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The Prognostic Value of Undetectable Highly Sensitive Cardiac Troponin I in Patients With Acute Pulmonary Embolism

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PODCAST

BACKGROUND: Elevated cardiac troponin levels have been shown to be associated with adverse outcomes in patients with acute pulmonary embolism (PE). However, few data address the management implications of undetectable cardiac troponin I (cTnI) using a highly sensitive assay. We hypothesized that undetectable cTnI predicts very low in-hospital adverse event rates.

METHODS: In a retrospective cohort study, we classified patients with confirmed acute PE according to cTnI detectability into cTnI+ ($\geq$0.012 ng/mL) and cTnI− ($<$0.012 ng/mL) groups. The Pulmonary Embolism Severity Index (PESI) was used for clinical risk determination. The primary outcome was a composite of hard events defined as in-hospital death, CPR, or thrombolytic therapy. The secondary outcome was a composite of soft events defined as ICU admission or inferior vena cava filter placement.

RESULTS: Among 298 consecutive patients with confirmed acute PE, 161 (55%) were cTnI+ and 137 (45%) cTnI−. No deaths occurred in the cTnI− group vs nine (6%) in the cTnI+ group ($P = .004$). No hard events were observed in the cTnI− group vs 15 (9%) in the cTnI+ group ($P < .001$). Soft events were observed at a lower rate in the cTnI– group (21[15%] vs 69 [43%], $P < .001$). Patients in the cTnI− group had a higher survival rate free of hard ($P = .001$) or soft ($P < .001$) events, irrespective of clinical risk. Furthermore, cTnI provided incremental prognostic value beyond clinical, ECG, and imaging data ($P < .001$).

CONCLUSIONS: Highly sensitive cTnI assay provides an excellent prognostic negative predictive value; thus, it plays a role in identifying candidates for out-of-hospital treatment of acute PE.

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ABBREVIATIONS: CTA = CT angiography; cTn = cardiac troponin; cTnI = cardiac troponin I; IVC = inferior vena cava; PE = pulmonary embolism; PESI = Pulmonary Embolism Severity Index

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An estimated 300,000 to 600,000 cases of VTE are diagnosed annually in the United States, with 10% to 30% mortality at 30-days occurring mostly among patients with acute pulmonary embolism (PE).[1] However, a great disparity exists in mortality rate, ranging from < 1% in low-risk PE to as high as 50% to 65% for massive PE.[2-4] Therefore, the initial patient triage and management should be tailored to patient risk.[5] A variety of clinical, ECG, echocardiographic, and CT angiographic parameters and biomarkers have been found to be useful in helping clinicians to risk stratify patients with acute PE.[3,4,6-15] This is important because outpatient management of low-risk acute PE has been under investigation in recent years.[16] The role of cardiac troponin (cTn) in identifying patients with low-risk acute PE as candidates for outpatient management is not well defined.[16]

It is well established that elevated cTn levels are associated with adverse outcomes, signifying acute right ventricular strain and ischemic injury caused by a high-burden PE.[15,17] Nonetheless, the prognostic negative predictive value of cTn using older assays has not been shown to be clinically useful because "negative" troponin was still associated with mortality events, albeit at a low rate.[15] Therefore, older troponin assays with higher

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detection thresholds are not sensitive enough to identify very-low-risk patients who may be suitable for early discharge and outpatient management.[15] In recent years, highly sensitive cTn assays have become widely available, enabling the detection of lower levels with higher accuracy.[18] Being highly sensitive, these assays may serve as a screening tool for right ventricular injury caused by high-burden acute PE. We hypothesized that undetectable cardiac troponin I (cTnI) levels measured by a highly sensitive assay predict very low in-hospital adverse events and, thus, can identify patients with acute PE who may be candidates for out-of-hospital management.

Materials and Methods

Patients

A retrospective cohort study design was implemented. We queried the electronic health records of John H. Stroger, Jr. Hospital of Cook County (Chicago, Illinois) for consecutive admissions with a discharge diagnosis of acute PE from January 1, 2008, to December 31, 2012. Diagnosis of acute PE was confirmed by pulmonary CT angiography (CTA), high-probability ventilation/perfusion scan, or invasive pulmonary angiography.[5] According to the initial cTnI level obtained within 24 h from diagnosis, patients were classified into two study groups: cTnI+ (≥ 0.012 ng/mL) and cTnI− (< 0.012 ng/mL).

