

Single Cardiac Troponin T Measurement Predicts Risk for Adverse Outcome in Decompensated Heart Failure

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Abstract

Background: The slight increase in cardiac troponin in the blood of patients with heart failure (HF) suggests that myofibrils are degraded in the myocardium and released in the circulation, reflecting a continuous and progressive injury process in the contractile system.

Objective: To correlate the serum levels of cardiac troponin T (TnT) at the hospital admission of patients with decompensated HF and prognosis.

Methods: A total of 79 consecutive patients, hospitalized due to decompensated HF, with LVEF \leq 45%, were included in the study. Patients were followed for 8 months. We excluded patients using intravenous inotropic agents, as well as those with acute coronary syndrome, pulmonary thromboembolism, creatinine levels $>$ 2.5 mg%, liver failure, or neuromuscular diseases.

Results: High levels of TnT (\geq 0.02 ng/ml) were detected in 37 patients (46.84%). The global mortality was 35.4%. In the groups with high TnT and low TnT levels ($<$ 0.02 ng/ml) there were, respectively, 19 versus 9 deaths (RR=2.4; 95%CI 1.24-4.63; $p=0.011$), 5 versus 4 heart transplants (RR=1.42; 95%CI 0.41-4.89; $p=0.73$), 11 versus 7 patients needed IV inotropic agents (RR=1.78; 95%CI 0.77-4.12; $p=0.26$) and 14 versus 10 patients were re-hospitalized (RR=1.85; 95%CI 0.95-3.6; $p=0.10$). Mean troponin levels were significantly higher in those individuals who died (0.071 ± 0.119 vs 0.032 ± 0.046 ; $p=0.004$). At the multivariate analysis, the persistence of the third sound and the need for IV inotropic agents showed to be independent predictors of death; however, we observed a higher tendency towards mortality for patients presenting high TnT when compared to those with low troponin levels (HR=2.64; 95%CI 0.91-7.63; $p=0.07$).

Conclusion: The single troponin measurement at hospital admission in patients with decompensated HF predicts adverse outcomes and should be considered at the early stratification of long-term morbimortality. (Arq Bras Cardiol 2010; 94(4):495-501)

Key words: Heart failure; prognostic; troponin T/administration & dosage.

Introduction

The deterioration process of chronic heart failure (HF) normally includes several hospitalizations due to acute decompensations. In this context, myocardial cells are probably lost due to apoptosis and necrosis, which contributes to the evolution of myocardial dysfunction^{1,2}. Clinical studies in unstable angina^{3,4} using cardiac troponin, a highly sensitive marker that is specific for cardiomyocyte lesions, have shown that patients with slight increased levels, but lower than those found in acute myocardial infarction, presented a worse prognosis when compared to those that presented values that were persistently within the normal range. These patients benefit from a more aggressive therapeutic approach with low-molecular weight heparin,

use of IIb-IIIa glycoprotein and more invasive strategies, such as early coronary angiography and myocardial revascularization procedures. Similarly, several studies have evaluated the role of serum levels of cardiac troponin in HF⁵⁻²¹ and tried to correlate them with the disease prognosis, demonstrating that the serum levels of these markers were high in a high number of patients with decompensated heart failure (DHF) and could function as predictors of morbimortality of this syndrome. The objective of the present study is to investigate whether the serum levels of cardiac troponin T (TnT) \geq 0.02 ng/ml at a single measurement at hospital admission can correlate with an adverse prognosis in patients with DHF.

Methods

Patients

This is a prospective cohort study in patients hospitalized due to DHF, followed for 8 months. The study included 79 consecutive patients hospitalized due to DHF at 3 general

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hospitals, namely the IC Unit and Cardiac Transplant of Clinica Cardiologica do Hospital Felício Rocho-BH, the Infirmary of the Internal Medicine Clinic of Hospital Odilon Behrens-BH and the Infirmary of the Internal Medicine Clinic of Hospital Joao XXIII-BH, from March 2003 to March 2004.

The study was approved by the Ethics Committee in Research of the institutions. The patients agreed to participate in the study and signed the Free and Informed Consent Form.

