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Urine high sensitive Troponin I measuring in patients with hypertension

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ABSTRACT

High sensitive troponin I (hsTnI) is one of the markers of cardiac damage. Its values increase two to three hours after a heart attack and remain elevated for days. Recent studies have shown that kidneys are the main organ of elimination of troponin from blood. Our previous studies have shown that troponin I is removed and concentrated in the first morning urine.
Increased blood pressure is one of the most common comorbidities today. By measuring blood pressure, we can see the current value of the pressure, but we do not know what the values are during the rest of the day. The aim of our research was to determine if there is a difference in the concentration of troponin I in urine among patients suffering from hypertension and among healthy individuals.
The study involved 20 participants divided into two groups. In the first group were healthy individuals, while in the second group were individuals with hypertension. The first morning urine was sampled and the hsTnI was measured using a high-sensitivity test on the Immuno-enzymatic analyser Abbott Architect i1000SR.
Within the normotensive group, the mean value of hsTnI in the first morning urine was 14.95 pg/mL, while in the group of participants with elevated blood pressure, the mean value of hsTnI in the first morning urine was 26.59 pg/mL. The difference between these two groups was statistically significant with p=0.0451 (p<0.05).
By measuring hsTnI in urine and determining the difference between healthy and those with hypertension, a new diagnostic test for hypertension monitoring and detection would be obtained.

Key words: troponin I, urin, hypertension

INTRODUCTION

Troponin is a protein molecule that makes a troponin complex. The troponin complex is composed of three types of troponin: Troponin I, Troponin T and Troponin C. Troponin T is a part of the troponin complex linked to tropomyosin, troponin I is an ATP-an activity inhibitor and prevents ATP consumption, while troponin C is the place on the complex where calcium (Ca2+) is attached. All troponin molecules together are part of the muscle cell contraction mechanism. (1)
High sensitive Troponin I (hsTnI) is determine as a marker of cardiac damage. It is a molecule of about 22.5 kDa. (2) Within the heart cells 2-6% of troponin is not related to the contractile system of the cell itself, but is found in cellular cytoplasm as free troponin. This troponin is responsible for rapid elevation of troponin levels after percutaneous coronary intervention. (3) There are numerous conditions that may increase the level of troponin in the blood (myocardial infarction, pulmonary embolism, cardiac damage, etc.), but they are all commonly associated with damage/necrosis of cardiac muscle cells. Two to three hours after cardiac events, the troponin concentration increases, its maximum value reaches approximately 24 hours of damage and remains elevated for up to eight days. (4)
Within the heart cells, daily changes of old proteins with new ones, including troponin, occur. There is also a natural daily loss of cardiac cells. These facts are one of the reasons why there is a presence of troponin molecules in the blood of a healthy population. These concentrations are not large, but with the development of new detection tests, they have become measurable and range around 0.1-0.2 ng/L. (5)
While the synthesis and presence of troponin molecules in the blood today is well known, the method of excretion or removal (clearance) from the blood is still relatively unknown. Several papers have recently attempted to explain how troponin is removed from the blood. Some data suggests that troponin is removed in a reticuloendothelial system where it is cleaved into smaller fragments. (6) There are also studies that show that enzymes such as caspases and calpain cleavage the troponin molecule into small fragments (4), which are then removed from the circulation. Until recently, there have been only two references of the presence of troponin in the urine. The first proved that troponin T and troponin I (7) can be proved in urine, while the second is an abstract presented at a congress that deals only with troponin I. (8) Our previous study showed the possibility of detecting hsTnI in urine by using an immunosensitive analyte Abbott Architect i1000SR. The values we received were 10 times greater than the concentration in the blood of a healthy population, indicating its possible ability to concentrate in the

urine. (9)
The aim of this study was to investigate if there is a difference in the concentration of hsTnI in the first morning urine between people without hypertension and those who have hypertension. The secondary goal was to investigate the ability to determine hsTnI in the first morning urine as a new method for detecting elevated blood pressure.

MATERIALS AND METHODS

The study included a total of 20 participants divided into two groups of 10. The participants in the first group were without elevated blood pressure (HT-), not at elevated risk of cardiovascular disease, have regular laboratory of cardiac and kidney function, have no diagnosed illness and have no chronic therapy. With all of them blood pressure was measured three times and it was within normotensive values (<140/90mmHg).
The second group (HT+) includes 10 participants who have elevated blood pressure and who are regularly controlling their hypertension at Clinical Hospital Merkur. All members of this group were under chronic antihypertensive therapy with up to three antihypertensive drugs with normal renal function (estimated GFR > 60 ml min-11.73m2, using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula). Their blood pressure values were regulated by existing therapy within normotensive (6p) up to grade I hypertension (4p). The study was voluntary and all participants signed informed consent for participation. The study did not include subjects who had any form of night work last month.
HsTnI was determined in a sample of the first morning urine by the chemiluminescence immunochemical CMIA method, on the immunoassay analyser Abbott Architect i1000SR. The method for the determination of hsTnI in plasma (and also used for urine analysis) was accredited according to the international standard HRN ISO 15189: 2012, Medical Laboratory, Quality and Qualification Requirement. The HsTnI Limit of Quantification (LoQ) of 5.0 ng / L on the applied analytical system was determined according to CLSI EP17-A protocol.
The statistical analysis was made using the statistical program Statistics (version 13.1). Descriptive data analysis was performed for all attributes. A value $p<0.05$ was considered statistically significant.