The VITROS Troponin I ES Assay (Ortho-Clinical Diagnostics, Inc) was used in the study.[19] The lower detection limit of the assay is 0.012 ng/mL.[20] According to the assay manufacturer, the coefficient of variation at the 99th percentile upper reference limit (0.034 ng/mL) is 10%,[18,20] meeting the recommendations for acceptable imprecision in a high-sensitivity cTn assay.[21]

Clinical Data

Based on detailed chart review, we determined patient baseline demographics, vital signs, and oxygen saturation at presentation. Comorbidities, including congestive heart failure, sepsis, malignancy, and renal insufficiency, were tabulated. Patients' clinical risk was determined using the validated Pulmonary Embolism Severity Index (PESI) as illustrated in Table 1. The patients were classified into two subgroups: low clinical risk (very low or low PESI class) and high clinical risk (intermediate, high, or very high PESI class).[6,22]

ECG and Imaging Data

An investigator blinded to clinical and outcome data analyzed all ECG tracings for rate, rhythm, and signs of right ventricular strain defined as right bundle branch block or T-wave inversion in leads V_1 to V_3.[8,23] Echocardiography reports, as interpreted by an expert board-certified echocardiologist, were reviewed for pulmonary artery systolic pressure measurements and right ventricular dysfunction.[24] Whenever possible, the pulmonary arterial peak systolic pressure was calculated using the simplified Bernoulli equation.[25] Pulmonary CTA reports were reviewed to determine PE burden (saddle, main, lobar, segmental, and subsegmental) and to ascertain right ventricular dilatation, which was defined as a right ventricular-to-left ventricular diameter ratio of > 0.9 in the four-chamber view.[26,27] We established evidence of lower-extremity DVT from compression and duplex venous ultrasonography reports.

TABLE 1] Pulmonary Embolism Severity Index

Factor	Points
Age	1 per year
Male sex	10
History of cancer	30
History of heart failure	10
History of chronic lung disease	10
Heart rate ≥ 110/min	20
Systolic BP < 100 mm Hg	30
Respiratory rate ≥ 30/min	20
Temperature < 36°C	20
Altered mental status	60
Oxygen saturation < 90%	20
Risk classes	
I. Very low	≤ 65
II. Low	66-85
III. Intermediate	86-105
IV. High	106-125
V. Very high	> 125

Adapted with permission of the American Thoracic Society. Aujesky D et al. *Am J Respir Crit Care Med*. 2005;172(8):1041-1046.[6]

Outcome Assessment

We conducted a detailed chart review to determine the occurrence, date, and time (hour and minutes) of the following adverse events: death, CPR, IV thrombolytic therapy, ICU admission, and inferior vena cava (IVC) filter placement. The primary outcome was a composite of hard events defined as death, CPR, or the use of IV thrombolytic therapy. The secondary outcome was a composite of soft events defined as ICU admission or IVC filter placement. We considered IVC filter placement a soft event because it represents an escalation of care that necessitates inpatient management and a surrogate of perceived clinical deterioration. We further classified ICU admissions into hard and soft admissions. A hard ICU admission included the use of a nonrebreather oxygen face mask, noninvasive ventilatory support to maintain oxygen saturation $>92\%$, or vasopressors to maintain systolic BP ≥ 90 mm Hg after failure of IV fluid resuscitation. A soft ICU admission was for patient monitoring, systolic BP <90 mm Hg not requiring the use of vasopressors, or an indication other than acute PE (sepsis, myocardial infarction, congestive heart failure, arrhythmias, or GI bleeding).

Statistical Analysis

The χ^2 test was used to compare dichotomous variables, which were expressed as number (percentage). Fisher exact test was used to compare dichotomous variables when the absolute number of events was fewer than five. The two-tailed independent-sample Student *t* test was used to compare normally distributed continuous variables, which were expressed as mean ± SD. The Mann-Whitney *U* test was used to compare skewed continuous variables, which were expressed as median (interquartile range).

Kaplan-Meyer curves and the log-rank test were used to compare time-to-event survival. Time zero in the survival curves represents the time of diagnosis of an acute PE, whereas censoring was at the time of hospital discharge.

Stepwise multivariate logistic regression analysis models were used to determine the incremental prognostic value of the PESI score, ECG, right ventricular imaging, and cTnI level. The absolute increment in global χ^2 value of the model and the corresponding *P* value (Wald test) were used to determine the significance of the predictive value gained by each added variable. A two-tailed $P<.05$ was considered statistically significant. SPSS version 18 software (IBM) was used for all statistical analyses. The study was approved by the Institutional Review Board of John H. Stroger, Jr Hospital of Cook County (approval number: 13-065).

