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Short paper

Diagnostic and prognostic utility of cardiac troponin in post-cardiac arrest care

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Abstract

Background: Cardiac troponin is routinely tested in the post-cardiac arrest setting, but its utility in identifying ischaemic aetiology and predicting left ventricular systolic dysfunction (LVSD) and survival is not known.

Methods: In a retrospective single center registry, we identified 145 consecutive patients who had achieved return of spontaneous circulation after cardiac arrest and had undergone serial cardiac troponin T (cTnT) testing, echocardiogram, and expert adjudication of aetiology. Initial and peak cTnT were evaluated for assessing ischaemic aetiology, LVSD, and survival to discharge using area under the receiver operating characteristic curve (AUROC).

Results: Mean age was 61 ± 14 years and 71% were men. Of the 145 arrests, 19% had an ischaemic aetiology, 68% had LVSD post-arrest, and 55% survived to discharge. All patients had a positive initial cTnT at 0.01 ng/mL (clinical cut-off). Even at higher cut-offs of 10×, 100× and 1000×, initial cTnT performed poorly (AUROC 0.57, 0.56, and 0.56) and peak cTnT performed modestly (AUROC 0.55, 0.61, and 0.62) as diagnostic tests for ischaemic aetiology. Similarly, even at higher cut-offs, initial (AUROC 0.60, 0.62, 0.55) and peak (AUROC 0.57, 0.61, and 0.62) cTnT performed poorly to modestly at predicting LVSD. The test performed poorly for predicting survival to discharge (AUROC for all <0.6).

Conclusions: At both current and several-fold higher thresholds, cTnT does not perform sufficiently well to guide clinical decision-making or predict patient outcomes. Routine post-cardiac arrest testing of cTnT should be reevaluated.

Keywords: Cardiac troponin T, Post cardiac arrest, Cardiac ischaemia, Left ventricular, systolic dysfunction, Survival

Background

Nearly 350,000 people in the US and approximately 6,000,000 people globally suffer cardiac arrest annually, with acute myocardial infarction (AMI) the most common aetiology.[1,2] However, the identification of those among this population who may have coronary ischaemia and require immediate percutaneous coronary intervention (PCI) is challenging. Electrocardiograms (ECG), the usual initial diagnostic test in the evaluation of coronary ischaemia/infarction, do not reliably demonstrate ST-segment elevations in the post-arrest period, even in the setting of obstructive coronary artery disease.[3] ECG diagnosis of AMI in this population may be complicated by the presence of persistent left-bundle-branch-block and/or non-Q-wave myocardial infarction.[4–6] Other symptoms such as chest pain are difficult to discern, making accurate diagnosis difficult.[3,7] PCI has been associated with improved outcomes in patients with AMI who achieve ROSC.[3,7] Consequently, treatment guidelines now recommend urgent coronary angiography after successful return of spontaneous circulation (ROSC) in individuals with suspected AMI, even without evidence of ST-elevation on ECG.[8]

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Identifying patients who require immediate PCI after ROSC remains problematic, given non-specific clinical symptoms and low predictive values of ECG. Cardiac troponin T (cTnT) is a marker of myocardial injury that is routinely used in the evaluation of acute coronary syndrome, and is the most sensitive and specific marker for diagnosis of AMI.[9] The role of cTnT in determining aetiology of cardiac arrest and prognosticating outcomes in this population remains relatively unknown. Events other than coronary ischaemia may underlie elevations in cTnT levels after cardiac arrest, including mechanical injury to the myocardium from cardiopulmonary resuscitation (CPR) or decreased coronary blood flow from cardiac arrest.[6,10] This complicates post-ROSC treatment guidelines concerning the decision to perform coronary angiography.[11,12]

Here, we sought to assess the sensitivity and specificity of cTnT in the post-arrest setting, with regards to (1) the identification of an ischaemic aetiology, (2) prognostication of post-arrest left ventricular systolic dysfunction (LVSD) and (3) prediction of survival to hospital discharge.

