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High Sensitivity Troponin T Rules Out Acute Cardiac Insufficiency Trial (TACIT): An Observational Study to Identify Acute Heart Failure Patients at Low Risk for Re-hospitalization or Mortality

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Abstract

Background—Identifying low-risk acute heart failure (AHF) patients safe for discharge from the emergency department (ED) is a major unmet need.

Methods—A prospective, observational, multi-center pilot study targeting lower risk AHF patients to determine whether high sensitivity troponin T (hsTnT) identifies ED AHF patients at low risk for re-hospitalization and mortality. hsTnT was drawn at baseline and 3 hours. Phone follow up occurred at 30 and 90 days. The primary endpoint: composite of all-cause mortality, re-hospitalization, and ED visits at 90 days (changed from 30 days due to lack of mortality events), analyzed using logistic regression. Secondary endpoints: 30 and 90-day all-cause mortality. hsTnT values less than the 99th%ile were defined as 'low' hsTnT.

Results—Out of 527 enrolled patients, 499 comprised the initial analysis set. Of these, 332 had both 0 and 3-hour hsTnT drawn, of whom 319 completed 30 day follow up. The average age was 62, 60% male, and 57% Black. Median hsTnT was 26.4ng/L (IQR 15.1–44.3). There were 99 (21%) 30-day composite events, 13 (2.7%) deaths at 30 days and 25 deaths (8.2%) at 90 days. Serial hsTnT values below the 99^{tho}%ile were not associated with a lower risk for the 90-day primary composite endpoint (OR 0.79 (95% CI 0.42–1.50) p=0.4736). However, no deaths occurred in the low hsTnT group at 30 days with 1 death at 90 days.

Conclusions—hsTnT did not identify patients at low risk for the primary outcome of re-hospitalization, ED visits, and mortality at 90 days.

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Clinical Trial Registration—ClinicalTrials.gov; Unique Identifier: .

Nearly one million hospitalizations for acute heart failure (AHF) occur every year, at great personal and financial cost.[1, 2] The emergency department (ED) is the primary gatekeeper;[3] over 80% of AHF patients who present to the ED are hospitalized.[4, 5] While some patients clearly warrant hospitalization, up to 50% of AHF patients may be potential candidates for ED discharge or observation unit management.[6]

There are many contributors to these high admission rates. Nearly 30% of ED AHF patients die or return to the hospital within 30 days.[7, 8] They tend to be elderly, with multiple co-morbid conditions.[9, 10] The emergency physicians who care for these patients have low tolerance for risk. In fact, most consider discharge appropriate only for AHF patients with < 0.5% risk of mortality at 30 days, which may be unrealistic in this complex population with multiple comorbidities. [11] The absence of well-validated risk scores to identify low-risk ED patients compounds the problem. Lack of high-risk features identifies patients at relatively lower risk, but does not equate to the near zero mortality risk desired by providers.[12] Furthermore, current risk-scores in development include patients already known to be high risk.[13, 14] Including high risk patients improves model performance as a result of more events, but patients with high-risk features (such as low blood pressure or elevated troponin) would not be discharged. Whom to discharge among lower risk patients is the unmet clinical need. Clinical judgment discriminates poorly; discharged ED patients are at equal or greater risk for death than hospitalized patients.[15, 16] This difficulty in identifying low risk, combined with the inherent high morbidity and mortality of AHF, contributes to the current 80% admission rate.[17]

The absence of organ injury in AHF—particularly myocardial injury defined by serum troponin elevation—identifies lower risk patients.[18–20] As the sensitivity of troponin assays increases, lower or non-detectable troponin values may identify a cohort of patients at low enough risk to consider direct ED discharge.[18] A retrospective analysis of over 1000 AHF patients identified zero deaths in patients through 180 days with high sensitivity troponin T (hsTnT) values less than the 99th percentile.[18] However, this was a post-hoc analysis of a highly select clinical trial population. A real-world sample of lower-risk ED patients is necessary to determine the possible utility of this marker.

Thus, we conducted a prospective, observational study of lower risk ED AHF patients to determine the discriminatory value of hsTnT to identify patients at low risk for re-hospitalization or mortality.

Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request.

The TACIT (High Sensitivity cTnT Rules Out Acute Cardiac Insufficiency Trial) study has been previously described.[21] Briefly, TACIT was a prospective, observational, multi-center, cohort study to determine whether hsTnT identifies a cohort at low risk for morbidity and mortality among ED patients with signs and symptoms of AHF. Patients were enrolled as a

convenience sample, based on study personnel availability, from December 2015 to May 2018. Five hospitals within the United States participated, in 4 different cities. All patients were pre-screened in the ED, via IRB approved screening protocols of electronic health records.