Results

We identified 350 patients with a discharge diagnosis of acute PE confirmed by pulmonary CTA in 327 (93%) or ventilation/perfusion scan in 23 (7%). Fifty-two patients (15%) did not have a cTnI assay during their hospitalization, whereas 298 (85%) did; 161 patients (54%) were considered cTnI+ (≥ 0.012 ng/mL) and 137 (46%) cTnI− (<0.012 ng/mL). The baseline characteristics of the study groups are summarized in Table 2. Notably, the cTnI+ group was older, had a higher mean heart rate and lower oxygen saturation at presentation, and were at greater overall clinical risk as determined by PESI.

ECG analysis demonstrated that the cTnI+ group had a higher prevalence of sinus tachycardia, T-wave inversion in leads V_1 to V_3, or right bundle branch block (Table 3). They also were more likely to have right ventricular dysfunction and elevated pulmonary artery systolic pressures (Table 3). Pulmonary CTA demonstrated that patients in the cTn+ group had higher rates of right ventricular strain and saddle or main pulmonary artery embolism (Table 3).

Outcomes

After confirmatory acute PE diagnosis, the patients were followed for in-hospital events for a median of 5 days (interquartile range, 3-8 days). During follow-up, we observed nine deaths (3%), nine CPR events (3%), five IV thrombolytic therapy administrations (2%), 74 ICU admissions (25%), and 36 IVC filter placements (12%). All hard events (primary outcome), defined as a composite of death, CPR, or IV thrombolytic therapy, occurred in the cTnI+ group, and none were observed in the cTnI− group (15 [9%] vs 0 [0%], respectively, $P<.001$). The soft events (secondary outcome) defined as a composite of ICU admission or IVC filter placement, occurred more frequently in the cTnI+ group (69 [43%] vs 21 [15%], $P<.001$) (Table 4). ICU admissions occurred more frequently among patients in the cTnI+ group (38%) than those in the cTnI− group (9%, $P<.001$). Hard ICU admissions were observed in 26 (16%) in the cTnI+ group vs only three (2%) in the cTnI− group ($P<.001$). Nonetheless, we determined that three of 137 patients (2%) considered cTnI– had hard ICU admissions. Among these patients, one had a high-risk PESI class. Similarly, soft ICU admissions occurred more frequently in the cTnI+ group than in the cTnI– group (35 [22%] vs 10 [7%], respectively, $P<.001$). The rate of IVC filter placement was not significantly different between the study groups (Table 4). Length of stay after the diagnosis of acute PE was greater in the cTnI+ group ($P=.001$).

Kaplan-Meier analyses demonstrated that the cTnI− group had greater survival free of hard ($P=.001$) or soft ($P<.001$) adverse events, irrespective of clinical risk (Figs 1, 2). As illustrated in Figure 3, stepwise multivariate logistic regression analysis indicated that cTnI provided incremental predictive values for in-hospital hard and soft adverse events beyond PESI score, ECG, and right ventricular imaging (CTA or echocardiography) ($P<.001$).

Missing Troponin Values

The baseline characteristics of the 52 patients who did not undergo cTnI assay were similar to those who did,