The inclusion criteria were: hospitalization due to DHF, no intravenous inotropic agent use until the blood collection was performed, aged 18 and older, left ventricular ejection fraction (LVEF) $\leq 45\%$ and signing the agreement to participate in the study. The diagnosis of HF at hospitalization was carried out through clinical and radiological data, using the Boston criteria²² to define HF and Stevenson's criteria for the clinical-hemodynamic classification²³.

The exclusion criteria included LVEF $> 45\%$, acute phase of coronary diseases, creatinine levels > 2.5 mg%, use of intravenous inotropic agents before the blood collection for cardiac TnT analysis, age < 18 years, other comorbidities such as pulmonary diseases with pulmonary hypertension, suspected pulmonary thromboembolism, liver failure and neuromuscular or inflammatory diseases. Patients with cardiac valvular diseases with barrier characteristics, such as mitral and aortic stenosis were also excluded.

Definition of outcomes and follow-up

The primary outcome was mortality due to all causes, cardiac transplant and re-hospitalization due to DHF. The mechanism of cardiovascular death was defined as progressive HF and sudden death. The secondary outcomes were arterial hypotension (SAP < 90 mmHg or SAP-DAP \div SAP $< 25\%$)²³ with the need for inotropic drugs, persistent hyponatremia for more than 7 days ($\text{Na}^+ \leq 130$ meq/l) and persistence of the third heart sound for more than one week.

The patients were followed for a period of 8 months, with visits to the outpatient clinic at 2, 5 and 8 months. Patients that could not be examined by the researchers were contacted by telephone or the contact was made with the patients' family members or respective assistant physicians.

Aspects related to biochemical and echocardiographic assessment

Blood was collected during the first 120 hours after hospitalization. TnT measurements were carried out by clinical pathologists who were blinded to the identity of the patients, the clinical pictures and the outcomes of interest. Third-generation Troponin-T-STAT (Short-Turn-Around-Time), Elecsys™, Roche-Diagnosis, was used to measure troponin, which has a capacity to detect 0.01 to 25.0 ng/ml. Values below the lower detection limit were indicated as < 0.01 ng/ml.

Biochemical assessments such as urea, creatinine, ionogram and hemogram were carried out in all patients and compared between the groups.

The echocardiographic measurements were also analyzed. In addition to LVEF, the dimensions of the left atrium (LA), the left ventricular-end systolic diameter (LVESD), the left

ventricular-end diastolic diameter (LVEDD) and the LV-end systolic and diastolic volumes were also studied.

Statistical analysis

The data were analyzed using the Epi-Info program (CDC-Atlanta) release 3.2 of February 2004. For the calculation of the sample, an alpha error of 5% was considered, as well as a beta error of 20%, with a prevalence of cardiac troponin increase (≥ 0.02 ng/ml) in the group with DHF of a minimum of 20% and a maximum of 50%.

Qualitative variables were expressed through the relative and percentage values and the difference between the groups with or without cardiac TnT increase was assessed by Chi-square and Fisher's tests. The continuous variables were presented as means and standard deviations and the ANOVA and Kruskal-Wallis tests were applied to compare the groups according to the presence or not of parametric samples, respectively. The level of significance was set at $p < 0.05$. Relative risk was used to verify the association between TnT and the outcomes of interest. The Cox regression model was used for the multivariate analysis and the association of variables that were related with death were evaluated, considering a p value of up to 20%, the hazard ratio (HR) and the 95% confidence interval (95%CI). The survival curve for both groups was estimated using the Kaplan-Meier method and compared through the log-rank test.

To determine the cutoff of the TnT measurement that would be related with the death outcome, the 0.02 ng/ml value was submitted to the ROC curve, using the SPSS program (Chicago-Illinois), release 10.0.

Results

Characteristics at hospitalization of patients with DHF and their association with serum levels of cardiac TnT

The general characteristics of the patients with DHF are shown in Table 1. The mean level of cardiac TnT was 0.0046 ± 0.0081 ng/ml. Thirty-seven (46.84%) patients presented high cardiac TnT levels (TnT ≥ 0.02 ng/ml) and 42 presented low levels (TnT < 0.02 ng/ml). The groups did not show a statistically significant difference regarding the sex, age, hemodynamic profile, SAP, DAP and heart rate variables. Seventy-eight patients presented 8 or more Boston criteria for the diagnosis of Heart Failure (definitive diagnosis of HF) and only one presented 7 criteria only (possible diagnosis of HF). All individuals with high TnT levels presented definitive criteria for HF.

