Original articles

# Troponin I serum concentration: a new marker of left ventricular hypertrophy in patients with essential hypertension

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*Key words:*
**Left ventricular hypertrophy; Myocardial damage; Systemic hypertension; Troponin I.**

*Background.* **Troponin I, a specific cardiac muscle protein, has proven to be very helpful in detecting myocardial damage in ischemic heart disease. In order to assess if this laboratory test may also characterize some hypertensive subjects with proven cardiac damage, we compared troponin I serum concentrations of a group of patients affected by systemic hypertension and left ventricular hypertrophy (LVH) with troponin I serum concentrations of hypertensive patients without LVH and with normal controls.**

*Methods.* **Of 100 hypertensive patients consecutively enrolled in the study, 27 had an increased left ventricular mass by M-mode/two-dimensional echocardiographic examination. Of these, 4 were excluded for significant Holter ST-segment modification. Troponin I was measured in the remaining 23, in 23 age- and sex-matched hypertensive patients with normal left ventricular mass and in 23 normal controls.**

*Results.* **Troponin I serum concentration was higher than the upper limit of the normal values (0.5 ng/ml) in 12 of the 23 hypertensives with LVH. On the contrary, all hypertensives without LVH and all normal controls had troponin I serum concentration below the upper limit of the normal values. Consequently, the mean troponin I serum value was significantly higher in the group of hypertensive patients with LVH than in the group of patients without LVH (0.88 – 0.93 vs 0.27 – 0.08 ng/ml, p = 0.002) and in normal controls (0.88 – 0.93 vs 0.22 – 0.04 ng/ml, p = 0.0001).**

*Conclusions.* **Our data indicate that a significant proportion of patients affected by essential hypertension with LVH have slightly elevated troponin I serum concentrations. This test seems to identify two subgroups of hypertensive subjects with LVH, and, considering that troponin I is a marker of myocardial damage, higher serum values probably indicate a more important cardiac involvement in the setting of a hypertensive disease.**

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## Introduction

Myocardial involvement is an ominous complication of systemic hypertension. The first clinical evidence of hypertensive heart disease is left ventricular hypertrophy (LVH); its presence significantly increases the risk of angina pectoris, myocardial infarction, cardiac failure, lethal dysrhythmias, and sudden cardiac death[1,2].

In clinical practice, cardiac damage in hypertension is currently evaluated by means of instrumental methods, whereas laboratory data are commonly considered unsuitable for adding significant information to this field.

Recently, the troponin I serum concentrations have proven to be exceedingly useful in identifying subjects with acute myocardial infarction[3] and, even more important, subgroups of patients affected by evolving unstable angina[4]. Moreover, elevated troponin I serum concentrations were found in subjects affected by cardiac failure[5] and there are data supporting the hypothesis that high troponin levels may have an adverse prognostic implication in hemodialysis patients[6].

In order to assess if elevated troponin I serum concentrations may characterize some hypertensive patients with proven cardiac damage, we measured this protein in a group of hypertensives with LVH, in a group of hypertensives without LVH and in a group of normal controls.

## Methods

In order to obtain a group of hypertensive patients with LVH we studied 100 consecutive subjects affected by stage 1-2 essential hypertension[7] (76 males, 24 females, mean age 40.2 years, range 28-65 years).

In every patient, blood pressure was measured in the sitting position by a mercury manometer, using the first and the fifth Korotkoff sounds[7]. Patients were not receiving any antihypertensive nor any cardioactive medication at the time of the study and in the 4 weeks before. Patients with renal disease, diabetes, cerebrovascular disease, dyslipidemia and secondary forms of hypertension were excluded on the basis of the results of extensive clinical and laboratory tests. Moreover, subjects with overt coronary disease were excluded from the study.

Every hypertensive subject underwent a complete clinical and laboratory evaluation, repeated casual blood pressure measurements, standard ECG, M-mode and two-dimensional echocardiogram.

On the basis of the echocardiographic evaluation, 27 subjects with augmented left ventricular mass (> 134 g/m$^2$ for males and > 110 g/m$^2$ for females) underwent 24-hour Holter ECG. Four subjects with Holter ST-segment abnormalities were excluded from the study.