High risk patients were specifically excluded, as the goal was identification of patients potentially safe for discharge rather than further stratification of high-risk patients who are already identified by existing markers. This is compounded by the ED practice pattern of nearly universal hospital admission for AHF patients. Thus, we focused on a lower-risk cohort, relative to other risk-stratification instruments or scores. To be eligible, the following was required: 1) 21 years of age or older, 2) diagnosed with AHF by the treating ED physician, 3) received AHF therapy (defined by IV loop diuretic or vasodilator therapy by any route or non-invasive ventilation) in the ED, 4) SBP > 100mmHg, and 5) enrolled within 3 hours of first AHF therapy. Notable exclusion criteria were: 1) life expectancy < 6 months, 2) shock of any kind 3) temperature > 101.5°F, 4) presumed acute coronary syndrome (determined clinically by the emergency physician), 5) atrial fibrillation with heart rate > 130bpm, 6) transplant of any kind or ventricular assist device, or 7) end stage renal disease requiring dialysis. All sites had approval from their local ethics committee or institutional review board. The study was registered on ClinicalTrials.gov (NCT02592135).

Study Procedures

After written informed consent, patients underwent a baseline blood draw followed by a repeat draw at 3 hours (+/− 1 hour) for both hsTnT and NTproBNP. These were locally processed, stored, and then batched shipped per protocol to the central core lab at the lead site. Results were not available to the clinical team. Medical history, physical exam, EKG, CXR, and other lab tests were all performed at the discretion of the treating physicians. Management was per usual standard practice, no tests or therapies were mandated and no study site used the hsTnT in usual practice. For follow up, patients received a phone call as well as medical record review at 30 and 90 days post-discharge. (See Figure 1 for study outline) All data were entered into REDCap, a secure, web-based, electronic data capture application.

Troponin Thresholds

We used the Roche Elecsys Troponin T hs Assay, with a 99th percentile upper reference limit of 14ng/L for myocardial infarction and a coefficient of variation of ≤ 10% at 13ng/L. This reference threshold is per the package insert for clinical use in Europe. As the study began prior to FDA approval of this hsTnT assay in the United States (US), we utilized the labeled 99th percentile of 14 ng/L as the threshold of normal; values < 14ng/L were considered ‘low.’ However, shortly after the study started, the FDA approved the Roche assay for use in the US with a 99th percentile of 19ng/L as well as sex specific thresholds. Accordingly, we also explored outcomes using: 1) the US 99th percentile definition of 19ng/L; and 2) sex-specific 99th percentile thresholds defined in the US, namely 14ng/L for women and 21 ng/L for men. All samples were analyzed on the Cobas e411.

Endpoints

The primary objective was to test the hypothesis that single or serial (baseline and 3 hours) hsTnT levels below the 99%ile, will identify AHF patients at low risk for adverse outcomes. Our primary endpoint was a composite of 90-day all-cause mortality and all-cause re-hospitalization, including ED re-visits. This was changed from the initial 30-day primary endpoint after initial data review demonstrated a lower than expected event rate for mortality, as outlined below. Secondary endpoints included 30-day and 90-day all-cause mortality. Other pre-specified analyses included: 1) testing various thresholds of hsTnT and their association with the pre-specified exploratory endpoints, both at baseline and serially and (2) determining the association between change in hsTnT levels and pre-specified endpoints.

Sample Size Considerations

Based on previously published literature, we estimated approximately 25% of patients would meet the primary endpoint of death or rehospitalization by 30 days.[22, 23] This would require approximately 400 patients in order to achieve 100 events. With 100 events, we would be able to control the error in the sensitivity estimate within ±10% and the error in the specificity estimate within ±6%. Given our enrollment criteria targeting lower risk patients, we estimated a sample size of 500 patients to account for a slightly lower event rate and still achieve 100 events.

Statistical Analysis

Descriptive statistics included means and standard deviations, medians with interquartile range, or counts and percentages as appropriate. Categorical data were compared between hsTnT levels using Fisher's exact test. Group comparisons of continuous variables by hsTnT levels were performed using t-tests, analysis of variance models (ANOVA), Wilcoxon rank sum tests or Kruskal-Wallis tests, as appropriate. No correction was made to account for multiple testing.

The potential of serial hsTnT values below the 99% for prognosis (as well as baseline hsTnT alone) to identify low-risk patients was evaluated using logistic regression for the composite endpoints of 30-day and 90-day mortality and re-hospitalization. We used exact logistic regression for 30-day mortality, given the small number of events, and logistic regression for 90-day mortality. The co-variates of age and NTproBNP were chosen based on their known prognostic significance. Due to skewness in the data, NTproBNP was $\log_{10}$ transformed for modeling. We also performed site-stratified logistic regression and Cox proportional hazards regression models on the 90-day composite and mortality endpoints, both unadjusted and adjusted for the same covariates. (see supplemental tables) For the Cox models, those subjects without the endpoints were censored at the minimum of 90 days or length of follow-up.

