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# Increased level of high-sensitivity cardiac Troponin T in a geriatric population is determined by comorbidities compared to age

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ABSTRACT

High level of cardiac Troponin T (hs-cTnT) in geriatric population has been considered as an age-related phenomenon, which may question the interpretation of the increase of hs-cTnT in this population. The challenge is what is the primary cause of the increased hs-cTnT levels in elderly patients without AMI.

*Objective:* The aim of the current study was to determine the impact of aging on hs-cTnT levels in elderly patients without acute cardiac events but in the presence of comorbidities.

*Methods:* Sociodemographic and clinical data were collected from 6977 medical records of patients aged ≥65 years without acute coronary events but for whom hs-cTnT measurements were available. The patients were stratified based on age, troponin levels and the number of comorbidities.

*Results:* The results suggested that the likelihood of increased hs-cTnT was related to the presence of comorbidities independently of their number ($p < 0.05$). The adjusted odds ratio (AOR) for both advanced age and having comorbidity was statistically significant, however for the old group (74 ≥ age ≥ 84 years) the chance of having elevated troponin regarding age compared to the presence of comorbidity was 1.070 *vs.* 1.216, whereas for the old-old group (≥85 years) it was found to be 1.071 *vs.* 1.311. Besides statistical significance for age, from a clinical standpoint, the AOR of 1.070 may not be considered clinically relevant.

*Conclusion:* Increased hs-cTnT levels were associated with the presence of pre-existing comorbidities independently of age. Increased hs-cTnT levels in the elderly should always be considered as pathological, and a specific etiology should be searched.

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## 1. Introduction

Elderly patient, when experiencing myocardial infarction, frequently present with atypical symptoms, often lack chest pain, have non-diagnostic ECG and delay in diagnosis and treatment [1]. High sensitivity troponin can aid in the rightful diagnosis of primary type myocardial infarction (type 1/associated with primary coronary event) when interpreted appropriately. Making or excluding correctly a myocardial infarction diagnosis in due time is paramount, especially in the elderly population, since they are both prone to worse prognosis if left untreated and more complications from therapy than younger counterparts [2,3]. Correct interpretation of elevated troponin in the elderly requires understanding of the factors that influence the baseline level of that protein. Most of the available literature indicates a positive and independent association with aging and increased baseline troponin level, but few, if none, have compared directly the impact of aging itself to the comorbidity burden that may come with aging [4–6].

Coronary heart disease (CHD) events are well established as a leading cause of death among older people [7], but the relationships between age, comorbidities and the levels of cardiac biomarkers serving as indicators for cardiac events are still subject to debate. One such biomarker, cardiac troponin, is established as the best biomarker to detect myocardial necrosis [8].

With the growing clinical adoption of cardiac troponin, the diagnosis of acute myocardial infarction (AMI), or acute coronary syndrome (ACS), has shifted from a primarily clinical diagnosis predicated on electrocardiogram (ECG) findings and blood biomarker levels, to one essentially based on cardiac troponin assays, supported by clinical and ECG findings [9].

The importance of cardiac troponin becomes even more prominent in elderly patients [8], particularly those >80 years of age, for whom secondary diagnostic characteristics of ACS such as chest pain, electrocardiography, and biomarkers are often unreliable when trying to exclude AMI [10]. This is exacerbated by the high prevalence of multiple chronic

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conditions and comorbidities in elderly patients, which may result in "atypical" or "asymptomatic" presentations [11]. There is, however, only limited data about cTnT behavior in elderly patients, and even less knowledge about cTnT in the oldest bracket of patients with AMI in the presence of comorbidities [12]. Moreover, hs-cTnT assays have been shown to be associated with a higher frequency of false-positives for AMI in elderly patients [13]. As such, AMI misdiagnoses are frequent with very old patients [14] and an improved interpretation of elevated hs-cTnT in elderly patients with comorbidities could have a considerable influence on ACS risk stratification.

Our hypothesis is that, after excluding ACS in elderly patients, the increased cardiac troponin values are mainly associated with the presence of comorbidities and not with age. Therefore, the main objective of this research is to determine the differential effect of age and comorbidities on the increased plasma hs-cTnT levels in elderly patients without ACS.