TABLE 2] Baseline Characteristics

Characteristic	All Patients (N = 298)	cTnI+ (n = 161)	cTnI– (n = 137)	*P* Value
Age, y	56 ± 13	58 ± 13	54 ± 13	.02
Male sex	151 (51)	78 (48)	73 (53)	.41
Race				.32
Black	174 (58)	97 (60)	77 (56)	
White	60 (20)	33 (20)	27 (20)	
Hispanic	27 (9)	10 (6)	17 (12)	
BMI, kg/m^2	31 ± 8	31 ± 8	31 ± 9	.67
Heart rate, beats/min	99 ± 20	102 ± 21	96 ± 18	.01
Heart rate ≥ 110/min	95 (32)	63 (39)	32 (23)	.004
SBP, mm Hg	129 ± 23	131 ± 24	128 ± 22	.29
SBP ≤ 100 mm Hg	24 (8)	14 (9)	10 (7)	.66
DBP, mm Hg	78 ± 15	80 ± 16	76 ± 14	.04
Respiratory rate, breaths/min	21 ± 6	21 ± 6	20 ± 6	.21
Respiratory rate ≥ 30/min	10 (3)	7 (4)	3 (2)	.30
O_2 saturation, %	95 ± 4	95 ± 5	96 ± 3	< .001
O_2 saturation < 90%	23 (8)	19 (12)	4 (3)	.004
Hypothermia (temperature < 36°C)	2 (1)	0 (0)	2 (1)	.21
Comorbidities				
Cancer	68 (23)	36 (22)	32 (23)	.84
Heart failure	28 (9)	22 (14)	6 (4)	.006
Chronic lung disease	29 (10)	21 (13)	8 (6)	.04
Postoperative	16 (5)	10 (6)	6 (4)	.48
Renal insufficiency	21 (7)	17 (11)	4 (3)	.01
Sepsis	13 (4)	7 (4)	6 (4)	.99
PESI score	84 ± 31	90 ± 32	78 ± 28	.001
PESI risk class				.006
I. Very low	87 (29)	34 (21)	53 (39)	
II. Low	86 (29)	50 (31)	36 (26)	
III. Intermediate	64 (21)	35 (22)	29 (21)	
IV. High	34 (11)	25 (16)	9 (7)	
V. Very high	27 (9)	17 (11)	10 (7)	
Diagnosis modality				.02
Pulmonary CTA	275 (92)	143 (89)	132 (96)	
$\dot{V}/\dot{Q}$ scan	23 (8)	18 (11)	5 (4)	

Data are presented as mean ± SD or No. (%). CTA = CT angiography; cTnI = cardiac troponin I; DBP = diastolic BP; O_2 = oxygen; PESI = Pulmonary Embolism Severity Index; SBP = systolic BP; $\dot{V}/\dot{Q}$ = ventilation/perfusion.

except that patients without measured cTnI were more likely to have a known history of cancer (Table 5). Notably, the mean PESI scores of patients with and without measured cTnI were similar, as were the observed rates of hard or soft events (Table 5).

To demonstrate whether the missing cTnI values could have changed the overall results of the study, we performed sensitivity analyses examining two scenarios: one assuming that all patients with missing values were cTnI+ and the other assuming that all were cTnI–. In both scenarios, the cTnI+ status was predictive of hard and soft in-hospital events (all $P < .001$).

Discussion

To our knowledge, this study is the first to investigate the prognostic negative predictive value of a highly sensitive cTnI assay for in-hospital adverse events in

TABLE 3] ECG and Imaging Findings

Finding	All Patients	cTnI+	cTnI–	*P* Value
ECG (n = 289)				
Sinus tachycardia	99 (33)	63 (41)	33 (24)	.003
T-wave inversion (leads V_1-V_3)	86 (30)	61 (40)	25 (19)	< .001
Right bundle branch block	25 (9)	19 (12)	6 (4)	.02
Right axis deviation	28 (10)	18 (12)	10 (7)	.22
Atrial dysrhythmia	13 (4)	10 (6)	3 (2)	.08
Echocardiography (n = 175)				
Test performed	175 (59)	116 (72)	59 (43)	< .001
RV dilation	54 (31)	49 (42)	5 (8)	< .001
RV dysfunction	51 (29)	46 (40)	5 (8)	< .001
Ventricular septal flattening	17 (10)	14 (12)	3 (5)	.18
PASP estimated (n = 147)				
PASP	38 ± 16	41 ± 17	31 ± 10	< .001
PASP > 30 mm Hg	70 (48)	58 (59)	12 (25)	< .001
PASP > 50 mm Hg	25 (17)	23 (23)	2 (4)	.004
Pulmonary CTA (n = 275)				
RV strain	37 (13)	29 (20)	8 (6)	.001
Saddle or main PA embolus	109 (40)	71 (50)	38 (29)	< .001
Venous ultrasound (n = 136)				
Test performed	136 (46)	85 (53)	51 (37)	.007
DVT present	78 (57)	48 (56)	30 (59)	.79

Data are presented as No. (%) or mean ± SD. PA = pulmonary artery; PASP = pulmonary artery systolic pressure; RV = right ventricular. See Table 2 legend for expansion of other abbreviations.

