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Increased level of cardiac troponin I determined by a highly sensitive method: clinical significance beyond the assessment of the severity and prognosis of acute and chronic diseases

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For a long time, an increased blood concentration of cardiac troponin I (cTnI) has been used to detect acute and chronic cardiomyocyte damage. According to modern concepts, in order to verify myocardial damage, the blood cTnI concentration should exceed the 99th percentile of its level in healthy individuals [1, 2]. Therefore, for the proper use of each diagnostic tool, it is necessary to establish this value among those who will later use cTnI to detect myocardial injury. However, in practice, this rule is often disregarded, focusing on the recommendations of diagnostic kit manufacturer, which may be incorrect if the cTnI level among healthy individuals in a studied region is significantly higher or lower than where the initial study was carried out. So, according to the recommendations of the manufacturer of Architect Stat High Sensitive Troponin I kit (Abbott, USA), based on the US study with 766 healthy men aged 21-73 years who did not have elevated levels of brain natriuretic peptide (BNP) and glycated hemoglobin, the 99th percentile of the distribution is 34,2 pg/ml in men and 15,6 pg/ml in women [3]. And according to the analysis of 8121 people aged 54-74 years in 4 US communities who did not have a diagnosed cardiovascular disease (CVD), but with the possible cardiovascular risk factors, including hypertension (HTN), the 99th the percentile of cTnI concentration distribution, determined by the same method, was 46,8 pg/ml for men and 23,3 pg/ml for women [4].

With the development of methods for determining blood cTnI, which have high sensitivity, it became obvious that the determined concentration of this biomarker, which usually does not reach the value required to verify cardiomyocyte damage, can be recorded both in patients with some chronic diseases and myocardial pathologies (stable coronary artery disease, heart failure, left ventricular hypertrophy, etc.), and in persons who do not yet have any disease [2, 5]. Obviously, the averaged blood cTnI concentration and 99th percentile of its distribution will depend on how widespread these diseases are in the studied group.

The reasons for such an unexpressed increase in blood cTnI concentration are considered not so much cardiomyocyte necrosis due to ischemia, inflammation, or other active pathological processes, but apoptosis, accelerated cell replacement in the myocardium, and exocytosis [6].

It is known that a higher blood cTnI concentration in individuals who do not yet have obvious diseases leading to acute or chronic cardiomyocyte damage indicates an increased risk of cardiovascular death, coronary artery disease, myocardial infarction, ischemic stroke, heart failure-related hospitalization [4, 7-10]. At the same time, an increased high-sensitivity cTnI level has an independent prognostic value, regardless of other risk factors and blood level of other biomarkers (in particular, high-sensitivity C-reactive protein, BNP).

In general, it seems that an increased blood cTnI level, detected using high-sensitivity methods, is a marker of the presence and/or severity of clear or not yet diagnosed pathological processes that specify an increased risk of adverse outcomes.

Accordingly, data on the distribution of blood cTnI concentration of individuals living in a certain area is extremely important, since, on the one hand, it allows us to determine the 99th percentile of the distribution, which is necessary for the correct diagnosis of myocardial damage, and on the other hand, it makes it possible to identify individuals with a higher risk of cardiovascular events, based on previously obtained data on unfavorable prognostic concentration of blood cTnI. In addition, prospective observation of a large sample can help to clarify the unfavorable prognostic cTnI level characteristic of the studied population.

This issue of the journal presents the results of an observational cross-sectional study carried out on a representative sample of the Vologda region population, which included 1591 people aged 25-64 years [11]. Some of the selected individuals had prior myocardial infarction (MI) or stroke, but there was no clear CVD in 1120 (70,4%) patients. According to multivariate regression analysis, the blood concentration of cTnI, determined by high-sensitivity method Architect Stat High Sensitive Troponin I (Abbott, USA), was associated with age, sex (higher in men) and the presence of some cardiovascular risk factors — hypertension, obesity, low-density lipoprotein cholesterol ⩾3 mmol/L and an increased blood concentration of BNP. Similar patterns are showed in other studies [2, 4].

The 99th percentile of blood cTnI concentration distribution in the studied men (47,7 pg/ml) was significantly higher than in manufacturer recommendations (34,2 pg/ml) [3]. The authors of the Russian study note that this was due to a group of men aged 45-54 years, each of whom had prior coronary artery disease or hypertension, which shows the importance of assessing approaches to sampling when determining the 99th percentile of the distribution of the indicator in population.

To stratify the risk of adverse outcomes in this study, we used the cTnI concentration values, determined by the same method as in the Nord-Trøndelag Health Study (HUNT), which included 9005 subjects without established CVD at the time of inclusion (except for hypertension) [7]. The amount of hospitalizations with acute MI or heart failure, or cardiovascular deaths during long-term follow-up (median, 13,9 years) was significantly higher in individuals with moderately elevated blood cTnI levels (4-10 pg/ml in women and 6-12 pg/ml in men) and the highest with a more pronounced increase (>10 pg/ml in women and >12 pg/ml in men). These cTnI levels are proposed to be used to improve the accuracy of risk stratification of adverse outcomes in individuals who do not yet have CVD, which seems to be especially relevant for moderate-risk patients [12].

According to prospective population-based studies, determination of increased cTnI concentration using the Architect Stat High Sensitive Troponin I diagnostic kit (Abbott, USA), makes it possible to increase the informative value of risk stratification scales for adverse outcomes in persons without CVD and to reclassify the risk in some of them [4, 7, 8, 12]. In the study by Shalnova S.A. et al., assessing this parameter in persons without prior myocardial infarction or stroke also allowed to reclassify the risk of an unfavorable outcome, assessed using Systematic COronary Risk Evaluationon (SCORE), both upward and downward. However, since this study had cross-sectional design, the result obtained should be compared with the actual rate of adverse outcomes in the studied patient population.

In general, the data presented by Shalnova S.A. et al. in the article "**Pilot project to study the association of troponin I with cardiovascular events in the population of Russian region**" is an important step towards studying the clinical interpretation of an increased level of high-sensitivity cTnI in individuals living in Russia.

Relationships and Activities: none.

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