## 2. Methodology

### 2.1. Patients selection and database records

This retrospective observational cohort study in geriatric Caucasian population was undertaken at the University Hospital of Sherbrooke (Quebec, Canada) (CHUS) using administrative database of patient records. Selected patients were aged ≥65 years, admitted to the university hospital between January 2012 and December 2016 and for whom serial analysis of hs-cTnT levels had been performed. Patient records were reviewed, and demographic, clinical and hs-cTnT data were extracted.

Data records were obtained for all patients admitted for emergency evaluation suspecting acute coronary events (chest pain, sweeting, palpitations, vomiting, dyspnoea). The exclusion of ACS was based on the same diagnostic criteria applied in our hospital, namely, the serial measurement of hsTnT (0, 2 h and 6 h) and also the ECG. The first statistical step of analysis contained 7080 medical records. The database was refined by detecting and or removing corrupt, inaccurate, or unnecessary records from our data pool. Our refined data then was reduced to a sample of 6822 medical records with the presence of multiple comorbidities in all. The study protocol was approved by the local Ethical Committee of the CIUSSS de l'Estrie-CHUS (approbation # 2018-2441).

### 2.2. Variables

The main dependent variables were hs-cTnT values and the occurrence of the following concomitant comorbidities: diabetes, heart failure (HF), chronic obstructive pulmonary disease (COPD), renal insufficiency, cancers, hypertension, neurocognitive disorders, hypothyroidism, anemia, cardiomyopathy, pulmonary hypertension, pulmonary embolism, pneumonia, stroke, atherosclerotic vascular disease, subarachnoid hemorrhage and other non-acute cardiovascular disease. Demographic and independent variables were age and sex.

### 2.3. Hs-cTnT assay

The hs-cTnT was measured using the elecrochemiluminescence immunoassays with Roche Elecsys analyzers (Troponin T Stat, Roche Diagnostics, F. Hoffmann-La Roche Ltd., Basel, Switzerland), with a limit of detection of 3 ng/L.

All patients for whom the diagnosis was MI or ACS have been automatically excluded. Therefore, for the included patients only the first hs-cTnT measurement, collected at time of admission to the hospital or emergency department, was considered.

### 2.4. Statistical analysis

Continuous variables were expressed as means ± standard deviation (SD), median and quartiles. Categorical variables were expressed as absolute values and percentages of the total. Independent *t*-test (to compare the troponin levels between age groups), Chi-square tests or Pearson $\chi 2$ tests (to evaluate the differences in the prevalence of comorbidities according to troponin levels) and multivariate logistic regression (to determine the association between the risk of having high troponin levels with age and comorbidities) were applied. Data were analyzed using SPSS (v24; IBM, USA). The statistical significance level was set at $P < 0.05$.

## 3. Results

A total of 6977 medical records of patients aged ≥65 years were included in the study database. After excluding all medical records with a history of cardiac arrest, previous or post-operative AMI and/or missing medical information, a final sample of 6822 elderly patients remained.

Table 1 presents the demographic and clinical characteristics of the study cohort. The cohort was categorized into three age groups: patients aged 65 to 74 years (young-old), aged 75 to 84 years (old) and aged ≥85 years (old-old). The average age of our sample was 78.3 years, with the oldest patient aged 104 years. Subjects were also divided into three categories according to the tertile of hs-cTnT concentration: tertile 1 (0–14 ng/L = low level: normal, according to the manufacturer instructions), tertile 2 (15–31 ng/L = moderate level) and tertile 3 (≥32 ng/L = high level). The mean hs-cTnT level in our total sample was 79.9 ng/L.

The cohort was further categorized according to the occurrence of comorbidities: quartile 1 (one or two comorbidities), quartile 2 (three comorbidities), quartile 3 (four or five comorbidities) and quartile 4 (≥6 comorbidities). A large number of subjects ($n = 2414$; 35.4%) had six or more comorbidities. Arterial hypertension and cardiomyopathy were the most and the least frequently observed comorbidities, respectively.

Table 2 presents total and by-sex mean hs-cTnT levels according to the comorbidity quartiles. The standard deviation of total and all quartile from the mean of troponin level was found relatively high due to the dispersion of troponin values. The mean hs-cTnT was considered high across sexes, age groups and comorbidity quartiles.