patients with confirmed acute PE. We demonstrated that patients with acute PE with undetectable cTnI had exceedingly low rates of in-hospital hard events of death, CPR, and use of thrombolytic therapy, irrespective of clinical risk. Furthermore, undetectable cTnI was predictive of significantly lower rates of the soft events of ICU admissions or IVC filter placement, irrespective of clinical risk. Additionally, cTnI level provided incremental prognostic value beyond established clinical, ECG, and imaging risk predictors. These findings complement similar data regarding cardiac troponin T and lay the foundation to investigate outpatient treatment of suitable patients with acute PE who are at low clinical risk and have undetectable cTnI.[28-30]

It is well established that cTns play an important role in the risk stratification of acute PE[15] because they have been shown to independently predict in-hospital hemodynamic instability and death in normotensive patients with acute PE.[31,32] Nonetheless, older data indicated that patients with cTn levels below the normal reference value continue to experience adverse outcomes, albeit at lower rates than those with elevated levels.[33-37] These studies predominantly investigated low-sensitivity troponin assays or used higher diagnostic thresholds.[15,33-38] In concept, highly sensitive cTn assays allow for high-fidelity detection of right ventricular injury and, thus, better prediction of adverse outcome.[15,38] Lankeit et al[28,29] demonstrated that cardiac troponin T assay, combined with the PESI, improves risk stratification of acute PE and identifies possible candidates for out-of-hospital treatment. The present study demonstrates similar findings using highly sensitive cTnI assay. Moreover, we demonstrated that even among patients at high risk clinically, undetectable cTnI identified patients with subsequent low event rates, indicating that cTnI measurement can improve risk stratification across all risk strata. Additionally, we demonstrated that the prognostic value of cTnI was incremental to other risk predictors, namely ECG and right ventricular imaging. The analyses suggest that ECG and right ventricular imaging had substantial incremental value in predicting soft events (ie, ICU admission, IVC filter placement) (Fig 3). We suspect that decisions leading to ICU admission or IVC filter

TABLE 4] Outcomes

Outcome	All Patients (N = 298)	cTnI+ (n = 161)	cTnI− (n = 137)	*P* Value
Hard events	15 (5)	15 (9)	0 (0)	<.001
Death	9 (3)	9 (6)	0 (0)	.004
CPR	9 (3)	9 (6)	0 (0)	.004
Thrombolytic therapy	5 (2)	5 (3)	0 (0)	.06
Soft events	90 (30)	69 (43)	21 (15)	<.001
ICU admission	74 (25)	61 (38)	13 (9)	<.001
Hard admission	29 (10)	26 (16)	3 (2)	<.001
Soft admission	45 (15)	35 (22)	10 (7)	<.001
IVC filter placement	36 (12)	23 (14)	13 (10)	.21
Length of stay, d	5 (3-8)	5 (3-9)	4 (2-8)	.001

Data are presented as No. (%) or median (interquartile range). Hard ICU admission includes admission for hypoxemia requiring nonrebreather face mask or noninvasive ventilatory support to maintain oxygen saturation > 92% and need for vasopressors to maintain SBP > 90 mm Hg. Soft ICU admission includes admission for monitoring, SBP < 90 mm Hg that responded to fluid resuscitation, or an indication other than acute pulmonary embolism (sepsis, myocardial infarction, arrhythmia, congestive heart failure, GI bleeding). IVC = inferior vena cava. See Table 2 legend for expansion of other abbreviations.

placement were clinically biased by the ECG findings, right ventricular imaging, or cTnI assay.

Combining PESI and cTnI seems to improve risk prediction.[29] We illustrated this point statistically by demonstrating an incremental predictive value of cTnI− when used in combination with PESI (Fig 3). Thus, cTnI would function best as an adjunct to a comprehensive clinical evaluation by leveraging Bayes theorem to identify very-low-risk patients who may be considered for outpatient management.

In the present study, it seems that patients with a history of cancer were less likely to undergo cTnI assay (Table 5). Upon further examination, it appears that in some of these patients, the diagnosis of PE was established incidentally by chest CT scans performed during cancer staging. Because the diagnosis was evident in these cases, cTnI assay often was not performed. We also determined that cTnI was not assessed in some patients with metastatic cancer and grim prognosis.