Methods

We constructed a retrospective cohort of 145 consecutive patients admitted to the intensive care unit (ICU) at Tufts University Medical Center who had achieved return of spontaneous circulation (ROSC) after undergoing either in-hospital or out-of-hospital cardiac arrest. All patients had undergone serial assessment of cTnT during ICU care after achieving ROSC. These cTnT were obtained from chart review. For the purposes of our study, the first cTnT on arrival to the ICU was referred to as the "initial" troponin. "Peak" cTnT, the highest recorded cTnT during hospitalization, was also recorded. Standard troponin assay protocol was followed, wherein cTnT levels were tested every 6 h. The number of tests before peak cTnT levels were reached were not recorded.

Two cardiologists independently adjudicated the aetiology of cardiac arrest for all patients, and any discrepancies were resolved with mutual agreement. A transthoracic echocardiogram (TTE) had also been performed on all patients to assess presence of LVSD, defined as regional or generalized wall-motion abnormalities of left ventricular myocardium. Ejection fraction (EF) during the first 24-h period following cardiac arrest was measured. Lastly, survival to hospital discharge was also recorded.

Values of cTnT were iteratively evaluated at different thresholds to define a positive value, including 0.01 ng/mL (clinical cutoff), 0.1 ng/mL (10× clinical cutoff), 1.0 ng/mL (100× clinical cutoff), and 10 ng/mL (1000× clinical cutoff), to determine their clinical utility in predicting outcome variables using area under the receiver operating characteristic curves (AUROC).

Statistical analyses were conducted at the University of Texas Southwestern Medical Center using SAS software, release 9.3 (SAS Institute, Cary, NC) for Windows (Microsoft, Redmond, Washington). $P < 0.05$ was set as the level of statistical significance, and tests were two-sided.

Results

The average age of the cohort was 61 ± 14 years, and 71% (103/145) were male (Table 1). Nineteen percent (28/145) of the arrests had an acute ischaemic aetiology, 68% (99/145) developed LVSD following cardiac arrest, and 55% (80/145) survived to hospital discharge. Overall mean EF after arrest was 39% [Standard deviation (SD) 18%]. Among those with LVSD, mean EF was 31% (SD 15%). On echocardiography, 22% (32/145) had anterior/apical hypokinesis, 21% (31/145) had posterior/inferior hypokinesis, 5% (7/145) had septal hypokinesis, and 19% (28/145) had global hypokinesis, while 32% (47/145) did not exhibit any wall motion abnormalities. Median initial cTnT was 0.4 ng/mL (IQR 0.1–4.1) and peak cTnT was 5.8 ng/mL (IQR 0.7–32.5). Compared to those with a non-ischaemic aetiology, an ischaemic aetiology was associated with a 4-fold higher initial (median [IQR] 0.24 [0.04–1.9] vs 0.9 [0.2–9.0]) and an 8-fold higher peak (1.5 [0.3–23.7] vs 12.6 [2.2–43.8]) cTnT ($p < .01$), with wide variation in cTnT levels in both groups (Table 2). Further, compared to patients without LVSD, those with LVSD had a 6-fold higher initial (0.2 [0.04–1.4] vs 1.2 [0.2–6.1]) and a 9-fold higher peak (1.3 [0.2–12.6] vs 11.6 [1.3–43.8]) cTnT ($p < .01$). Survivors and non-survivors had similar initial cTnT (0.4 [0.1–3.9] vs 0.6 [0.1–4.4]) and peak cTnT (4.8 [0.5–26.1] vs 11.4 [1.2–32.7]) levels.

All patients had a positive initial cTnT at 0.01 ng/mL (clinical cut-off), 76% (110/145) at 0.1 ng/mL (10×), 43% (63/145) at 1.0 ng/mL (100×), and 17% (25/145) at 10 ng/mL (1000×). All patients also had a positive peak cTnT at 0.01 ng/mL (clinical cut-off), 91% (132/145) at 0.1 ng/mL (10×), 68% (99/145) at 1.0 ng/mL (100×), and 46% (67/145) at 10 ng/mL (1000×).

