBUTIONS

Authors: Gregory J. Fermann, Jon W. Shrock and Sean P. Collins contributed to the study concept and design. Cathy A. Jenkins, Dandan Liu and Karen F. Miller led data acquisition and analysis. All authors analyzed data and drafted sections of initial version of the manuscript. All authors contributed to the critical revision of the overall manuscript. Gregory J. Fermann takes final responsibility for the manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Fermann GJ, Schrock JW, Levy PD, et al. Troponin is unrelated to outcomes in heart failure patients discharged from the emergency department. *JACEP Open*. 2022;3:e12695. https://doi.org/10.1002/emp2.12695