The definition of high-sensitivity cTn assay has been evolving as a new generation of assays have become available, allowing for the detection of lower troponin levels with greater precision.[39-41] The latest generation of

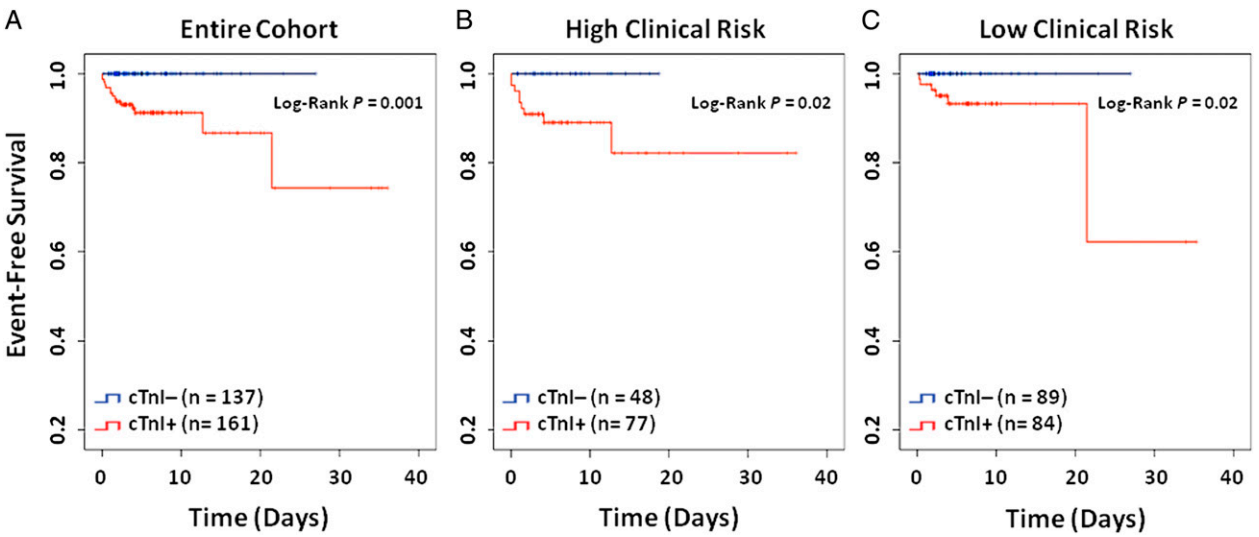

Figure 1 – *A-C, Kaplan-Meier survival curves: death, CPR, or thrombolytic therapy (hard events). A, Entire cohort. B, High clinical risk. C, Low clinical risk. High clinical risk was defined as intermediate-, high-, or very-high-risk class according to the Pulmonary Embolism Severity Index, whereas low clinical risk was defined as very-low-risk or low-risk class. cTnI− = undetectable highly sensitive cardiac troponin I; cTnI+ = detectable highly sensitive cardiac troponin I.*

