Blood levels of cardiac troponin I in the elderly women with and without dementia

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ABSTRACT

Objectives: We hypothesized that cardiac biomarker levels could be elevated in patients with dementia due to high frequency of cardiovascular risk factors in older patients with vascular and neurodegenerative type of this disease. The aim was to determine possible association between cardiac Troponin I (cTnI) blood levels and dementia.

Methods: The cross-sectional study included 88 patients, female gender, and mean age 81 years, who were recruited from specialized unit of the Health Care Hospice for persons with disabilities in Sarajevo, Bosnia and Herzegovina. According to the Hachinski ischemic score, 59 patients with dementia were classified in two groups- vascular (VD) and neurodegenerative dementia (ND), while 29, age-matched asymptomatic persons, were used as a control group(CG). The cTnI was measured using ELISA kit Humani Tn-I/TNNI3 (Elabscience Biotechnology Co., Ltd), using immunoanalyser STAT FAX 2100, USA.

Results: The Mini-Mental State Examination (MMSE)score was significantly lower in dementia patients than in control group (p<0.01). No significant difference in cardiac TnI levels was found in Alzheimer’s (AD), vascular dementia (VD) and control group (AD: Me = 3.41, VD: Me = 3.49, control group: Me=3.57; (p=0.737).

Conclusion: The participants’ age and comorbidities are probable factors causing no association between dementia and cTnI. It is known that troponins are associated with risk of dementia but cTnI levels are as well under influences of a possible epigenetic modification of cTnI that should be the objects of the future investigation.

Keywords: cTnI, dementia, cardiovascular risk

INTRODUCTION

Based on the latest Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria, dementia is classified as a major neurocognitive disorder, that comprises memory loss of different causes, thinking, social and behavioral disorders, which interfere with daily functioning. Therefore, dementia disrupts cognitive functions (memory, speech, language, judgment, reasoning, planning) and everyday activities [1]. The two main dementia entities are Alzheimer’s (AD) and vascular dementia (VD), preceded by a stage of cognitive impairment [2]. Elders represent the largest part of population affected by dementia, with AD as the most common primary neurodegenerative disorder [3]. Both conditions have been linked to cardiovascular diseases and cardiovascular risk factors, of which particularly studied are diabetes, stroke, hypertension, high levels of cholesterol, tobacco smoking and angina pectoris [2,4]. The term ‘cardiogenic dementia’ was originally introduced by Medical Journal Lancet in 1977 and used to describe a reduced cognitive function in the presence of cardiac failure [5]. Schneider and colleagues studied the association of high-sensitivity cardiac Troponin T (cTnT) with cognitive function and dementia and concluded that subclinical myocardial injury is associated with cognition and dementia [6]. Nevertheless, there are just several studies which investigated the association between cTnI and incidence of dementia. To conduct a clinical diagnosis of dementia can be difficult, and it would be very helpful to search for biomarkers that can predict who is a potential candidate for the disease and who is not. Therefore, there is a need to consider the abnormal levels of biomarkers and try to find a specific marker for a specific disease. The aim of this study was to determine whether cTnI blood levels are affected by dementia in elderly women.
METHODS

Subjects
A cross-sectional study included 88 female participants, of which 59 were patients with, and 29 subjects without dementia. Study group was comprised of 30 AD and 29 patients suffering from VD. Control group represented 29 age-matched elderly asymptomatic persons. The median age of participants was 81 year. The patients were institutionalized in a specialized unit of the Health Care Hospice for persons with disabilities in Sarajevo, Bosnia and Herzegovina. Participants with a history of cardiovascular or thyroid disease, chronic inflammatory disease (asthma and rheumatoid arthritis), hepatic or renal insufficiency and cancer were excluded from the three groups. Approval for the study was obtained from the local ethics committee. The study was performed according to the ethical principles outlined in the Declaration of Helsinki. The study participants and their caregivers were informed regarding the study procedure and provided the written informed consent.

Methods
The criteria based on the National Institute of Neurological and Communication Disorders and Stroke (NINCDS-ADRDA) for probable AD [7] and the National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l’Enseignement en Neurosciences (NINDSAIREN) for probable VD [8] were used by a senior staff neurologist and psychiatrist to set the clinical diagnosis. Global cognitive function was tested with the MMSE test [9-11] which has been used for rapid screening of those with cognitive and/or intellectual deficit. It assesses orientation, short term memory, serial subtraction, constructional capacities and use of language. The total score is 30. A score of 24 is considered abnormal. A score of less than 17 is considered dementia. All patients in the AD and VD groups had A score of ≥ 12 while subjects in the control group had a score of 26-30. The Hachinski ischemic score (HIS) helps differentiate patients with VD from those with AD. The original scale consists of 13 items; each scale item was assigned a numeric value with double weighting applied to specific clinical features. A score of 7 or more means vascular dementia. A score of 0-4 means Alzheimer’s dementia and a score of 4-7 means mixed dementia [11]. Our patients in the AD group had a score of 4 or less, and patients with VD had a score 7 or more. ELISA kit from Elabscience Biotechnology Co., Ltd (Elabscience) was used for in vitro quantitative determination of Human Tn-I/TNNI3 concentrations in serum, plasma and other biological fluids. Minimal detectable dose of Humanic Tn-I/TNN13 was 0.23 ng/ml, detection range 0.39-25ng/ml. The serum cTnI level was determined using the sandwich principle.

