Profile of patients with acute heart failure and elevated troponin I levels

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BACKGROUND: Elevation of troponin I (TnI), a sensitive marker of myocardial cell injury, has been described in a portion of patients with chronic heart failure and acute decompensated heart failure. The proportion and characteristics of patients with TnI elevation in an unselected population with acute left heart failure (AHF) are, however, not known.

PATIENTS AND METHODS: One hundred five consecutive patients with AHF as the leading diagnosis were included in the present study. TnI was routinely assessed at admission and 12 h to 24 h later. Patients with TnI 0.5 µg/L or greater (TnI+ group) and TnI less than 0.5 µg/L (TnI– group) were compared from demographic and clinical points of view.

RESULTS: TnI elevation was detected in a total of 28 patients with AHF (26.7%). The TnI+ patients had a significantly higher entry Killip stage (P<0.0001), lower time from onset of symptoms (P=0.002), higher baseline heart rate (P=0.003) and creatinine level (P=0.002), and lower body mass index (P=0.03). On the other hand, the TnI+ group did not differ from TnI– patients in demographic and some clinical parameters, such as age, sex, blood pressure, history of coronary artery disease, major electrocardiograph parameters and left ventricular ejection fraction.

CONCLUSIONS: TnI elevation was present in a substantial portion of unselected patients with AHF as the leading clinical diagnosis. Moreover, TnI+ patients differed from those with normal TnI in several clinical parameters.

Key Words: *Acute heart failure; Killip stage; Troponin I*

Heart failure is a significant cause of mortality and hospitalization worldwide. Both de novo acute left heart failure (AHF) and decompensated chronic heart failure can be induced and/or triggered by several different factors (acute coronary syndrome, hypertensive crisis, acute arrhythmia, valvular disease, myocarditis, volume overload, septicemia, etc) (1,2). Other probable factors in the pathogenesis of AHF include activation of the sympathetic nervous system, tachycardia, hypertension and ischemia.

Elevated serum levels of cardiac troponins (Tn) T and I, sensitive markers of myocardial cell injury, have been repeatedly detected in some patients with heart failure (3-5). Tn elevation is connected with worse prognosis in chronic heart failure, as has been described by different authors (6-9). Recently, this relationship has been proven for TnT and AHF (10-12). The precise mechanism of myocardial damage as detected by increased levels of Tn is still unclear. Some authors speculate elevated Tn is related to the extent of ventricular remodelling (13). Although coronary artery disease is often present in AHF (2,14-16), an acute coronary event is probably responsible for only some of these patients. Other possible causes of ischemia/hypoxia are volume/pressure overload or gas-exchange failure with global hypoxia.

Data dealing with the Tn elevation in unselected patients with AHF (including de novo AHF) are, unfortunately, very scarce. Furthermore, very little is known about the changes of TnI in AHF because the majority of studies have used TnT (10,12,13). The aim of our study was, therefore, to determine the rate of TnI elevation in unselected patients with AHF, and to describe possible differences in their demographic and clinical profile.

METHODS

Patient population

Medical record data from consecutive patients with AHF, admitted to University Hospital Kralovske Vinohrady between January and October 2006, were analyzed retrospectively. AHF as the leading diagnosis was the only inclusion criterion (ie, patients with acute coronary syndrome as the main diagnosis were not included); no specific exclusion criteria were defined. All records were reviewed for confirmation of diagnosis, however, none were excluded. Patients were then divided into two groups according to the TnI level (measured routinely at admission and 12 h to 24 h later): 0.5 µg/L or greater in either or both samples (TnI+ group), and both samples less than 0.5 µg/L TnI (TnI– group).