Regarding the hemodynamic profile of the DHF at hospital admission (Stevenson's classification), 64 patients (81%) presented in quadrant "B" (with congestion and absence of low perfusion), 3 (3.8%) in quadrant "L" (no congestion and low perfusion) and 12 in quadrant "C" (with congestion and low perfusion).

The comorbidities identified in the decompensated patients were smoking, alcoholism and thyroid disease, with no statistically significant differences between the groups. Atrial fibrillation and atrioventricular conduction dysfunction were observed in 18 (25.31%) and 58 (73.41%) patients, respectively.

The types of medication used at the hospital admission

Table 1 - Characteristics at hospitalization of 79 patients with decompensated heart failure (DHF) according to cardiac troponin-T (TnT) levels

Characteristics	TnT > 0.02 ng/ml (n=37)	TnT < 0.02 ng/ml (n=42)	p
Male sex (%)	70.3	52.3	0.16
Age (years)	57.08±18.35	53.90±16.74	0.42
Hemodynamic criterion (n)			
B	28	36	0.39
L	1	2	1.00
C	8	4	0.23
SAP (mmHg)	117±24	118±25	0.82
DAP (mmHg)	75±16	80±16	0.23
Heart rate (bpm)	90±25	88±18	0.68
Echocardiographic measures			
LVEF (%)	25.78±6.44	28.11±7.76	0.15
Left atrium (mm)	48.94±6.32	47.42±6.75	0.32
LVESD (mm)	59.08±10.33	58.03±10.95	0.67
LVEDD (mm)	67.89±10.17	67.68±10.98	0.93
Biochemical analyses			
Hemoglobin (g%)	13.28±1.59	12.93±1.85	0.33
Global leukocytes (mm ³)	7.455±2.815	7.599±2.318	0.82
Creatinine (mg%)	1.41±0.39	1.17±0.35	0.004
Sodium (meq/l)	133.24±5.52	135.52±5.76	0.07
Potassium (meq/l)	4.10±0.39	4.08±0.51	0.07
Etiologies (n)			
Hypertensive	7	9	0.91
Dilated cardiomyopathy	5	10	0.38
Ischemic	6	8	0.97
Chagas' disease	9	4	0.14
Alcohol	3	2	0.88
Valvular	2	3	1.00
Peripartum	1	2	1.00
Diabetes mellitus	0	1	1.00
Post-chemotherapy	0	1	1.00
Miscellaneous	4	2	0.41

SAP - systolic arterial pressure; DAP - diastolic arterial pressure; LVEF - left ventricular ejection fraction; LVESD - left ventricular end systolic diameter; LVEDD - left ventricular end diastolic diameter.

were angiotensin-converting enzyme inhibitors (ACEI) by 58 (73.4%), digitalis by 40 (50.6%), aldosterone antagonists by 38 (48.1%) and beta-blockers by 14 (17.7%) patients. The proportion of these specific drugs was similar in the two groups, with no statistical difference.

The mean left ventricular ejection fraction (LVEF) was

27.02% and most patients (75/94.9%) presented LVEF < 40% with only one patient presenting a LVEF = 44%. When the mean LVEF was analyzed in the groups, the group with low (28.11±7.76%) and high (25.78±6.44%) cardiac TnT levels, no statistically significant difference was observed between them (p=0.15). The same occurred with the analysis of the left atrium (LA) measurements, the left ventricular-end systolic diameter (LVESD) and the left ventricular-end diastolic diameter (LVEDD), as well as the analysis of serum levels of hemoglobin, leukocytes, sodium and potassium. The mean serum creatinine levels were higher in the group of patients with cardiac TnT ≥ 0.02 ng/ml (1.41±0.39 versus 1.17±1.85, p=0.004).

Regarding the etiologies, there was no statistical difference between the groups with low and high TnT levels. The main HF etiology was hypertension, followed by idiopathic dilated cardiomyopathy, ischemic and Chagasic etiologies.