At higher cut-offs of 10×, 100×, and 1000× of the clinical cut-off, initial cTnT performed poorly (AUROC 0.57, 0.56, and 0.56), and peak cTnT performed modestly (AUROC 0.55, 0.61, and 0.62) as

Table 1 – Cohort characteristics.

N	145
Age (Mean ± SD)	61 ± 14 years
Men	71%
Coronary artery disease	36%
Initial creatinine (Mean ± SD)	1.9 ± 1.8
LV dysfunction	68%
STEMI	19%
Ischaemic aetiology	54%
Survival to discharge	55%
Cardiac arrest characteristics	
Cardiac arrest type	
VT/VF	57%
PEA/asystole	43%
In-hospital location	45%
Initial troponin T	
Median, IQR in ng/mL	0.45 (0.12–4.06)
>0.01 (clinical cut-off)	100%
>0.1 (10×)	76%
>1 (100×)	43%
>10 (1000×)	17%
Peak Troponin T	
Median, IQR in ng/mL	5.84 (0.56–32.46)
>0.01 (clinical cut-off)	100%
>0.1 (10×)	91%
>1 (100×)	68%
>10 (1000×)	46%

Abbreviations: SD: standard deviation; LV: left ventricle; STEMI: ST elevation myocardial infarction; VT: ventricular tachycardia; VF: ventricular fibrillation; PEA: pulseless electrical activity; IQR: inter-quartile range.

Table 2 – Cardiac troponin t levels by outcome.

	Initial troponin, Median (IQR), ng/mL	
	Yes	No
Ischaemic aetiology*	0.9 (0.2–9.0)	0.24 (0.04–1.9)
LV dysfunction*	1.2 (0.2–6.1)	0.2 (0.04–1.4)
Survived	0.4 (0.1–3.9)	0.6 (0.1–4.4)
Peak troponin, Median (IQR)		
Yes	No	
Ischaemic aetiology*	12.6 (2.2–43.8)	1.5 (0.3–23.7)
LV dysfunction*	11.6 (1.3–43.8)	1.3 (0.2–12.6)
Survived	4.8 (0.5–26.1)	11.4 (1.2–32.7)

Abbreviations: IQR: inter-quartile range; LV: left ventricle.
* p-value <0.01.

diagnostic tests for ischaemic aetiology (Fig. 1). Similarly, even at higher cut-offs, initial (AUROC 0.60, 0.62, 0.55) and peak (AUROC 0.57, 0.61, and 0.62) cTnT performed poorly to modestly at predicting LVSD. The test performed poorly for predicting survival to discharge, and AUROC for all troponin thresholds was 0.5.

Discussion

In this single-center cohort study of 145 patients who underwent cardiac arrest, we identified several limitations of the routine evaluation of cTnT in the post-arrest setting. Despite early PCI being recommended in post-arrest patients, identifying individuals with AMI is difficult in routine practice. Troponin testing is often part of post-arrest protocols to help guide clinical decision-making. We found that both initial and peak cTnT values of the patients enrolled in our study did not exhibit sufficiently high prediction thresholds for clinical utility, specifically regarding the differentiation of arrest aetiology, prognosis, and survival to discharge. Modifying the cTnT cutoffs to 10, 100, and 1000 times the current clinical cutoff of 0.01 ng/mL did not improve prediction of the aforementioned outcome variables of interest. The corresponding AUROC c-statistics for all analyses at all cutoff levels correlated with poor to modest diagnostic/predictive values well below clinical relevance.