Two other groups of subjects were studied. The former included 23 patients affected by stage 1-2 essential hypertension[7] with a normal left ventricular mass on the basis of the echocardiographic examination. These subjects were sex- and age-matched with the hypertensive patients with LVH and had normal 24-hour Holter recordings. They were not receiving any antihypertensive nor cardioactive medication at the time of the study and in the 4 weeks before, and were free of renal disease, diabetes, cerebrovascular disease, dyslipidemia and secondary forms of hypertension. The latter group was formed of 23 normal subjects without any known disease, who were not receiving any medication and had a normal clinical, echocardiographic, echo-color Doppler and ECG evaluation.

The sera were collected after an overnight fast, immediately centrifuged and frozen at -80 C until assayed. Troponin I was measured in the serum using an IRMA method (Opus plus, Behringwerke AG, Hannover, Germany). All samples were assayed in duplicate, and the mean of the obtained values was used for further analysis. Data were analyzed with the Mann-Whitney test[8]. Informed consent was obtained from every subject. The protocol was in accordance with the Helsinki Declaration of 1975 revised in 1983.

**Echocardiographic methods.** M-mode/two-dimensional echocardiography was performed by Hewlett-Packard Sonos 1000 (Andover, MA, USA) with the patients in partial left decumbent position using a 2.5 MHz transducer.

Echocardiographic recordings were coded and blindly and randomly assessed by two investigators who were unaware of the subject s blood pressure or other clinical data. Only tracings with optimal visualization of left ventricular interfaces were considered. Left ventricular measurements were calculated according to the recommendations of the American Society of Echocardiography and Penn Convention[9].

End-diastolic measurements of interventricular septal thickness (IVS), left ventricular internal dimension (LVID), and posterior wall thickness (PWT) were taken according to the Penn Convention protocol to calculate left ventricular mass. This was calculated by a simple anatomically validated formula:

$$LVM = 1.04\ [(IVS + LVID + PWT)^3 - LVID^3)] - 13.6$$

To minimize the impact of body size variation, left ventricular mass was indexed for body surface area.

Similarly to other authors[10,11] we chose a cut-off value of 134 g/m$^2$ body surface area to define LVH in men and of 110 g/m$^2$ in women.

**Continuous Holter monitoring.** Continuous 24-hour Holter monitoring was performed using a Del Mar Avionics model 563 (Del Mar Medical Systems, Irvine, CA, USA).

The ECG was recorded continuously on tape using a cassette system. The two-lead systems used were $V_5$ and $V_1$. Electrode position was selected to minimize patient discomfort, noise, skin-electrode impedance, polarization or other malfunction.

Abnormal ST-segment changes were defined as 1 mm of ST-segment depression occurring 80 ms after the J point, lasting for 1 min and separated from other episodes by 1 min.

## Results

Among the 100 subjects enrolled in our study and submitted to echocardiographic examination, 23 were excluded for the suboptimal visualization of the left ventricular interfaces. Of the remaining 77, 27 (35%, 20 males and 7 females) had LVH on the basis of the echocardiographic parameters described above. Four of these 27 subjects (14.8%, 3 males) showed episodes of myocardial ischemia during the 24-hour ECG recording and were excluded from further evaluation.

Age, sex, and mean blood pressure of the three groups studied are summarized in table I. Age and mean blood pressure of patients with hypertension and LVH were not significantly different from those of hypertensive patients without LVH.

**Table I.** Age, sex and mean blood pressure of hypertensives with left ventricular hypertrophy (SH + LVH), of hypertensives without left ventricular hypertrophy (SH) and of normal controls (NC).

| | Age range (years) | Mean age (years) | Males (n=) | Females (n=) | Mean blood pressure (mmHg) |
|---|---|---|---|---|---|
| SH + LVH (n = 23) | 32-55 | 38.6 | 17 | 6 | 116.6 |
| SH (n = 23) | 32-55 | 38.6 | 17 | 6 | 116.9 |
| NC (n = 23) | 21-38 | 28.8 | 15 | 8 | 89.1 |

Troponin I serum values in the 23 patients with hypertension and LVH ranged between 0.2 and 3.6 ng/ml; 12 of these subjects (53.2%) had troponin I serum concentrations > 0.5 ng/ml, that is the upper limit of normal values when the IRMA method is used, and 4 had troponin I serum concentrations > 2 ng/ml.