Association between the serum levels of cardiac troponin T and clinical outcomes

The adverse events were more often observed in patients with high levels of cardiac TnT. There were 28 cardiovascular deaths (19 deaths due to refractory HF and 9 sudden deaths) during the follow-up, which corresponds to a mortality rate of 35.4%, with 19 deaths in the group with high TnT and 9 in the group with low TnT (RR=2.40; 95%CI: 1.24-4.63, p=0.011). There was no statistically significant difference between the groups regarding the re-hospitalization, the risk of heart transplant, arterial hypotension with the need for intravenous inotropic agents and persistent hyponatremia for more than one week (Na⁺ ≤ 130 meq/l). Patients with high levels of TnT presented a higher risk (RR=1.94; 95%CI: 1.23-3.08; p=0.005) of persistent third sound for more than one week and this finding was observed in 39 patients, 25 of which (64.1%) belonged to the group with high-troponin levels (Table 2).

The analysis of the Kaplan-Meier curve showed that the probability of survival was lower in the group with high troponin levels (log-rank, p=0.007), which highlighted the curve divergence since the beginning of the study (Fig.1). The HF etiology was not associated with the increased risk of death in the studied cohort, even when it was stratified for high or low TnT. It is noteworthy the fact that the Chagasic etiology contributed with 13 patients, 9 of which (69%) presented high TnT levels, with 6 deaths in this group, but no increased risk when compared to Chagasic patients with low TnT (Table 3).

ROC curve analysis

The cutoff of TnT measurement for death was 0.02ng/ml, with an area under the ROC curve of 69.7% (95%CI: 0.577-0.816), with a sensitivity of 67% and specificity of 66% (Fig.2). The area under the curve for the combined outcomes of death and transplant, for the same cutoff, was 67.4% (95%CI: 0.533-0.795).

Serum concentrations of TnT in hospitalized patients with DHF and their effect on the studied outcomes

The mean serum concentrations of cardiac TnT at hospital admission was higher in patients that died during the follow-up. Similarly, the mean concentrations were higher in patients that

Table 2 - Association between high levels of cardiac troponin-T with the outcomes of interest in patients with DHF

Outcomes	Total n (%)	TnTc > 0.02 ng/ml n (%)	TnTc < 0.02 ng/ml n (%)	Relative risk	95% CI	p
Death	28 (35.4)	19 (67.9)	9 (32.1)	2.40	1.24-4.63	0.011
Heart transplant	9 (11.4)	5 (55.5)	4 (45.5)	1.42	0.41-4.89	0.73
Re-hospitalizations	24 (30.4)	14 (58.3)	10 (41.7)	1.85	0.95-3.60	0.10
Hypotension/use of inotropic agents	18 (22.9)	11 (61.1)	7 (38.9)	1.78	0.77-4.12	0.26
Hyponatremia-persistent	21 (26.6)	13 (61.9)	8 (38.1)	1.85	0.87-3.95	0.17
B3-persistent	39 (49.4)	25 (64.1)	14 (35.9)	1.94	1.23-3.08	0.005

Table 3 - Risk of death during the follow-up (8 months) according to the HF etiology in 37 decompensated patients, with cardiac TnT levels ≥ 0.02 ng/ml at the hospitalization

Etiology(n)	TnTc > 0.02 ng/ml (n)	Deaths n (%)	RR (IC 95%)	p
Hypertensive (16)	7	5(71)	1.53 (0.84-2.80)	0.40
Dilated idiopathic (15)	5	2(40)	1.20 (1.44-2.77)	1
Ischemic (14)	6	3(50)	0.97 (0.41-2.31)	1
Chagas' disease (13)	9	3(33)	0.58 (0.22-1.55)	0.26
Alcohol (5)	3	1(33)	0.63 (0.12-2.2)	0.60
Valvular (5)	2	1(50)	0.97 (0.23-2.77)	1
Peripartum (3)	1	1(100)	2 (1.44-2.77)	1
Diabetic (1)	0	0	-	-
Actinic (1)	0	0	-	-
Miscellaneous (6)	4	2(50)	0.97 (0.34-2.73)	0.97
Total (79)	37	18(48.6)		