After enrollment of approximately 20% of patients a review of demographics and outcomes, blinded to hsTnT values, was undertaken. At that time, the follow up period was extended to 90 days due to a lower than expected number of events. The primary endpoint was also changed from 30 to 90 days. We did not mandate sites to follow up all patients, as some sites

were required to re-obtain written informed consent for the longer study period. The 30 and 90-day endpoint period was counted from time of enrollment.

All analysis were performed using SAS version 9.4.

Results

Out of 527 enrolled patients, 499 completed follow up, with 493 having at least one hsTnT drawn; the 499 patients comprise the initial analysis set. Of these, 332 completed the full protocol with both 0 and 3-hour hsTnT drawn, of whom 319 completed 30 day follow up. Exclusions from the analysis were primarily due to hemolyzed samples that could not be analyzed. (Figure 2) Overall, the cohort was relatively young (age 62 SD 14), predominantly Black (57.3%), and male (60.3%). (Table 1) One-third of patients had a HF visit to the ED or hospital in the previous 6 months. Less than 5% were discharged from the ED, with 6.6% going to observation status.

Patients with lower hsTnT values were younger and more likely to be female. There were no differences in heart rate, blood pressure, ejection fraction, history of MI, hypertension, or chronic HF between patients with high or low hsTnT. More patients with high hsTnT values had chronic kidney disease. Serum creatinine and NTproBNP levels were higher in the high hsTnT group.

In patients with non-hemolyzed samples, hsTnT value < 14 ng/L was observed in 22.5% at baseline, and 21.1% at 3-hours. Using the US cut-points of 19ng/L and sex-based thresholds increased the proportion of patients with low-troponin values to 35.2% and 33.3%, respectively.

A description of events is shown in Table 2. The primary endpoint of death/ED revisits/re-hospitalization occurred in 21% of patients within 30 days and 49% within 90 days. For the primary endpoint, the unadjusted analysis for the 90-day composite outcome demonstrated no difference with both serial hsTnT values below 14 ng/L compared to patients with at least one hsTnT value above this threshold (OR 0.79 (95% CI 0.42–1.50), p=0.4736). There was also no difference for the same endpoint at 30 days (OR 1.24 (95% CI 0.63–2.43), p=0.5316). Additionally, there were no differences in the composite endpoint when using hsTnT threshold of < 19, or when using single vs. serial measurements. Supplemental table 1 shows the results from stratified Cox proportional hazards regression models on time to 90 day composite outcome which also showed no differences for any of the hsTnT thresholds.

Secondary Mortality Endpoints

All-cause mortality was 3% at 30 days and 8% at 90 days. Table 3 and Table 4 explore the relationship between various hsTnT cutpoints and 30 and 90 day all-cause mortality. No patient with a low hsTnT – regardless of baseline or 3-hour draw or cut-point – died within 30 days. Only one patient with a hsTnT < 14ng/L at baseline died within 90 days. Among patients with serial troponins, no patient with hsTnT < 14 ng/L at 0 and 3 hours died by 90 days. After adjustment for age and $\log_{10}$ (NTproBNP) for 90-day mortality, hsTnT was no longer significant. However, $\log_{10}$ (NTproBNP) remained significant. (Supplemental Table

2) Results from site-stratified logistic regression models on 90-day mortality provided similar findings (Supplemental Tables 3 and 4). Additionally, results from site-stratified Cox proportional hazards regression models on time to 90-day mortality provided similar findings (Supplemental Table 5).

Discussion

In this prospective, ED-based, observational, cohort study, over 95% of patients were hospitalized, despite excluding high risk patients at baseline. This demonstrates the low threshold for admission by emergency physicians and the need to better identify patients suitable for outpatient therapy. Depending on the cut-point (99%ile US. vs. Europe), 23–33% had baseline hsTnT values less than the 99%ile: 21% experienced the composite outcome of 30-day death/ED re-visit/re-hospitalization, including a 3% mortality, an event rate greater than or equal to clinical trials.[24, 25] Low hsTnT values did not identify lower risk for the composite outcome.

Unlike prior HF clinical trials, where myocardial injury with higher sensitivity assays above the MI threshold exceeds 90%,[18, 26] the proportion of patients with myocardial injury was much lower in our cohort; 66% to 77% depending on the threshold. Despite a smaller proportion of myocardial injury patients, 30-day outcomes were similar. This supports the assertion that lower risk patients can be identified, but risk may not be low enough for safe ED discharge. In addition, our results represent an undifferentiated ED-based cohort, rather than a highly selective clinical trial patient population. Importantly, we deliberately enrolled a lower risk cohort. High-risk features are already known; patients with them won't be sent home. The gap in knowledge is the identification of patients at low enough risk to be considered for ED discharge.