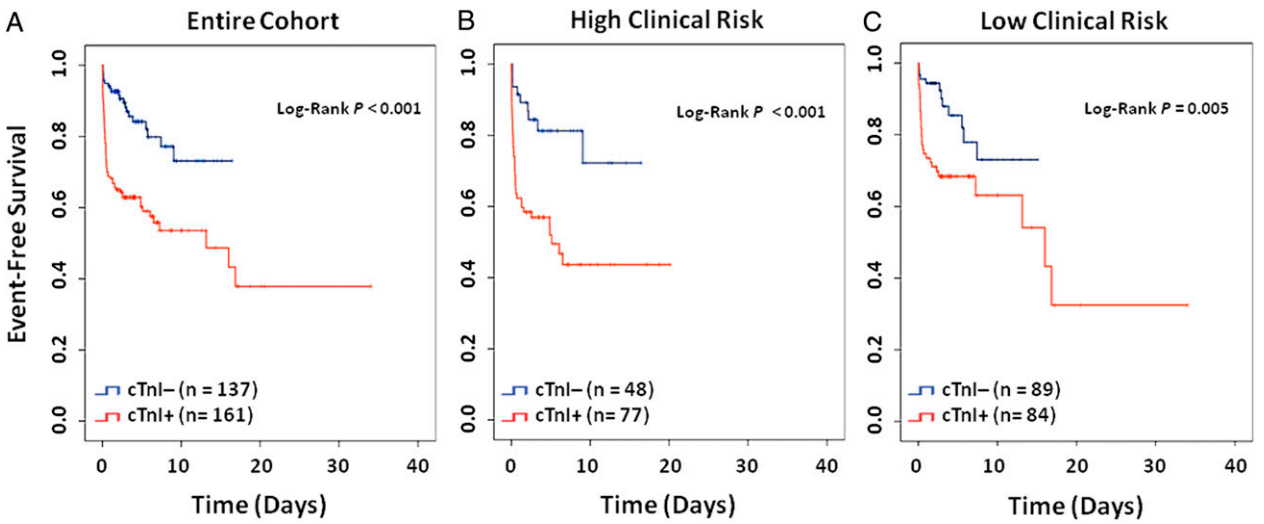

Figure 2 – *A-C, Kaplan-Meier survival curves: ICU admission or inferior vena cava filter placement (soft events). A, Entire cohort. B, High clinical risk. C, Low clinical risk. High clinical risk was defined as intermediate-, high-, or very-high-risk class according to the Pulmonary Embolism Severity Index, whereas low clinical risk was defined as very-low-risk or low-risk class. See Figure 1 legend for expansion of abbreviations.*

assays may allow for even greater prognostic negative predictive value than the one investigated in this study.

The current American College of Chest Physicians clinical practice guidelines on the management of venous thromboembolic disease state that early discharge after a few days of admission is feasible for patients with low-risk acute PE and good home circumstances.[42] In a recent systematic review of 11 studies,[16] including three randomized controlled trials and eight prospective cohort studies comparing early discharge to conventional hospital management in patients with low-risk symptomatic acute PE, a variety of risk assessment methods were used to identify low-risk acute PE, such as clinical gestalt, clinical scoring systems, and

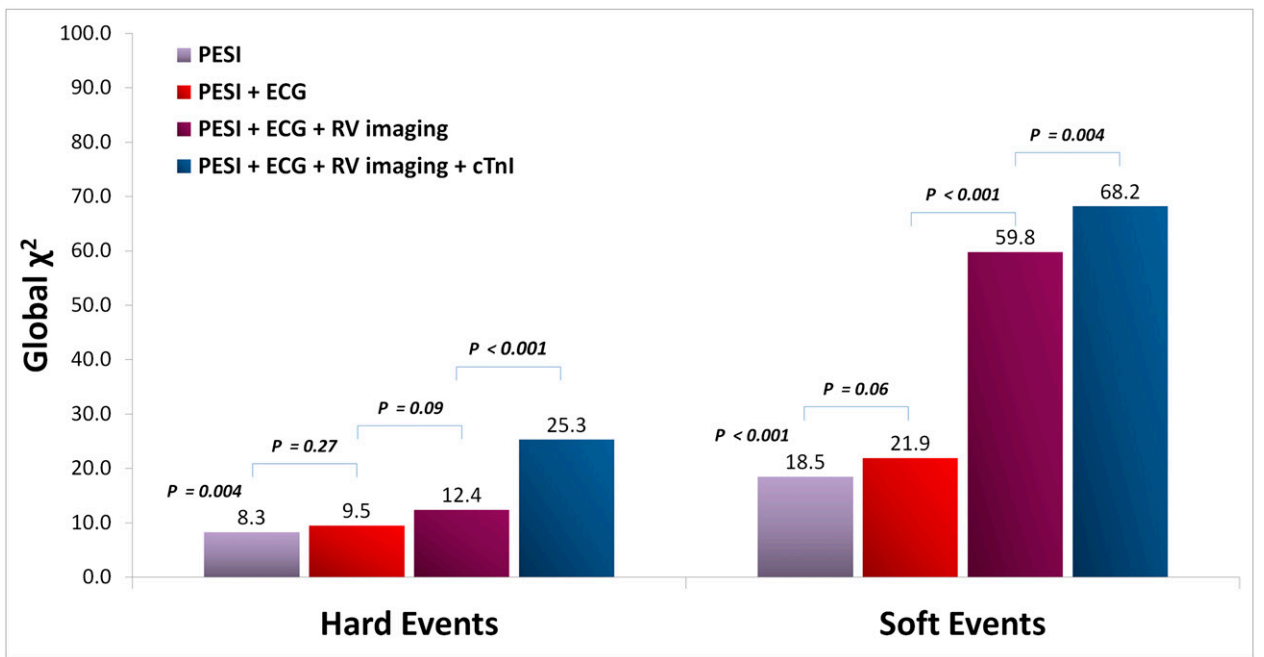

Figure 3 – *Incremental prognostic value. Hard events (primary outcome) were defined as death, CPR, or thrombolytic therapy. Soft events (secondary outcome) were defined as ICU admission or inferior vena cava filter placement. Outcome predictors in acute pulmonary embolism, including the PESI score, ECG (right bundle branch block or T-wave inversion in leads V_1-V_3), RV dilatation (by echocardiography or pulmonary CT angiography), and detectable cTnI level, were introduced in a stepwise fashion into two multivariable logistic regression models in which hard and soft events were the respective outcome variables. The gain in the global χ^2 value was used to determine the significance of the incremental predictive value provided by each predictor. cTnI = cardiac troponin I; PESI = Pulmonary Embolism Severity Index; RV = right ventricular.*