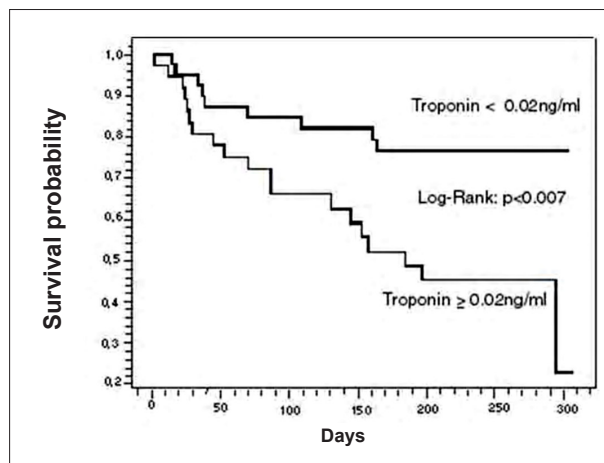


Figure 1 - Kaplan-Meier Curve for death.

were submitted to heart transplant or died (combined outcome), in those who persisted with the third sound and in those that presented hyponatremia for more than one week. The TnT concentrations were not statistically different between patients that received heart transplants and the ones that did not, as well as in those that developed or not arterial hypotension, with the subsequent need for intravenous inotropic agents (Table 4).

Cox model for the analysis of survival

The proportional Cox model was used to analyze the variables related with the risk of death, if these variables reached statistical significance ($p \leq 0.20$) at the univariate analysis. Ten variables were selected: cardiac TnT ≥ 0.02 ng/ml (HR=2.86; $p=0.009$), hyponatremia (HR=2.31; $p=0.03$), persistence of the third sound (HR=3.89; $p=0.008$), LVEF $\leq 27\%$ (HR=1.9; $p=0.09$), systemic arterial hypotension that needed intravenous inotropic agents (HR=3.6; $p=0.002$), increase in creatinine levels (HR=1.7; $p=0.14$), LVEDD >

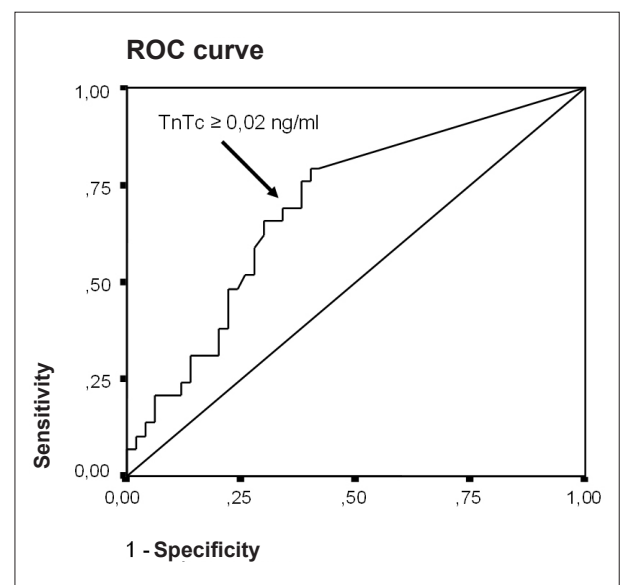


Figure 2 - ROC curve (receiver operating curve) to estimate the serum level cutoff of death-related cardiac troponin T (TnT) to determine the risk of death due to HF.

Table 4 - Serum levels of cardiac troponin-T in hospitalized patients with DHF and their association with outcomes of interest

	TnT levels (ng/ml)		p value
	Yes	No	
Death	0.071±0.119	0.032±0.046	0.004
Heart transplant	0.028±0.024	0.048±0.086	0.891
Tx combined with death	0.061±0.105	0.033±0.050	0.005
Re-hospitalizations	0.045±0.054	0.046±0.096	0.153
Hypotension and use of IV inotropic agents	0.037±0.045	0.048±0.089	0.50
Hyponatremia	0.073±0.132	0.036±0.051	0.037
B3-persistent	0.057±0.101	0.037±0.060	0.009

Tx - heart transplant.

69 mm (HR=2.1; p=0.06), LVESD > 58 mm (HR=2.3; p=0.04), use of aldosterone antagonists (HR=1.86; p=0.11) and age > 59 years (HR=0.57; p=0.14). The etiology of the cardiomyopathy, the left atrium diameter (\geq 49 mm), the presence of diabetes mellitus and the use of ACEI and beta-blockers did not reach statistical significance.