Previous retrospective work examining the potential of hsTnT to identify a lower risk cohort of AHF patients observed zero deaths at 180 days in a cohort of clinical trial patients with a hsTnT value below the 99th percentile for MI (14ng/L cut-point).[18] Other studies of troponin have focused on their prognostic value, not their potential to identify low-risk patients who could be considered for safe ED discharge.[19, 27] The preponderance of evidence supports troponin as an adverse prognostic marker; however, not all studies have found troponin to be a risk factor for mortality.[26, 28] In the era of newer, more highly sensitive assays, how to best interpret an elevated troponin is also not well known. While we utilized the value the 4th Universal Definition of Myocardial Infarction[29] as the diagnostic threshold for myocardial injury in the setting of suspected ACS, these are unlikely to be the ideal cut-points for risk in AHF. While these newer assays have been used outside of the US for multiple years, it is unknown whether absence of myocardial injury at a specific threshold sufficiently identifies an AHF patient who is low enough risk to safely discharge. This is in marked contrast to ACS, where numerous studies have focused on accelerated diagnostic protocols to identify the population safe for discharge or observation.[30–32]

HsTnT did not differentiate the composite of re-hospitalization and mortality in TACIT. Previous work demonstrates an association of hsTnT with mortality but in our cohort, it appeared unrelated to re-hospitalization. While re-hospitalization is an important endpoint as

it relates to healthcare costs, what impacts mortality likely differs from re-hospitalization.[33] Self-care issues, access to care, numeracy, literacy, economic status and comorbidities can strongly influence readmission.[34] Further, it is unlikely that myocardial injury can sufficiently risk-stratify patients who might return to the hospital for non-cardiovascular causes.[33] An acceptable compromise may be minimizing the risk for death while keeping re-hospitalization rates similar to admitted patients in comparison to those directly discharged from the ED. Importantly, this may be a critical step towards future work. Given that over 80% of patients are currently hospitalized, robust evidence of safety will be required to change this practice. Our secondary analyses suggests a very low risk for mortality with low hsTnT, but underpowered to draw any significant conclusions. Nevertheless, if a cohort of patients at low risk for death can be identified, future work may build upon this cohort; either to further stratify risk or build strategies of care to mitigate re-hospitalization risk.

Limitations

As an observational study, the finding that a lower number of events occurred in patients with low hsTnT values is not a causal relationship. Furthermore, no correction was made to account for multiple testing. Given the number of statistical analyses and the small number of events, it is possible significant results were due to chance. However, the absolute number of events in the low hsTnT groups was either zero or very small. A larger cohort would be required to confirm our results. As most patients were hospitalized, whether hospitalization itself altered the outcome, especially readmission, is unknown. However, no AHF therapy is known to decrease myocardial injury or mortality. Furthermore, no specific strategies of care or management plans were mandated, with every institution having transitional care programs to reduce 30-day readmissions. Additionally, a number of enrolled patients could not be analyzed because of hemolyzed samples or lost to follow up. As the primary endpoint was changed, we were unable to obtain follow up for all previously enrolled patients due to the requirement for a re-consent for this additional information. In regards to hemolysis, in clinical practice, these samples would have been redrawn and the assay repeated. This was not feasible given our study design.

Conclusions

In this lower risk, observational cohort of ED AHF patients, over 95% of patients were hospitalized. While the composite event rate of re-hospitalization and mortality is consistent with other studies, mortality rates overall were low. hsTnT did not predict the primary composite endpoint; troponin alone may not be a good marker to identify low risk for re-hospitalization and mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is new?

- Identification of lower risk patients with AHF safe for ED discharge remains a challenge. Past work demonstrates myocardial injury, as defined by troponin elevation, is associated with worse outcomes.
- In our prospective, observational cohort study, we found lower high sensitivity troponin values were not associated with sufficiently low enough risk for re-hospitalization/mortality for ED discharge.

What are the clinical implications?

- Use of high sensitivity troponin alone at the 99th percentile threshold should not be used for risk-stratification to decide who is at low risk for re-hospitalization or mortality.