TABLE 5] Patients Without Troponin Assay

Characteristic	cTnI Not Available (n = 52)	cTnI Available (n = 298)	*P* Value
Age, y	52 ± 16	56 ± 13	.09
Male sex	29 (56)	147 (49)	.39
Heart rate, beats/min	98 ± 20	99 ± 20	.61
Heart rate ≥ 110/min	16 (31)	95 (32)	.87
SBP, mm Hg	130 ± 24	129 ± 23	.84
SBP < 100 mm Hg	6 (12)	24 (8)	.41
Respiratory rate, breaths/min	19 ± 2	21 ± 6	.08
Respiratory rate ≥ 30/min	0 (0)	10 (3)	.18
O_2 saturation, %	96 ± 4	95 ± 4	.68
O_2 saturation < 90%	5 (10)	23 (8)	.64
Comorbidities			
Cancer	24 (46)	68 (23)	< .001
Heart failure	3 (6)	28 (9)	.40
Chronic lung disease	4 (8)	29 (10)	.64
PESI score	87 ± 35	84 ± 31	.58
PESI risk class			.06
I. Very low	16 (31)	87 (29)	
II. Low	7 (14)	86 (29)	
III. Intermediate	11 (21)	64 (21)	
IV. High	12 (23)	34 (11)	
V. Very high	6 (12)	27 (9)	
Clinical risk (PESI)			.06
Low	23 (44)	173 (58)	
High	29 (56)	125 (42)	
Hard events	2 (4)	15 (5)	1.0
Death	2 (4)	9 (3)	.67
CPR	0 (0)	9 (3)	.37
Thrombolytic therapy	0 (0)	5 (2)	1.0
Soft events	12 (23)	90 (30)	.30
ICU admission	10 (19)	74 (25)	.38
IVC filter placement	5 (10)	36 (12)	.61

Data are presented as mean ± SD or No. (%). See Table 2 and 4 legends for expansion of abbreviations.

N-terminal pro-B-type natriuretic peptide level.[43-52] Only one study took cTn level into consideration.[53] This meta-analysis showed that early discharge was associated with 3-month rates of recurrent VTE, fatal acute PE, and mortality of 1.47%, 0.47%, and 1.58%, respectively.[16] Unlike complex clinical scoring systems, cTn assay allows for dichotomous decision-making, which simplifies and improves the triage process by identifying patients at very low risk of adverse events who may be candidates for early discharge after the initiation of antithrombin and oral anticoagulation therapies.[42,54] Moreover, cTnI assay use is likely to be clinically effective because 45% of patients in the present study had undetectable cTnI; thus, these patients are candidates for early discharge with ensuing cost savings.[1] The present data strongly argue for the routine implementation of cTn measurement in the risk assessment and triage of patients with acute PE. In this regard, we emphasize that the decision for early outpatient management in acute PE is complex and entails an assessment of clinical status, chemical biomarkers, imaging studies, comorbidities, bleeding risk, psychosocial status, and follow-up plans.

This study has some limitations. The most obvious is the single-center, retrospective design. Additionally,

15% of all patients with acute PE did not have cTnI levels measured and, thus, were excluded from the analysis. However, we demonstrated that patients without measured cTnI levels had similar clinical characteristics, PESI scores, and event rates as those with measured cTnI levels. Therefore, it is likely that patient selection for cTnI measurement was nondifferential, except for patients with a history of cancer. Furthermore, sensitivity analyses demonstrated that having included the patients with missing troponin values could not have changed the overall results of the study. It is unknown, however, whether the risk of hard events would remain at zero having had cTn levels from all patients.

Conclusions

Highly sensitive cTnI assay provides an excellent prognostic negative predictive value and thus, plays a role in identifying patients at low risk for adverse events who may be considered for out-of-hospital management of acute PE. The prognostic value of cTnI is incremental to clinical, ECG, and radiographic data. These findings support the implementation of cTnI as a pivotal risk stratification tool in acute PE.

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