In the final model, the persistence of the third sound (HR=2.9; 95%CI: 1.001-8.447; p=0.049) and the need for intravenous inotropic agents (HR=2.6; 95%CI: 1.06-6.43; p=0.036) emerged as independent predictors of death; however, we observed a tendency towards higher mortality among patients with cardiac TnT \geq 0.02 ng/ml when compared to those with TnT < 0.02 ng/ml (HR=2.64; 95%CI: 0.91-7.63; p=0.07).

Discussion

This study corroborates the evidence of myocardial cell loss in patients with DHF without acute coronary disease. The observation of the slight increase of cardiac TnT in a single blood sample was associated with the increased risk of adverse events in the eight months following hospitalization. The high level of cardiac TnT was a marginal predictor of death in the long term, and, in spite of its statistical value (p=0.072), the cardiac TnT measurement can be considered a predictor of the risk of death in patients with DHF. This statistically borderline value probably reflects the small sample size.

Similar findings in previous studies have been observed in outpatients with compensated HF⁵⁻¹² and in hospitalized patients with decompensated HF¹³⁻²¹, with a large variability among the techniques used to measure cardiac troponin, as well as the cutoffs associated with the studied outcomes. The present study did not use seriate measurements of troponin, thus differing from others that used a cutoff identical to ours, such as Sato et al¹⁰ and Del Carlo et al¹⁵, which demonstrated an association between high TnT and adverse cardiac events at short and long-term. Recently, Perna et al²⁰ reported that the cardiac TnT at hospital admission was an independent predictor, associated with an increased risk of death or hospitalization,

differently from the measurement carried out at the hospital discharge. The present study did not use seriate samples and it was observed that a single cardiac troponin measurement carried out within 120 hours after hospitalization due to DHF was associated with the risk of death in the following 8 months. We also observed that the increase in this marker was associated with the risk of developing the persistence of the third heart sound, which, in turn, has a prognostic role that has been previously documented in HF²⁴.

Differently from most studies with DHF that did not mention the use of intravenous inotropic agents, we excluded patients using these drugs before the blood collection for the measurement of this marker. These were patients with low systemic output that needed these drugs even at the emergency room. The reason for excluding these patients is the potential of these drugs to worsen the subendocardial coronary perfusion, increasing heart rate and the myocardial oxygen consumption, leading to ischemia and death of the myocyte and consequently increasing the serum levels of cardiac TnT^{25,26}.

Homogeneity of the study groups

The patients from the groups with high and low TnT did not present a statistically significant difference regarding sex, age, HF severity and medication at hospitalization. Some authors demonstrated a predominance of the ischemic etiology in their populations^{5,12}. However, in the present study, there was no predominance of the ischemic etiology, which corresponded to only 17.7% of the causes, with no statistically significant difference between the groups.

The study by Horwich et al⁸ showed a predominance of the population with ischemic HF (50%) when compared to dilated cardiomyopathy (33%); however, the troponin was detected in 48% of those with ischemic disease and in 52% of those with dilated cardiomyopathy. Similarly, Ishii et al¹⁴ observed comparable concentrations of cardiac troponin T and I in patients with ischemic and non-ischemic etiologies. The hypothesis that the continuous death of myocytes would have an important role in the physiopathology of HF, regardless of the presence or not of coronary disease, is also corroborated by the study of Logeart et al²⁷, which only studied patients with non-ischemic cardiomyopathy and did not observe more significant alterations in ventricular remodeling and a higher level of BNP in the group with higher troponin levels. In the ADHERE registry, Peacock et al²¹ defined as high levels > 0.1µg/l for cardiac troponin T and > 1.0µg/l for cardiac troponin-I at hospital admission, occurring in 6.2% patients and associated with a higher rate of intrahospital mortality rate. When the troponin was assessed as a continuous variable, higher levels were also associated with higher mortality rates. Although the ischemic etiology did not discriminate the troponin "status" and was not a predictor of mortality, most patients from both groups presented coronary disease or risk factors for this disease.

In spite of the several studies on the role of the cardiac troponins in HF, there is no record of these markers in HF caused by Chagasic cardiopathy. In the present study, although it was not the objective of the study design, it was demonstrated that the proportion of patients with cardiac TnT

was higher among Chagas patients, although that did not implicate in a higher risk of death.