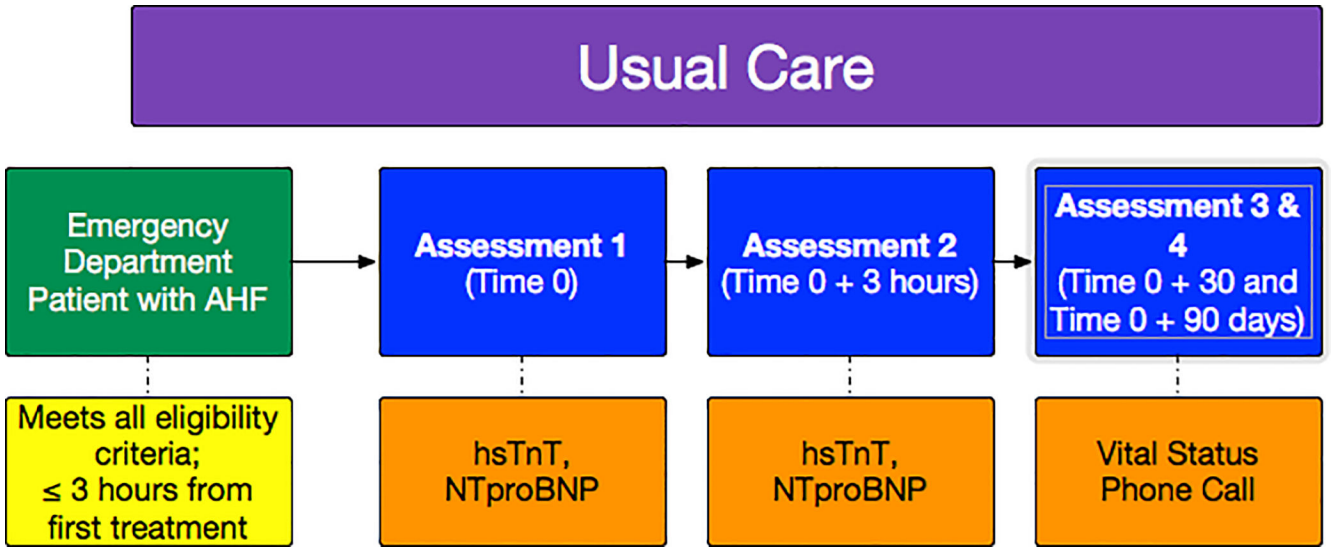

Figure 1:
Trial Flow Diagram

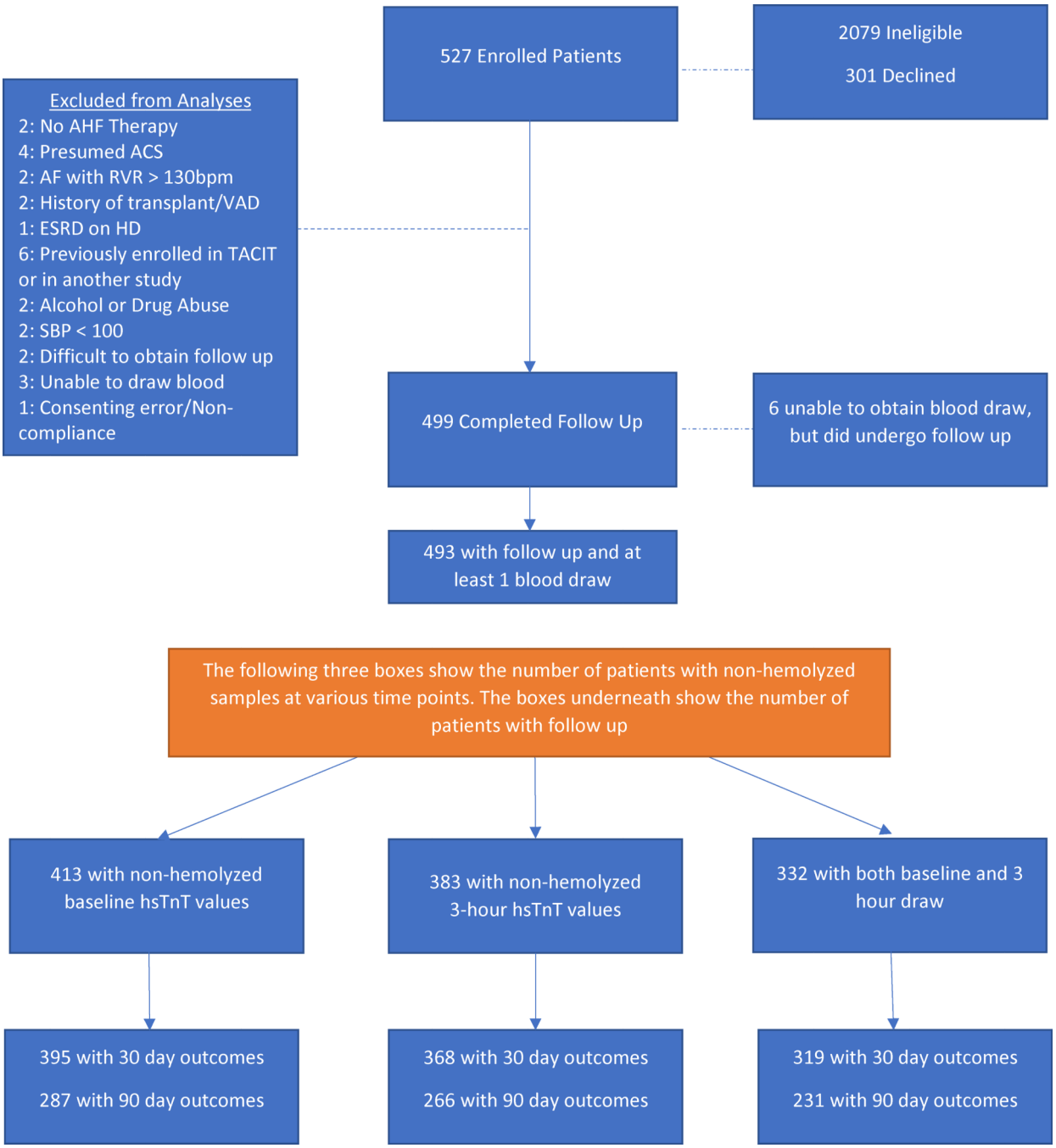

Figure 2:
Description of Final Patient Cohort

Table 1:

Baseline Characteristics by Troponin Level

*n (%) or mean +/− SD or median (IQR)	Overall N=499	Baseline Troponin > 14ng/L (n=320)	Baseline Troponin < 14ng/L (n=93)	p-value	Troponin Serial Values Both High > 14 ng/L N=253	Troponin Serial Values Either High N=17	Troponin Serial Values Both Low < 14 ng/L N=62	p-value
Age at Initial Presentation (n =492)	62.0 ± 14.0	62.6 ± 13.9 (n=316)	58.0 ± 13.7 (n=92)	0.005	62.7 ± 14.5 (n=250)	61.6 ± 11.1	57.7 ± 14.3 (n=61)	0.05
Male gender	301 (60.3%)	221 (69.1%)	24 (25.8%)	<.001	180 (71.1%)	7 (41.2%)	20 (32.3%)	<.001
Hispanic (n=496)	6 (1.2%)	4 (1.3%) (n=318)	1 (1.1%)	1.00	4 (1.6%) (n=251)	0 (0.0%)	1 (1.6%)	1.00
Black	284 (57.3%)	175 (54.9%)	62 (66.7%)	0.044	131 (52.0%)	11 (64.7%)	40 (64.5%)	0.45
Study Site				<.001				<.001
Cincinnati	84 (16.8%)	39 (12.2%)	25 (26.9%)		30 (11.9%)	4 (23.5%)	14 (22.6%)	
Detroit	150 (30.1%)	88 (27.5%)	38 (40.9%)		56 (22.1%)	10 (58.8%)	25 (40.3%)	
Eskenazi	25 (5.0%)	22 (6.9%)	1 (1.1%)		21 (8.3%)	0 (0.0%)	1 (1.6%)	
Methodist	91 (18.2%)	62 (19.4%)	13 (14.0%)		54 (21.3%)	0 (0.0%)	11 (17.7%)	
Nashville	46 (9.2%)	42 (13.1%)	0 (0.0%)		36 (14.2%)	0 (0.0%)	0 (0.0%)	
Vanderbilt	103 (20.6%)	67 (20.9%)	16 (17.2%)		56 (22.1%)	3 (17.6%)	11 (17.7%)	
Any ED Visit or hospitalization in the past 6 months (n=497)	275 (55.3%)	175 (54.7%)	48 (51.6%)	0.64	139 (54.9%)	11 (64.7%)	30 (48.4%)	0.45
Any HF-related ED Visit or hospitalization in the past 6 months (n=491)	165 (33.6%)	105 (33.1%) (n=317)	27 (29.3%) (n=92)	0.53	85 (33.9%) (n=251)	5 (29.4%)	17 (27.4%)	0.62
ED Disposition (n=498)		(n=319)		0.038	(n=252)			0.35
AMA	1 (0.2%)	1 (0.3%)	0 (0.0%)		1 (0.4%)	0 (0.0%)	0 (0.0%)	
Deceased	3 (0.6%)	2 (0.6%)	0 (0.0%)		2 (0.8%)	0 (0.0%)	0 (0.0%)	
Home	21 (4.2%)	10 (3.1%)	5 (5.4%)		6 (2.4%)	2 (11.8%)	2 (3.2%)	
ICU/CCU	41 (8.2%)	24 (7.5%)	8 (8.6%)		19 (7.5%)	2 (11.8%)	4 (6.5%)	
Intermediate Care	54 (10.8%)	26 (8.2%)	13 (14.0%)		19 (7.5%)	1 (5.9%)	7 (11.3%)	
Nursing home/Assisted living	1 (0.2%)	0 (0.0%)	1 (1.1%)		0 (0.0%)	0 (0.0%)	1 (1.6%)	
Observation	33 (6.6%)	25 (7.8%)	5 (5.4%)		21 (8.3%)	1 (5.9%)	2 (3.2%)	