Prior studies vary regarding the predictive values of cTnT in patients after cardiac arrest. Some demonstrated clinical utility as a triage tool, with suggested cut-offs ranging from 0.6 to 4 ng/mL.[6,13] We did not find that any such thresholds had sufficient sensitivity or specificity to be useful in the clinical setting. Dumas et al also found a similarly modest predictive value of cardiac troponin for coronary occlusion.[10]

There are several possible explanations for the low/modest predictive value of cTnT that was observed. Increased levels of cTnT in patients with non-cardiac causes of cardiac arrest are common after ROSC.[11,14] Reasons for elevated cTnT include common comorbidities such as heart failure (HF), tachycardia, sepsis, or renal failure.[15–18] CPR and defibrillation have also been associated with cTnT release, though studies show inconsistent results.[6,18,19]

Currently, the prognosis for patients with cardiac arrest remain poor. The role of cTnT should be reevaluated in decisions to pursue diagnostic cardiac catheterization in post-cardiac arrest patients, given that early PCI may have prognostic value.

Our findings should be interpreted in the context of certain limitations. Our observations are based on assessments at a single center over a short time period. However, variation in prior studies suggests that our conclusions regarding the uncertain value of troponin testing in the post-arrest setting may hold for clinical practice. Both in-hospital and out-of-hospital arrest data were used, which may add variation in the results of troponin testing. However, the management algorithms for post-arrest care are similar across settings. The use of clinical data obtained after the episode of care may be associated with heterogeneity in cTnT testing. However, provider treatment plans often differ in urgent situations, making variation likely. Data about the timing of TTE after arrest was not

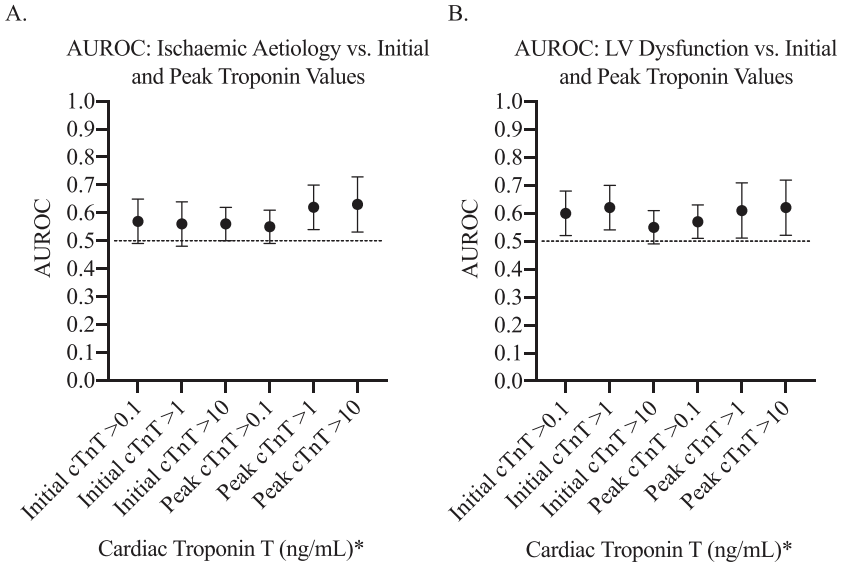

Fig. 1 – AUROC: Ischaemic Aetiology and LV Dysfunction vs. Initial and Peak Troponin Values.
***Clinical cut-off (0.01 ng/mL) was positive for all patients**
Abbreviations: AUROCarea under the receiver operating characteristic curve; LVleft ventricular; cTnTcardiac troponin T.

collected during patient admission and was subsequently unavailable for analysis. And we acknowledge that the determination of ischaemic vs non-ischaemic aetiology of arrest is sometimes difficult, and in this study (as well as any clinical study) inaccuracy of this determination may be present. The retrospective study design may not account for all potential confounders. Finally, our results did not evaluate the value offered by the more precise high-sensitivity troponin test, but there is limited evidence supporting its use in the post-arrest setting, and it is not yet widely available.[20]

Overall, our study underscores the challenges with the use of cTnT to guide clinical management of the post-cardiac arrest patient and encourages a reevaluation of the routine testing of cTnT in this setting.

Conflicts of interest

None.

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