Our analysis did not show any significant differences regarding the presence of comorbidities and, similarly to the study by Ishii et al¹⁴, the treatment with beta-blockers, digitalis and ACEI at hospital admission did not differ between the groups with high and low troponin levels. Differently, the study by Perna et al¹⁷ observed, with statistical difference, a higher number of patients with high cardiac TnT levels using ACEI and nitrates, before and after hospitalization. Horwich et al⁸ also observed, at the first assessment of their patients, a higher incidence of ACEI use in the group with high troponin levels; however, the use of beta-blockers was similar in those with high and normal troponin levels. Nevertheless, during the follow-up, the use of beta-blockers was associated with significantly lower rates of mortality, when compared to those that did not receive this type of medication.

Some authors observed the association and sometimes, the correlation, between the increase in troponin levels and left ventricular dysfunction. Our results did not reproduce the findings of these authors^{5,7,13} that detected a negative correlation between the serum level of this marker and the LVEF of these patients with HF. Horwich et al⁸ found similar LVEF values at the beginning of the study of patients with low and high TnI; however, at the six-month follow-up, the group with high TnI showed a higher tendency towards the development of ventricular deterioration, with statistical significance.

In the present study, we did not observe statistically significant differences regarding the LVEF between the groups with high and low cardiac TnT levels. The same observations were reported by Setsuta et al⁶ and Logeart et al²⁷, who also observed a lack of association between the LVEF and the troponin levels at the hospital admission of patients with DHF.

Horwich et al⁸ and Perna et al^{12,16,17} did not observe differences in creatinine levels regarding the troponin measurements. The present study showed a higher mean serum creatinine in patients with increased troponin levels, with a statistically significant difference, a finding that can be explained by the higher level of hemodynamic, neurohormonal and catabolic involvement of the patients in this group. However, the kidney dysfunction was not a predictor of the death outcome at the multivariate analysis.

The lack of significant differences between the groups of the present study supported our findings that higher cardiac TnT levels predict a worse prognosis and has a discriminating characteristic, regardless of other factors, such as the ischemic etiology, the use of beta-blockers, kidney involvement and the deterioration of the left ventricular function.

TnT measurement cutoff

Although the serum levels of troponin were quite lower than those found in patients with AMI, the measurement of this myocardial cell injury marker is simple and can be a quite useful prognostic method in HF. However, it is necessary to better define the available techniques, as there is a great variability among the cutoffs and their associations with the outcomes.

Missov et al⁹, in their first report of the detection of cardiac troponin elevation in patients with HF, used a more sensitive

technique, with the capacity to measure in picograms (10^{-12} g) per milliliter. As in previous studies^{8,11,12,15}, we used a third-generation technique to measure the troponin; however, this technique has a capacity to measure in nanogramas per milliliter (10^{-9} g). Wallace et al²⁸ estimated the prevalence of cardiac TnT in the general population as 0.7% and suggested that the upper limit of the normal range would be 0.01ng/ml. A cardiac TnT cutoff of 0.02 ng/ml was previously used in the literature in HF studies^{15,29}, which corresponds to twice the value observed in normal individuals²⁸. According to our results, this cutoff corresponded to the area under the ROC curve of 67.9%, with a sensitivity of 68% and a specificity of 64%, for the prediction of the death outcome, corroborating previously published data^{15,29}.

Study limitations

Although the sample had the statistical power calculated to show differences between the groups, the confidence intervals of the results at the multivariate analyses were broad, demonstrating the need for a larger sample size.

The evaluation of re-hospitalization was influenced by other factors that are not solely related with the severity of the patients' disease. Potential confounding factors for its measurement include the socioeconomic level, the access to medical services, availability of medication and family support. Thus, the re-hospitalization rates might have been underestimated, in situations that involved other hospital environments or even in the hospitals participating in the study.

Conclusion

The increase in cardiac TnT was highly prevalent (46.8%) in patients with DHF at hospital admission. The increase in cardiac TnT ≥ 0.02 ng/ml, in a single measurement performed up to 5 days of hospitalization, increased the risk of death by 2.4-fold during the following 8 months and can be considered a predictor of mortality in this population. An important aspect of the present study is the role of this marker of cellular injury as a prognostic predictor and collaborator in the risk stratification of patients with HF, mainly those that are hospitalized due to decompensation. However, additional studies are necessary to define detection techniques for troponin levels with a broad diagnostic window, high sensitivity and specificity, as well as a cutoff that can really determine the level of myocardial injury that will correlate with risk.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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