Study design

Groups were compared according to several demographic characteristics (age, sex, body mass index [BMI], smoking status), history of noncardiac disease (diabetes, hypertension, dyslipidemia, chronic obstructive pulmonary disease, thyroid disease), history of cardiac disease (history of ischemic heart disease, percutaneous coronary intervention, coronary artery bypass graft, pacemaker implantation, heart failure, time from

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TABLE 1
Demographic data and history of noncardiac diseases

	Troponin I+ n=28	Troponin I– n=77	P
Age, years	76.14±1.98	74.75±1.30	0.57
Female, n (%)	13 (46.4)	39 (50.6)	0.83
BMI, kg/m^2	25.64±0.79	28.13±0.63	0.03
Smoker, n (%)	16 (57.1)	36 (46.8)	0.38
Diabetes, n (%)	15 (53.6)	38 (49.4)	0.83
Hypertension, n (%)	20 (71.4)	56 (72.7)	1.00
Dyslipidemia, n (%)	11 (39.3)	10 (13.0)	0.005
COPD, n (%)	15 (53.6)	26 (33.8)	0.07
Thyroid disease, n (%)	6 (21.4)	21 (27.3)	0.62

Data are expressed as means ± SEM for continuous variables and absolute (and relative) frequencies for categorical variables. P<0.05 was considered to be statistically significant. BMI Body mass index; COPD Chronic obstructive pulmonary disease; + Positive; – Negative

TABLE 2
History of cardiac diseases

	Troponin I+ n=28	Troponin I– n=77	P
Decompensation	3.96±1.31	16.60±2.32	0.002
Heart disease	2.00±0.62	3.71±0.54	0.08
IHD, n (%)	16 (57.1)	36 (46.8)	0.38
PCI or CABG, n (%)	8 (28.6)	12 (15.6)	0.16
PM, n (%)	4 (14.3)	7 (9.1)	0.48
History of HF, n (%)	9 (32.1)	33 (42.9)	0.37

Data are expressed as means ± SEM for continuous variables and absolute (and relative) frequencies for categorical variables; P<0.05 was considered to be statistically significant. Decompensation, time from the onset of symptoms in days; Heart disease, time from the diagnosis of the first cardiac disease in years. CABG Coronary artery bypass graft; HF Heart failure; IHD Ischemic heart disease; PCI Percutaneous coronary intervention; PM Permanent pacemaker; + Positive; – Negative

onset of symptoms, time from the first heart disease diagnosis), major clinical findings (Killip stage, blood pressure, heart rate, pleural effusion, hemoglobin and serum creatinine levels, and length of hospitalization), and finally in major electrocardiograph (ECG) and echocardiographic (ECHO) data.

Definitions

For the review of medical records, AHF was defined as dyspnea at rest or with minimal exertion or shock, and the presence of at least one of the following: S3 gallop, pulmonary rales, x-ray proof of pulmonary congestions or pulmonary capillary wedge pressure greater than 25 mmHg. The severity of AHF was estimated using Killip classification (17): stage 1 – no heart failure, stage 2 – heart failure, stage 3 – pulmonary edema, stage 4 – cardiogenic shock; the mean Killip stage was calculated for each group. For the blood pressure and heart rate data, the earliest values recorded at admission were analyzed. Decompensation was defined as the time (in days) from the first symptoms of AHF to admission. History of any cardiac disease was defined as the presence of any documented significant heart abnormality and the time (in years) from the first detection to admission was calculated. The admission 12-lead ECG summaries and results of ECHO performed within 48 h of admission were analyzed; if more than one was performed, the first was analyzed. For the mitral regurgitation severity assessment, the semiquantitative method according to Miyatake et al (18) was used and the mean for each group was calculated. For the other possible valve disorders, only moderate to severe diseases were registered and classified.

TnI measurement

The first blood samples for TnI assessment were taken routinely at admission; the second samples 12 h to 24 h later. The samples were immediately transferred to the local laboratory and TnI levels were determined by an automated monoclonal antibody solid phase enzyme immunoassay (IMMULITE Turbo Troponin I using IMMULITE analyzer, DPC, USA).

Statistical analysis

Mean ± SEM were calculated for continuous variables and absolute and relative frequencies for categorical variables. Comparison between groups was performed with unpaired Student's *t* test for continuous variables and Fisher's exact test for categorical variables. P<0.05 was considered to be statistically significant in all analyses.

RESULTS

The study population comprised 105 patients with AHF: 42 patients (40%) had a history of heart failure and 70 patients (66.7%) had a history of any cardiac disease. Elevated levels of TnI were detected in 28 patients with AHF (26.7%), and the remaining 77 patients (73.3%) had both TnI samples within the normal range.