**Table 1**
Demographic and clinical characteristics of the study cohort.

| Age: $\bar{x}$ ± SD | 65–74 years old ($n = 2555$) 69 ± 2.83 | 75–84 years old ($n = 2490$) 79 ± 2.88 | ≥85 years old ($n = 1777$) 89 ± 3.62 | All patients ($n = 6822$) 78.3 ± 8.30 |
|---|---|---|---|---|
| Men (%) | 1456 (57%) | 1294 (52%) | 649 (36%) | 3439 (50.4%) |
| Women (%) | 1098 (43%) | 1196 (48%) | 1128 (64%) | 3383 (49.6%) |
| Hs-cTnT ng/L ($\bar{x}$ ± SD) | 93 ± 312.15 | 77 ± 234.46 | 63 ± 162.73 | 79 ± 252.14 |
| Men | 104 ± 353.0 | 80 ± 183.73 | 70 ± 125.32 | 89 ± 264.64 |
| Women | 78 ± 242.34 | 74 ± 279.19 | 59 ± 180.71 | 70 ± 238.45 |
| Comorbidities (N, %) | | | | |
| Quartile I (1291, 19.4) | | | | |
| Men | 283.48 | 228.52 | 132.61 | 643.48 |
| Women | 349.52 | 207.48 | 83.49 | 684.52 |
| Quartile II (1048, 15.4) | | | | |
| Men | 169.39 | 188.48 | 149.58 | 506.48 |
| Women | 263.61 | 204.52 | 78.42 | 545.52 |
| Quartile III (2030, 19.8) | | | | |
| Men | 313.41 | 355.48 | 354.67 | 1022.51 |
| Women | 442.59 | 392.52 | 174.33 | 1008.49 |
| Quartile IV (2414, 35.4) | | | | |
| Men | 294.43 | 425.46 | 493.61 | 1212.51 |
| Women | 397.56 | 491.54 | 314.39 | 1202.49 |

Hs-cTnT (High-sensitivity cardiac Troponin T), ng/L = nanogram/L Quartiles (I = 1–2 comorbidities, II = 3 comorbidities, III = 4–5 comorbidities, IV = ≥6 comorbidities).

**Table 2**
Levels of hs-cTnT (ng/L) by sex and comorbidity quartiles.

| | Total ($\bar{X} \pm SD$) | Men ($\bar{X} \pm SD$) | Women ($\bar{X} \pm SD$) | P-value |
|---|---|---|---|---|
| Q I | 79 ± 324.68 | 93 ± 416.20 | 65 ± 181.78 | $p > 0.05$ |
| Q II | 81 ± 290.86 | 89 ± 263.39 | 71 ± 317.80 | $p > 0.05$ |
| Q III | 89 ± 264.02 | 97 ± 242.62 | 81 ± 283.43 | $p > 0.05$ |
| Q IV | 71 ± 161.85 | 66 ± 203.50 | 76 ± 119.84 | $p > 0.05$ |

Quartiles (I = 1–2 comorbidities, II = 3 comorbidities, III = 4–5 comorbidities, IV = ≥6 comorbidities), Hs-cTnT (High-sensitivity cardiac Troponin T), SD (standard deviation).

**Table 3**
Median and quartiles of hs-cTnT, by sex and age.

| | Male | Female |
|---|---|---|
| | Median [Q1; Q3] | Median [Q1; Q3] |
| 65–74 years | 24.0 [13.0; 57.2] | 19,0 [9.0; 45.2] |
| 75–84 years | 33.0 [19.0; 63.0] | 24,0 [14.0; 48.0] |
| 85+ years | 39.0 [25.0; 67.2] | 31,0 [20.0; 52.0] |

Q1: 25 percentile; Q3: 75 percentiles.

According to our primary data analysis, the probability of having raised levels of troponin was increased with all types of comorbidities. In our pooled analysis of patients' medical records, plasma levels of hs-cTnT had a non-parametric distribution as the hs-cTnT values were abnormally distributed. In other words, the level of hs-cTnT was extremely dispersed above the reference range, that means a lot of patients had raised hs-cTnT level >33 ng/L whereas the standard deviation that was of greater magnitude than its mean. It can be exemplified by an individual with an Hs-cTnT value of 9258 ng/L (which would probably be clinically correct) which could influence the Mean ($\bar{x}$).