Statistical analysis
Statistical analysis has been done using the SPSS software version 19. Normality of data distribution was tested by Shapiro Wilk test. The descriptive statistics such as median with the range of 25th-75th percentile was used due to abnormal data distribution. The difference between groups was tested by Kruskal-Wallis test followed by Mann Whitney test. Data have been shown using table and figure. The statistical significance was set at p<0.05.

RESULTS
Out of a total of 88 female subjects involved in the study, 29 (33%) were control group, 30 (34%) were subjects with AD, and 29 (33%) were subjects with VD. The degree of dementia of the subjects in the study was measured by the Mini-mental status score (MMS) instrument. Samples did not statistically differ significantly from the mean age of the patient with the real probability of p<0.144, which is confirmed by the median age values shown in Table 1. (Control: Me = 80, AD: Me = 79.75, VD: Me = 79). The Kruskal Wallis test confirmed a statistically significant difference between the average scores of the MMS scales between the tested groups (p<0.001). Subjects in experimental groups had statistically significantly lower average scores of MMS scales (AD: Me = 9, 25th = 7, 75th = 12.75 and VD: Me = 12, 25th = 7, 75th = 16) compared to subjects in the control group, where the medians of the same scale were significantly higher (control: Me = 28, 25th = 27, 75th = 29), as shown in Table 1.

Table 1. Basic characteristics of the study participants

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control (n=29)</th>
<th>AD group (n=30)</th>
<th>VD group (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>(77,5-83.0)</td>
<td>(79,75-87,00)</td>
<td>(76,5-87)</td>
</tr>
<tr>
<td>MMS (points)</td>
<td>28(27-29)**</td>
<td>9(7-12,75)</td>
<td>12(7-16)</td>
</tr>
</tbody>
</table>

Data are presented as median value and range between 25th-75th percentiles. ** p<0.001 in comparison with dementia groups; MMS-Mini-mental status score; AD-Alzheimer dementia; VD-vascular dementia;

Figure 1. shows median, percentile and interquartile ranges of cTnI in relation to three groups of participants: control group, AD group and VD group. Fifty percent of the participants in the control group had a cTnI score of 3.57 or less, while the other 50% of
participants had the same value or higher. When it comes to participants from experimental groups, there are slightly lower values of cTnI (AD: Me = 3.41, VD: Me = 3.49).

Kruskal Wallis independent sample test showed no statistically significant difference in the mean cTnI values between the tested groups (p=0.737).

**DISCUSSION**

Cardiac troponin is the gold standard for diagnosing, risk stratification and prognosis of the acute coronary syndrome (12).

Elevated cTnI in the blood points at myocardial damage but not mechanisms the damage is based on what means that cTnI is specific for myocardial damage but not for specific disease.

There is evidence that elevated troponins in the blood are associated with the risk of dementia. It is known that mild subclinical myocardial injury leads to cognitive impairment but it is also possible that brain injury associated with cognitive dysfunction causes cardiac injury.

Impaired endothelial function as the major finding of atherosclerotic disease contributing to cognitive impairment and elevated troponins is the most likely pathomechanism for simultaneous cardiac and brain damage [13].

Besides the non-acute clinical conditions that cause cTnI elevation in blood such as chronic heart failure, chronic kidney disease, arterial hypertension, coronary artery disease, cTnI values are under the valuable influence of the age. There are contradictory data about TnI in the blood of the elderly people which points that this population requires additional investigation of cTnI blood levels in order to set proper threshold value for elevated TnI. Baseline values are higher in the people older than 60 years compared to those younger than 60 [14].

The study of Kuster and associates [15] stated that hsTnT increases exponentially after the age of the 65 regardless the comorbidities. Masson et al [16] reported higher baseline cTnI concentrations in elderly individuals [73 ± 5 years]. Contrary to the previous statements related to age influence on cTnI blood level, Myint PK and associates stated that troponin rise in older people is not as intensive as in the young people despite having a similar extent of cardiac damage due to age-related physiological changes in cardiac myocytes that may influence the response to injury [17].

In addition, epigenetic modifications of cTnI gene such as methylation of DNA and histone acetylation reduces cTnI expression in aging heart that might result in a reduced cTnI blood level and diastolic dysfunction in the elderly [18].

Data regarding elderly people cardiac TnI level especially with dementia are scarce. In the present study, two groups of dementia patients and control group were compared in the term of blood cTnI level. There was no difference between observed groups of elderly woman.

So we can speculate that the TnI values are under the influence of the age and also comorbidities that are common for that age but the dementia does not significantly influence the cTnI. The researches done with hs-cTnT found elevated cTnT associated with lower cognitive test scores at baseline and increased dementia hospitalization risk [6].

Hilal et al. [19] stated that higher hs-cTnT as marker of cardiac dysfunction is only associated with dementia if cerebrovascular disease is present independently of other vascular risk factors. It was found that values of cTnT were elevated during overt myocardial stress and injury but also during the early phases of vascular pathology. The higher hsTnT as marker of cardiac dysfunction is only associated with dementia if cerebrovascular disease is present independently of other vascular risk factors.

It was not possible to establish the temporal association of cTnI and the cognitive impairment due to cross-sectional study design. In order to find the subtle differences between the considered groups the further research should be done using hs-TnI.

**CONCLUSION**

No association between dementia and cTnI was found due to the influence of age and co-morbidities as additional factors. It is known that troponins are associated with risk of dementia but their levels in blood are also under the influence of a possible epigenetic modification that should be the objects of the future investigation.
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DECLARATION OF INTEREST

Authors declare no conflict of interest.

REFERENCES