The 23 hypertensive patients without LVH and the 23 normal subjects had troponin I serum concentrations < 0.5 ng/ml.

The mean troponin I serum value of the 23 hypertensive patients with LVH was significantly higher than that of hypertensive patients without LVH (0.88 – 0.93 vs 0.27 – 0.08 ng/ml, $Z = 3.05$, $p < 0.002$) and that of normal controls (0.88 – 0.93 vs 0.22 – 0.04 ng/ml, $Z = 3.86$, $p < 0.0001$). No significant difference was found between the mean troponin I serum value of hypertensive patients without LVH and that of controls (Fig. 1).

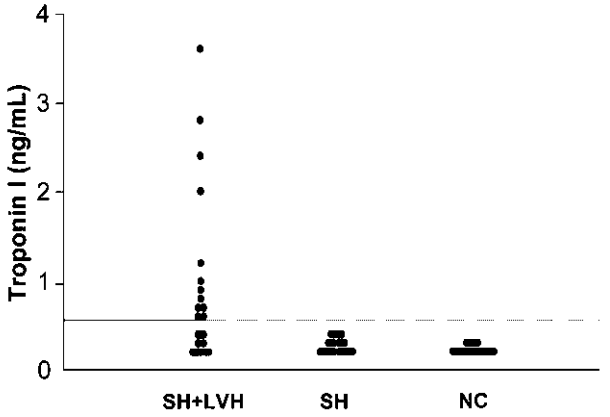


**Figure 1.** *Troponin I serum values in the group of patients with systemic hypertension and left ventricular hypertrophy (SH + LVH), in the group of patients with systemic hypertension without left ventricular hypertrophy (SH) and in normal controls (NC). The* dotted line *indicates the upper limit of troponin I normal range.*

## Discussion

Our data suggest that a significant proportion of patients with grade 1-2 essential hypertension and LVH have slightly elevated troponin I serum concentrations. On the contrary, sex- and age-matched patients with the same grade of hypertension but without LVH and normal subjects have troponin I serum values in the normal range. Consequently, the mean troponin I serum value in patients with hypertension and LVH is significantly higher than that of hypertensives without LVH and of normal controls.

While planning our study, we were aware of the high incidence of silent ischemic heart disease in subjects with essential hypertension and, consequently, we performed a 24-hour ECG recording in all subjects examined for troponin I measurement. On the basis of an ischemic 24-hour ECG recording, we excluded 4 of the 27 hypertensive patients with increased left ventricular mass (14.8%) from further evaluation. This percentage is similar to that reported among mild-to-moderate hypertensive patients in Italy[12].

The presence of elevated troponin I serum values only in hypertensive patients with an augmented left ventricular mass is probably directly linked to the pathophysiology of LVH. High troponin I serum concentrations are likely due to a leakage of this protein into the serum from hypertrophic cardiac myocytes. A fraction of the troponin cellular content is free in the cytosol[13] and may leak out if membrane damage occurs. Several studies identified different cellular and subcellular alterations in cardiac myocytes during the so-called hypertrophic response . In particular, increased mechanical stress, induced *in vivo* by beta-adrenergic stimulation or *in vitro* by the pacing of cultured myocytes, may cause significant alterations in plasma membrane permeability and, subsequently, the leakage of macromolecules out of the cell[14,15]. However, even if the subjects with significant Holter ST-segment depression were excluded from the study, we cannot rule out that chronic ischemia determined by the remodeled coronary microcirculation of the hypertensive heart may contribute to the leakage of troponin I across the plasma membrane in some patients with hypertension and LVH[16,17].

In the group of hypertensive patients with LVH, the troponin I serum determination allows us to identify two patient subgroups. Although the role of troponin I in patients with LVH is not completely understood, according to the mechanisms proposed for the troponin I leakage into the blood, it seems likely that higher troponin I serum values may be a marker of a more important cardiac involvement in the setting of a hypertensive disease. However, a larger cohort of patients and an adequate follow-up are necessary to clarify whether a slight troponin I serum elevation can help to better define subjects

with a more severe hypertensive cardiac damage and to predict adverse cardiovascular events.

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