By analyzing hs-cTnT across age groups when corrected for comorbid disease there was a significant decrease of baseline hs-cTnT in male patients and an insignificant trend in female patients (Table 3).

When participants with elevated Hs-cTnT were compared with participants with troponin levels within the reference range using the adjusted odds ratio, there was a significantly increased probability of having an increased level of troponin in the moderate or high-level range that came with age but also with each comorbidity (Table 4). For example, male participants of >84 years old had a crude odds ratio of 5.61 ($p < 0.001$) for having an increased level of hs-cTnT but this did not account for comorbid diseases of that group (Table 4).

**Table 5**
Adjusted odds ratio for one comorbidity and for a year of aging.

| Tertile of hs-cTnT | AOR | 95% CI | P value |
|---|---|---|---|
| 2 | | | |
| Burden of disease | 1.216 | [1.178, 1.255] | $p < 0.001$ |
| Age | 1.070 | [1.061, 1.080] | $p < 0.001$ |
| 3 | | | |
| Burden of disease | 1.311 | [1.272, 1.352] | $p < 0.001$ |
| Age | 1.073 | [1.064, 1.082] | $p < 0.001$ |

Reference category is: 1, CI = confidence interval. AOR = adjusted odds ratio.

In order to determine whether the observed increases in troponin were attributable to advancing age or the occurrence of comorbidities, adjusted OR (AOR) were included into our logistical regression model (Table 5). By analyzing the risk of having increased troponin levels with the adjusted odds ratio (AOR) still taking the population with normal troponin levels as the reference range, the relative impact of each added comorbidity surpasses the effect of one year of aging as shown in Table 4. Each year of aging confers an AOR of having a high level of hs-cTnT of 1.073 ($p < 0.001$) which is far less than the impact of one added comorbid disease which confers an AOR of 1.311 ($p < 0.001$).

The main disadvantage of the mean ($\bar{x}$) in statistical analysis refers to its susceptibility to the impact of outliners, so the mean cannot be representative of the values in the sample. Therefore, in this situation, it would be preferred to have a more accurate measure of central tendency. In this case, from a statistical point of view, the use of the Median [Q1: 25 percentile; Q3: 75 percentiles] which is not influenced by extreme values, seems more precise. Therefore, we applied the median to present Hs-cTnT values (interquartile range).

The occurrence of more comorbidity appears to have a greater influence on troponin levels, compared to age, in both hs-cTnT tertiles. In other words, among the elderly, age may not be a risk factor for increased cardiac troponin levels.

## 4. Discussion

Although the hs-cTnT is a marker that has made a significant contribution to the diagnosis of acute myocardial events, the interpretation of abnormal hs-cTnT levels remain as a debate among geriatric cardiologists. It could become a challenging clinical issue for the elderly patients with vague ischemic symptoms, atypical ECG and

**Table 4**
Odd ratios of having moderate or high levels of hs-cTnT in men and women, by age groups and the occurrence of comorbidities.

| | Hs-cTnT (0-14 ng/L) = Low level | | | Hs-cTnT (15-31 ng/L) = moderate level | | | Hs-cTnT (≥32 ng/L) = high level | | |
|---|---|---|---|---|---|---|---|---|---|
| Men | $N = 666$ | | | $N = 1125$ | | | $N = 1648$ | | |
| Women | $N = 860$ | | | $N = 1176$ | | | $N = 1342$ | | |
| | OR | 95% CI | P value | OR | 95% CI | P value | OR | 95% CI | P value |
| Sum of the comorbidities for men | 1.22 | [1.16; 1.28] | $p < 0.001$ | 1.38 | [1.31; 1.44] | $p < 0.001$ | | | |
| Sum of the comorbidities for women | 1.23 | [1.18; 1.28] | $p < 0.001$ | 1.26 | [1.21; 1.32] | $p < 0.001$ | | | |
| Old group [75–84 years old] | | | | | | | | | |
| Men | 2.03 | [1.63; 2.52] | $p < 0.001$ | 2.13 | [1.73; 2.63] | $p < 0.001$ | | | |
| Women | 1.53 | [1.25; 1.89] | $p < 0.001$ | 1.70 | [1.37; 2.10] | $p < 0.001$ | | | |
| Old-old group [≥85 years old] | | | | | | | | | |
| Men | 4.49 | [3.10; 6.50] | $p < 0.001$ | 5.61 | [3.92; 8.03] | $p < 0.001$ | | | |
| Women | 4.45 | [3.42; 5.70] | $p < 0.001$ | 4.55 | [3.53; 5.82] | $p < 0.001$ | | | |
| Young-old group [65–74 years old] | | | | | | | | | |
| Men | 1 | | | 1 | | | | | |
| Women | 1 | | | 1 | | | | | |