*n (%) or mean +/− SD or median (IQR)	Overall N=499	Baseline Troponin > 14ng/L (n=320)	Baseline Troponin < 14ng/L (n=93)	p-value	Troponin Serial Values Both High > 14 ng/L N=253	Troponin Serial Values Either High N=17	Troponin Serial Values Both Low < 14 ng/L N=62	p-value
Stepdown or other level of care	34 (6.8%)	18 (5.6%)	12 (12.9%)		14 (5.6%)	1 (5.9%)	8 (12.9%)	
Ward	310 (62.2%)	213 (66.8%)	49 (52.7%)		170 (67.5%)	10 (58.8%)	38 (61.3%)	
Heart rate mean ± SD	88 ± 18.8	88 ± 19.5	89 ± 17.1	0.63	88 ± 19.7	88 ± 14.4	86 ± 15.1	0.83
Systolic blood pressure mean ± SD	151.5 ± 29.4	151 ± 30.6	155 ± 28.1	0.26	151 ± 30.7	151 ± 23.0	155 ± 30.2	0.62
Diastolic blood pressure (n=497) mean ± SD	88 ± 22.1	88 ± 22.7 (n=318)	90 ± 22.0	0.32	87 ± 22.9 (n=252)	88 ± 21.5	88 ± 21.4	0.96
Heart Failure (n=494)	391 (79.1%)	251 (79.7%) (n=315)	72 (77.4%)	0.66	194 (78.2%) (n=248)	17 (100.0%)	47 (75.8%)	0.06
Ejection Fraction (n=303) mean ± SD	41.5 ± 18.0	41.2 ± 17.8 (n=188)\	44.6 ± 16.9 (n=56)	0.20	41.5 ± 18.0 (n=149)	41.1 ± 15.4 (n=14)	44.2 ± 17.8 (n=37)	0.71
Myocardial Infarction (MI) (n=491)	117 (23.8%)	66 (20.9%) (n=316)	22 (24.2%) (n=91)	0.56	56 (22.4%) (n=250)	0 (0.0%)	14 (23.3%) (n=60)	0.07
Hypertension (HTN) (n=496)	432 (87.1%)	282 (88.1%)	78 (84.8%) (n=92)	0.38	220 (87.0%)	17 (100.0%)	54 (87.1%)	0.34
Hyperlipidemia (n=490)	289 (59.0%)	192 (60.6%) (n=317)	52 (57.1%) (n=91)	0.63	145 (57.8%) (n=251)	11 (64.7%)	35 (58.3%) (n=60)	0.91
Diabetes (n=496)	233 (47.0%)	155 (48.7%) (n=318)	37 (40.2%) (n=92)	0.16	114 (45.4%) (n=251)	9 (52.9%)	27 (44.3%) (n=61)	0.84
Chronic Kidney Disease (n=495)	128 (25.9%)	94 (29.7%) (n=317)	15 (16.3%) (n=92)	0.011	74 (29.4%) (n=252)	3 (17.6%)	10 (16.4%) (n=61)	0.09
Laboratory Values								
Sodium value mean ± SD	139.3 ± 3.6	139.2 ± 3.5	140.0 ± 3.5	0.07	139.2 ± 3.4	140.3 ± 3.5	139.9 ± 3.8	0.19
Creatinine value (n=498) Median(IQR)	1.2 (0.5–8.5)	1.3 (0.5–8.5) (n=319)	0.9 (0.5–8.2)	<0.001	1.2 (1.0–1.7) (n=252)	1.3 (0.9–1.4)	0.9 (0.8–1.2)	<0.001
NT-proBNP (n=488) Median(IQR)	3160 (1174 – 6800)	3619 (1521–7685) (n=318)	1024 (450–3158)	<.001	3748 (1521–8155) (n=251)	2155 (1124–4273)	1107 (450–2813)	<.001
hsTnT T0 (n=413) Median (IQR)	26.4 (15.1 – 44.3)	32.5 (22.6–51.8)	7.1 (3.0–11.2)	<.001	33.3 (23.6–52.5)	14.1 (11.5–16.7)	6.8 (3.0 – 11.1)	<.001

*n (%) or mean +/− SD or median (IQR)	Overall N=499	Baseline Troponin > 14ng/L (n=320)	Baseline Troponin < 14ng/L (n=93)	p-value	Troponin Serial Values Both High > 14 ng/L N=253	Troponin Serial Values Either High N=17	Troponin Serial Values Both Low < 14 ng/L N=62	p-value
hsTnT T1 (n=383) Median (IQR)	27.4 (16.0 – 44.0)	32.1 (23.5–53.5) (n=262)	8.4 (3.3–11.3) (n=70)	<.001	33.0 (24.9–54.0)	13.8 (12.5 – 14.8)	7.9 (3.0–10.7)	<.001

Abbreviations: hsTnT – high sensitivity Troponin T

Table 2:

Event Rates based on Troponin Value

	Overall	Baseline Troponin > 14ng/L (n=320)	Baseline Troponin < 14ng/L (n=93)	p-value*	Troponin Serial Values Both High > 14 ng/L N=253	Troponin Serial Values Either High N=17	Troponin Serial Values Both Low < 14 ng/L N=62	p-value *
30-day all-cause mortality/ED/ hospitalization (n=476)	99 (20.8%)	56 (18.5%) (n=303)	20 (21.7%) (n=92)	0.4880	47 (19.5%) (n=241)	3 (17.6%)	14 (23.0%) (n=61)	0.8085
90-day all-cause mortality/ED/ hospitalization (n=344)	169 (49.1%)	106 (48.6%) (n=218)	33 (47.8%) (n=69)	0.9080	85 (49.4%) (n=172)	8 (66.7%) (n=12)	21 (44.7%) (n=47)	0.4091
30-day all-cause mortality (n=475)	13(2.7%)	10 (3.3%) (n=303)	0 (0.0%) (n=91)	0.0699 **	10 (4.1%) (n=242)	0 (0.0%) (n=16)	0 (0.0%) (n=61)	0.1900 **
90-day all-cause mortality (n=305)	25 (8.2%)	19 (9.5%) (n=201)	1 (1.7%) (n=58)	0.0855	17 (10.6%) (n=161)	2 (20.0%) (n=10)	0 (0.0%) (n=40)	0.0542 **