With respect to the demographic characteristics and history of noncardiac disease, patients with high and normal TnI were of similar age and had similar proportions of females, smokers, history of diabetes, hypertension, chronic obstructive pulmonary disease and thyroid disease. On the other hand, lower mean BMI and less dyslipidemia were observed in the TnI+ group (Table 1). There was no difference in the presence of a history of ischemic heart disease or heart failure between TnI+ and TnI– groups, and rates of previous percutaneous coronary intervention, coronary artery bypass graft and pacemaker implantations were also comparable. Moreover, the time from the first diagnosis of cardiac disease was not significantly different between the groups; duration of acute decompensation was, however, significantly shorter in the TnI+ group (Table 2).

As far as the clinical findings are concerned, TnI+ patients had more severe AHF (according to the mean Killip stage), higher entry heart rate and higher creatinine level. On the other hand, entry blood pressure, incidence of pleural effusion, mean hemoglobin level, length of hospitalization, and suspected causes or precipitating factors of AHF were comparable in both groups (Table 3). No significant differences were observed in the presence of valvular heart disease, mean left ventricle ejection fraction, incidence of pericardial effusion or major ECG findings (ST-depression, negative T waves, pathological Q waves, and left or right bundle branch block) (Table 4).

DISCUSSION

The major observations of our study are that a substantial proportion of an unselected population with AHF as the leading diagnosis had elevated TnI, and that individuals with elevated TnI differed in several major characteristics.

TABLE 3
Clinical data at admission

	Troponin I+ n=28	Troponin I– n=77	P
Killip stage	2.64±0.13	2.10±0.05	<0.0001
SBP (mmHg)	153.4±8.8	146.4±3.9	0.40
DBP (mmHg)	85.2±4.0	82.4±1.9	0.49
HR (beats/min)	113.0±4.7	95.0±3.1	0.003
Pleural effusion	23 (82.1)	58 (75.3)	0.60
Hemoglobin (g/L)	124.0±4.3	127.0±2.4	0.45
Creatinine (µmol/L)	146.5±19.9	104.3±3.9	0.002
Hospitalization (days)	10.3±1.1	9.7±0.7	0.67
Hypertensive crisis	5 (18)	18 (23)	0.61
Severe aortic valve stenosis	4 (14)	7 (9)	0.48
Moderate to severe mitral valve regurgitation	9 (32)	36 (47)	0.26
Acute arrhythmia	5 (18)	17 (22)	0.79
Lack of compliance with medical treatment	0 (0)	2 (3)	1.00
Acute infection	3 (11)	7 (9)	0.72

Data are expressed as means ± SEM for continuous variables and absolute (and relative) frequencies for categorical variables; P<0.05 was considered to be statistically significant. DBP Diastolic blood pressure; HR Heart rate; SBP Systolic blood pressure; + Positive; – Negative

TABLE 4
Selected electrocardiograph and echocardiographic findings

	Troponin I+ n=28	Troponin I– n=77	P
Electrocardiograph			
ST depression	5 (17.9)	10 (13.0)	0.54
Negative T waves	19 (67.9)	42 (54.5)	0.27
Pathological Q waves	5 (17.9)	4 (5.2)	0.05
Left bundle branch block	4 (14.3)	14 (18.2)	0.77
Right bundle branch block	3 (10.7)	6 (7.8)	0.70
Echocardiography			
LVEF (%)	35.0±2.7	39.2±1.8	0.22
MR	1.6±0.1	1.9±0.1	0.10
MS	0 (0)	1 (1.3)	1.00
AR	5 (17.9)	18 (23.4)	0.61
AS	7 (25)	18 (23.4)	1.00
PH	19 (67.9)	55 (71.4)	0.81
Pericardial effusion	7 (25)	17 (18.2)	0.42

Data are expressed as means ± SEM for continuous variables and absolute (and relative) frequencies for categorical variables; P<0.05 was considered to be statistically significant. AR Moderate to severe aortic regurgitation; AS Moderate to severe aortic stenosis; LVEF Left ventricular ejection fraction; MR Mitral-valve regurgitation expressed as mean grade assessed by a semi-quantitative method (1+ to 4+); MS Moderate to severe mitral stenosis; PH Signs of pulmonary hypertension; + Positive; – Negative