Reference group: 1, CI = confidence interval. Multivariate logistic regressions were performed to quantify the risk of having a high level of troponin according to age and comorbidities. For both the old and old-old age groups and for both sexes, we observed a greater risk of having higher levels of hs-cTnT. After calculating odds ratio, with each increase in age, in all age groups of both sexes, the risk of having a moderate and high level of hs-cTnT has shown to be increased.

abnormal cTnT levels, to diagnose whether the patient suffer from ACS, since it is proven that certain adverse outcomes due to acute coronary events increase with age [15].

This study aimed to determine the influence of age on the value of hs-cTnT in older adults without acute cardiac events, but with one or more comorbidities, to improve the diagnostic prediction of acute coronary events in elderly.

The results of the present study have shown that, in elderly and very elderly patients suffering from different comorbidities, the presence of comorbidities compared with advancing age has more effect to rising hs-cTnT level. In other words, the raised cardiac troponin in the absence of AMI or ACS in the elderly population resulted from the presence of comorbidities and not from their age.

The main significant novelty of the present study is to exclude acute cardiac events (ACE) in order to eliminate the role of cardiac injury on increasing hs-cTnT levels, and to consider the comorbidities in the sample pools as well. That means that the effects of advancing age and ACE, as confounding biases, are diminished.

In our literature review, among the comorbidities that have been included in the different studies, almost all papers indicated that the renal dysfunction and congestive heart failure are the main reasons for the increased hs-cTnT values in geriatric patients [16,17].

In almost all previous similar studies where the individuals were screened to rule out ACS, the majority of these studies have justified the increased hs-cTnT level as related to the advanced age if the ACS could be excluded. Although in these studies the comorbidities were presented, the authors only indicated that the reason for the increased hs-cTnT levels was the advanced age [8,18–25]. In other words, the age has been considered as the main factor for explaining the elevated hs-cTnT.

Although a few studies have suggested the influence of comorbidities on raised hs-cTnT, they were still more attributed to the effect of advancing age [26]. Several studies have considered the influence of age on hs-cTnT as significant; consequently, they have underestimated the diagnostic role of hs-cTnT assay in ACE profiles [16,17]. While, our data analysis suggests a different interpretation of the rising hs-cTnT levels in elderly, namely the hs-cTnT could still be a sensitive and very useful acute cardiac biomarker to detect acute coronary events, and could play a more significant role in ACS diagnosis in aged patients, mainly in old-old patients if other reasons of its elevation are taken into consideration such as other causes (co-morbidities) leading to increased hs-cTnT levels.

A study of factors affecting hs-cTnT values has shown that the hs-cTnT levels are higher in men and increases with age in both men and women [27]. Our results fit with the first part of mentioned study, which means that the basic levels of hs-cTnT are increased in men compared to women, but in contrast our results have shown that the hs-cTnT levels are not showing clinically significant change with advancing age in both sexes.

As the previous studies have significantly interpreted the elevated of hs-cTnT values as an effect of advancing age [13,19], our data analysis shows that the possible causes of the increased hs-cTnT in elderly population are the presence of different comorbidities, and not advancing age. Our results are also not in agreement with those of Kuster et al. showing that hs-cTnT concentration, independently of comorbidities, increases exponentially with age after 65 years [6]. However, in their study the authors had used Cox regression to analyze their data which was not possible in our condition due to abnormal distribution of the hs-cTnT values. If the elevated hs-cTnT value considered as a result of advancing age, it may be assumed that the hs-cTnT assay is not a reliable criterion to exclude ACE in diagnosis of geriatric patients. However, at the absence of a thrombotic complication of coronary artery disease in elderly patients, an elevated hs-cTnT could be the result of undiagnosed comorbidities. Considering our pool of patients, it could be concluded that among elderly patients of either sex, with abnormal hs-cTnT values, older patients were more likely to have an elevated troponin level compared to the younger cohorts due to the presence of comorbidities, but not to age ($p < 0.001$).