* P-values from logistic regression

** P-values from exact logistic regression

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Table 3:

Low hsTnT and 30-day All-Cause Mortality

	Alive	Dead	OR (Mortality)	p-value
Troponin Baseline	N=384	N=10		
Low (<14ng/L)	91 (23.7%)	0 (0%)	0.23 (0.00–1.15)	0.0699
3-Hour Troponin	N=357	N=11		
Low (<14ng/L)	79 (22.1%)	0 (0%)	0.23 (0.00–1.13)	0.0672
Troponin Baseline	N=384	N=10		
Low (<19ng/L)	135 (35.2%)	0 (0%)	0.13 (0.00–0.65)	0.0142
3-Hour Troponin	N=357	N=11		
Low (<19ng/L)	119 (33.3%)	0 (0%)	0.13 (0.00 – 0.64)	0.0127
Troponin Baseline	N=384	N=10		
Low (<14/22ng/L) (m/f)	130 (33.9%)	0 (0%)	0.14 (0.00–0.69)	0.0172
3-Hour Troponin	N=357	N=11		
Low (<14/22ng/L) (m/f)	127 (35.6%)	0 (0%)	0.12 (0.00 – 0.58)	0.0088
SERIAL TROPONIN VALUES				
Both Low Vs. Either/Both High	N=309	N=10		
Low (<14ng/L)	61 (19.7%)	0 (0%)	0.29 (0.00–1.46)	0.1157
Both Low Vs. Either/Both High	N=309	N=10		
Low (<19ng/L)	98 (31.7%)	0 (0%)	0.16 (0.00–0.77)	0.0239
Both Low Vs. Either/Both High	N=309	N=10		
Low (<14/22ng/L) (m/f)	97 (31.44%)	0 (0%)	0.16 (0.00–0.78)	0.0250

All analyses by univariate exact logistic regression

m = male, f = female

Table 4:

hsTnT and 90-day All-Cause Mortality

			Unadjusted Analysis		Adjusted Analysis	
	Alive	**Dead**	**OR (Mortality)**	**p-value**	**OR (Mortality)**	**p-value**
Troponin Baseline	N=239	N=20				
Low (<14ng/L)	57 (23.8%)	1 (5%)	0.17 (0.02–1.28)	0.0855	0.37 (0.05–2.96)	0.3463
3-Hour Troponin	N=217	N=20				
Low (<14ng/L)	49 (22.6%)	1 (5%)	0.18 (0.02–1.39)	0.0993	0.35 (0.04–2.84)	0.3283
Troponin Baseline	N=239	N=20				
Low (<19ng/L)	90 (37.7%)	2 (10%)	0.18 (0.04–0.81)	0.0254	0.44 (0.09–2.13)	0.3072
3-Hour Troponin	N=217	N=20				
Low (<19ng/L)	78 (35.9%)	2 (10%)	0.20 (0.04–0.88)	0.0328	0.45 (0.09–2.15)	0.3156
Troponin Baseline	N=239	N=20				
Low (<14/22ng/L) (M/F)	85 (35.6%)	1 (5%)	0.10 (0.01–0.72)	0.0231	0.19 (0.02–1.53)	0.1199
3-Hour Troponin	N=217	N=20				
Low (<14/22ng/L) (M/F)	84 (38.7%)	2 (10%)	0.18 (0.04–0.78)	0.0219	0.34 (0.07–1.59)	0.1705
Serial Troponin Values						
Both Low Vs. Either/Both High	N=192	N=19				
Low (<14ng/L)	40 (20.8%)	0 (0%)	0.14 (0.00–0.68)	0.0150*	N/A	N/A
Both Low Vs. Either/Both High	N=192	N=19				
Low (<19ng/L)	64 (33.3%)	2 (10.5%)	0.24 (0.05–1.05)	0.0579	0.48 (0.10–2.28)	0.3533
Both Low Vs. Either/Both High	N=192	N=19				
Low (<14/22ng/L) (m/f)	65 (33.9%)	1 (5.3%)	0.11 (0.01–0.83)	0.0325	0.19 (0.02–1.55)	0.1218

All analyses by logistic regression except for these results by exact logistic regression

Adjusted analysis covariates: Age, Log_{10}(NTproBNP)

Key: f = female; m= male