RESULTS

Within the normotensive group (HT-), the mean value of troponin (hsTnI) in the first morning urine was 14.95 pg/mL (Standard Deviation, SD 9.09). The range of hsTnI in urine was from 3.3 to 29.3 pg/mL. The participants of this group were ages 25 to 59, while the mean age was 37 years. There were six males (60%).
In the hypertension group (HT+), the mean value of hsTnI in the first morning urine was 26.59 pg/mL (SD 14.48). The range of hsTnI in urine in this group was from 3.3 to 56.6 pg/mL. The participants of this group were ages 30 to 68 years, while the mean age was 55.5 years. In this group there were four male (40%).
The data are presented in Table 1.
The difference in the concentrations of hsTnI in urine among participants suffering from hypertension and healthy ones was statistically analysed by the following tests: first we tested the distribution of groups by Kolmogorov-Smirnov test. Test value was D=0.3444 with value p=0.167. We therefore decided for the Student T Test for Independent Samples. The T value obtained with 18 degrees of freedom was 2.153 with $p = 0.0451$ indicating that the difference between the groups was statistically significant ($p< 0.05$).

DISCUSSION

Increased blood pressure today is one of the most common comorbidities. It is one of the key risk factors for cardiovascular, renal and cerebral events. Maintaining its values within normal limits is necessary to reduce the risk of cardiovascular adverse events for patients. Timely recognition of hypertension is sometimes not easy since patients very often have no symptoms. By measuring blood pressure, we can only see the current value of the pressure, while we do not know what values are during the rest of the day. Night-time hypertension is not recognized by conventional pressure measurement methods except by using continuous pressure measurements for 24 hours (KMAT). (10)
This research has shown that it is possible to determine the level of troponin in urine and that the average values of hsTnI in the first morning urine is about 15 pg/mL in healthy participants and about 26.7 pg/mL in hypertensive participants. The obtained values suggest that people with high blood pressure have elevated values of hsTnI in the first morning urine. The range of values

Table 1. Values of high sensitive troponin I in urine (hsTnI pg/ml)

	HT-	**HT+**
N	10	10
hsTnI (pg/mL)	14,95	26,59
SD	9,08897378	14,47806387
Min.levels of hsTnI	3,3	3,3
Max. levels hsTnI	29,3	56,6
AGE(years)	37	55,5
Min.years	25	30
Max.years	59	68

HT -, healthy subjects
HT+, hypertensive subjects
HsThI, high sensitive troponin I
N, number
SD, standard deviation

indicates that the minimum values of hsTnI in urine are equal for both groups and are 3.3 pg/ml while the upper (maximum) values differ. An explanation of the difference in the maximum values of hsTnI in urine is possible due to the age difference between healthy and hypertensive subjects. Lower (minimum) overlaps may be due to good regulation of high blood pressure of this group of subjects. Stratification by age was not possible to match to ideal parameters since most healthy subjects are age <50 years, and most of the subjects with hypertension are >50 years old.

We decided to measure the concentration of troponin I in urine instead of troponin T due to physiological (9) and practical reasons, since hsTnI is routinely determined in an Emergency Room.

Measuring troponin in urine has shown that kidneys are the main organ of troponin elimination from the blood. Given that it is not always easy to recognize or measure elevated blood pressure (e.g. night hypertension) by measuring hsTnI in the first morning urine it could be a test of the screening for elevated or poorly regulated blood pressure.

CONCLUSION

This study suggests that people with hypertension have elevated values of hsTnI in the urine. Due to its practicality, simplicity and cost-effectiveness this could be a new tool in diagnosing and monitoring people with hypertension.

REFERENCES

1. Farah CS, Reinach FC. The troponin complex and regulation of muscle contrraction. Faseb J 1995; 9: 755-67.
2. Labugger R, Organ L, Collier C, Atar D, Van Eyk JE. Extensive troponin T and I modification detected in serum from patient with acute myocardial infarction. Circulation 2000; 102: 1221-6.
3. Wu AH, Feng YJ. Biochemical differences between cTnT and cTnI and their significance for diagnosis of acute coronary syndromes. Eur Heart J. 1998; 19:25-9.
4. Michielsen EC, Diris JH, Kleijnen VW, Wodzig WK, Van Dieijen-Visser MP. Investigation of release and degradation of cardiac troponin T in patients with acute myocardial infarction.Clin Biochem 2007; 40 (12): 851-5.
5. Missov ED, De Marco T. Clinical insights on the use of highly sensitive cardiac troponin assays. Clin Chim Acta. 1999; 284(2):175-85.
6. Freda BJ, Tang WH, Van Lente F, Peacock WF, Francis GS. Cardiac troponins in renal insufficiency: review and clinical implications. J Am Coll Cardiol. 2002; 40(12): 2065-71.
7. Ziebig R, Lun A, Hocher B, Priem F, Altermann C, Asmus G, et all. Renal elimination of troponin T and troponin I. Clin Chem 2003; 49(7): 1191-3.
8. Maruta T, Li T, Morrissey J, Blood J, Macy E, Bach R, Townsend R, Boyle W. Urinary cardiac troponin I is detectable in patients with myocardial injury using a high-sensitive immunoassay. Critical Care Medicine 2012; 40 (12): 1-328 (Abstract).
9. Pervan P, Svagusa T, Perkov S, Prkacin I. Određivanje vrijednosti troponina I u urinu. Acta Medica Croatica 2017; (in press).
10. Prkacin I, Balenovic D, Djermanovic-Dobrota V, Lukac I, Drazic P, Pranjic IK. Resistant hypertension and chronotherapy. Mater Sociomed. 2015; 27(2): 118-21.