To our knowledge, this is the first study to document that advancing age has a less role to play in elderly patients with high hs-cTnT concentrations. Based on the results of the present study, the elevated levels of hs-cTnT in aged patients without any ACE are further due to other causes which should be thoroughly investigated.

## 5. Conclusion

It is shown that there is an overall increase of hs-cTnT values in all groups of elderly patients with comorbidities. Our findings suggest that in elderly patients the association of elevated hs-cTnT is mostly explained by the presence of comorbidity than by advancing age. Consequently, an increased hs-cTnT value in an elderly subject that is not associated to the occurrence of ACS should be always be investigated for other underlying clinical problems.

## 6. Study strengths

In the current study, our sample size was large, so in our statistical analysis the *t*-test has so much power that even a minuscule difference was flagged as statistically significant. On the other hand, we recruited the medical records of a large heterogeneous elderly population, who were divided into three main aged groups with seventeen comorbidities, so our results could be applied or generated to represent group of elderly patients, as a whole. Thus, the main result of the study showing that age is not the main cause for hs-cTnT can be most probably generalized.

## 7. Study limitations

In our study, the evaluation of hs-cTnT accuracy was limited since the data was collected only on elderly patients with different comorbidities, without having much awareness of their concomitant therapy. In other words, it is not possible to quantify the presence of different comorbidity, how much it could increase the level of hs-cTnT values. Therefore, we cannot speculate the variance of the hs-cTnT values in elderly patients who were affected by different concomitant diseases with respect to their comorbidity.

Lastly, in this study, although the data were included from a large cohort of patients, these data are observational.

## 8. Future directions

Features of acute coronary events in elderly and very elderly patients comprise life-threatening conditions that require immediate and efficient medical intervention to improve prospective outcomes, particularly in the presence of atypical signs and symptoms. Judicious interpretation of increased hs-cTnT levels is essential in different fields of medicine, particularly in emergency wards, intensive care units and geriatric cardiology. Clinical assessment with use of para-clinical data is critical for an accurate and prompt diagnosis followed by appropriate management. Thoughtful interpretation of hs-cTnT levels may yield insight into physio-pathological mechanism of the concomitant condition that causes the raised hs-cTnT in elderly. Furthermore, future directions should aim to find the cut-off level for hs-cTnT levels at the presence of different comorbidities in acute coronary events, and study the relationship between mortality and increased levels of troponin in elderly patients with different comorbidities as well.

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## Conflict of interest

- The authors do not declare any competing interest.
- A part of these results was presented as a poster at the ESC Congress 2018, Munich, Germany.

## Disclosures

No actual or potential conflict of interest in relation to this study to declare. We also testify that we have no relationships with industry in connection with this study.

## References

[1] K.P. Alexander, L.K. Newby, C.P. Cannon, P.W. Armstrong, W.B. Gibler, M.W. Rich, F. Van de Werf, H.D. White, W.D. Weaver, M.D. Naylor, J.M. Gore, H.M. Krumholz, E.M. Ohman, American Heart Association Council on Clinical C, Society of Geriatric C. Acute coronary care in the elderly, part I: non-ST-segment-elevation acute coronary syndromes: a scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology: in collaboration with the Society of Geriatric Cardiology, Circulation 115 (2007) 2549–2569.

[2] A. Saraswat, A. Rahman, K. Singh, An invasive vs a conservative approach in elderly patients with non-ST-segment elevation myocardial infarction: systematic review and meta-analysis, Can J Cardiol 34 (2018) 274–280.

[3] M. Gierlotka, M. Gasior, M. Tajstra, M. Hawranek, T. Osadnik, K. Wilczek, Z. Kalarus, A. Lekston, M. Zembala, L. Polonski, Outcomes of invasive treatment in very elderly Polish patients with non-ST-segment-elevation myocardial infarction from 2003–2009 (from the PL-ACS registry), Cardiol. J. 20 (2013) 34–43.

[4] A. Garg, L. Garg, M. Agarwal, A. Rout, H. Raheja, S. Agrawal, S.V. Rao, M. Cohen, Routine invasive versus selective invasive strategy in elderly patients older than 75 years with non-ST-segment elevation acute coronary syndrome: a systematic review and meta-analysis, Mayo Clin. Proc. 93 (2018) 436–444.