The population analyzed in the present study had different causes of heart failure, based on the inclusion criterion of 'AHF as the leading diagnosis'. Excluded were all patients with AHF induced by acute coronary syndrome with ST elevation, the majority of individuals with AHF caused by acute coronary syndrome without ST elevation, and some patients with AHF as a result of noncardiac diagnosis (severe renal failure, anemia, etc). Two-thirds of our population had a history of cardiac disease; however, only two-fifths were admitted with a known diagnosis of heart failure. The majority of our population (60%) had, therefore, de novo AHF. However, underestimation of heart failure in the past cannot be excluded.

Elevation of TnI was detected in 26.7% of our AHF population. This proportion corresponds with the observations by Perna et al (10,13) and Ishii et al (11), who found an elevation of TnT or TnI in a broad range of patients (15% to 77%) with acute decompensation of chronic heart failure. Although ischemic heart disease is often present and is a factor in the pathogenesis of AHF, TnI elevation is not entirely associated with coronary artery disease (4,19). Clinical significance of Tn estimation has been repeatedly demonstrated in patients with chronic heart failure (6-9). Recently, it was found that elevation of TnT is associated with a worse prognosis in some individuals with acutely decompensated chronic heart failure (10,11) or selected patients with AHF (12).

Our study has shown that TnI+ patients have a significantly shorter time from the onset (or worsening) of symptoms to admission than patients with normal TnI. The explanation of this observation is not clear; however, it can be speculated that more severe AHF leading to TnI elevation is associated with faster progression of symptoms. This hypothesis is supported by our observation that TnI+ patients have a significantly higher mean Killip stage compared with the TnI– group. On the other hand, Perna et al (10,13) did not observe significant differences in AHF severity of TnT+ versus TnT– patients. The reason for this discord could be the differences between our population and populations in other studies – while more than one-half of our patients were de novo AHF, in studies by Perna et al (10,13) the population exclusively comprised individuals with acutely decompensated chronic heart failure. Significantly higher entry heart rate in patients with TnI elevation is another observation that can be related to the severity of heart failure and possibly to the cardiac overload and activation of the sympathetic nervous system. This finding is in contradiction to other studies (10,13); this difference may be again explained by the different AHF population.

The creatinine level in TnI+ patients was significantly higher than in patients with normal TnI. This observation reflects the impaired renal function, which may decrease the clearance of Tn. Tn elevation was described in patients with chronic renal failure and correlated with the worse prognosis in these patients (20). However, our study was not designed to determine if TnI elevation in AHF patients is accentuated or caused by renal failure, or whether increased creatinine is more a marker of severely impaired circulatory status.

TnI+ patients had significantly less frequent dyslipidemia; this finding is consistent with the study by Perna et al (13). Furthermore, BMI was significantly lower in TnI+ patients. This result is in agreement with the paper by Romero-Corral et al (21) describing lower total mortality in overweight people than in people with a normal BMI.

Similar to studies in patients with acutely decompensated chronic heart failure, we did not observe differences between TnI+ and TnI– groups in ECG and ECHO parameters. These data are in contradiction with Perna et al (13), who described differences in several ECHO parameters of left ventricular

function between TnI+ and TnI– groups; they suggested a link between Tn elevation and enhanced left ventricular remodeling. In a more recent study (10), they did not observe this difference in patients with acutely decompensated chronic heart failure.

Several limitations of our study should be taken into consideration. Possible biases come from the retrospective design and relatively low number of patients. Also, the inclusion criterion 'AHF as the leading diagnosis' may be questionable, because it is not always easy to determine the leading diagnosis retrospectively. A further limitation was the use of a relatively low sensitivity TnI assay.

CONCLUSION

TnI elevation was observed in a substantial number of AHF patients, and these individuals had highly significant differences in several characteristics, including duration of decompensation, Killip stage and entry heart rate. Because the elevation of Tn seems to be a strong independent predictor of worse prognosis in patients with heart failure, our study provides additional data for admission at-risk stratification of patients with AHF.

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