[5] J.N. Boeckel, L. Palapies, J. Klotsche, T. Zeller, B. von Jeinsen, M.F. Perret, S.L. Kleinhaus, L. Pieper, S. Tzikas, D. Leistner, C. Bickel, G.K. Stalla, H. Lehnert, B. Lindahl, H.U. Wittchen, S. Silber, S. Baldus, W. Maerz, S. Dimmeler, S. Blankenberg, T. Munzel, A.M. Zeiher, T. Keller, Adjusted troponin I for improved evaluation of patients with chest pain, Sci. Rep. 8 (2018) 8087.

[6] N. Kuster, K. Monnier, G. Baptista, A.M. Dupuy, S. Badiou, A.S. Bargnoux, C. Jeandel, J.P. Cristol, Estimation of age- and comorbidities-adjusted percentiles of high-sensitivity cardiac troponin T levels in the elderly, Clin. Chem. Lab. Med. 53 (2015) 691–698.

[7] P. Scarborough, K. Wickramasinghe, P. Bhatnagar, M. Rayner, Trends in Coronary Heart Disease 1961–2011, London: British Heart Foundation 2011 (2011).

[8] M.G. Rains, C.A. Laney, A.L. Bailey, C.L. Campbell, Biomarkers of acute myocardial infarction in the elderly: troponin and beyond, Clin. Interv. Aging 9 (2014) 1081–1090.

[9] T. Nguyen Dang, B.W. Karlson, T. Karlsson, J. Herlitz, Characteristics of and outcomes for elderly patients with acute myocardial infarction: differences between females and males, Clin. Interv. Aging 2016 (11) (2016) 1309–1316.

[10] H.V. Barron, L.J. Bowlby, T. Breen, W.J. Rogers, J.G. Canto, Y. Zhang, A.J. Tiefenbrunn, W.D. Weaver, Use of reperfusion therapy for acute myocardial infarction in the United States: data from the National Registry of Myocardial Infarction 2, Circulation 97 (1998) 1150–1156.

[11] B. Elbarouni, S.G. Goodman, R.T. Yan, R.C. Welsh, J.M. Kornder, J.P. Deyoung, G.C. Wong, B. Rose, F.R. Grondin, R. Gallo, M. Tan, A. Casanova, K.A. Eagle, A.T. Yan, Canadian Global Registry of Acute Coronary Events I. Validation of the Global Registry of Acute Coronary Event (GRACE) risk score for in-hospital mortality in patients with acute coronary syndrome in Canada, Am. Heart J. 158 (2009) 392–399.

[12] R. Inbar, Y. Shoenfeld, Elevated cardiac troponins: the ultimate marker for myocardial necrosis, but not without a differential diagnosis, Isr. Med. Assoc. J. 11 (2009) 50–53.

[13] F. Ferri, Ferri's Best Test. A Practical Guide to Clincal Laboratory Medicine and Diagnostic Imaging, Third Edition ELSEVIER SAUNDERS, Philadelphia, 2015.

[14] C. Borna, K.L. Frostred, U. Ekelund, Predictive role of high sensitivity troponin T within four hours from presentation of acute coronary syndrome in elderly patients, BMC Emerg Med 16 (1) (2016).

[15] A. Ngako, A. Santin, F. Hemery, M. Salloum, M.J. Calmettes, J. Herve, J.C. Grego, E. Roupie, P. Maison, B. Renaud, Prediction of myocardial infarction risk in older patients with acute coronary syndrome, Am. J. Emerg. Med. 27 (2009) 675–682.

[16] N. Mahajan, Y. Mehta, M. Rose, J. Shani, E. Lichstein, Elevated troponin level is not synonymous with myocardial infarction, Int. J. Cardiol. 111 (3) (2006) 442–449, https://doi.org/10.1016/j.ijcard.2005.1008.1029.

[17] E.J. Lamb, M.C. Webb, N.A. Abbas, The significance of serum troponin T in patients with kidney disease: a review of the literature, Ann. Clin. Biochem. 41 (2004) 1–9.

[18] M.O. Gore, S.L. Seliger, C.R. Defilippi, V. Nambi, R.H. Christenson, I.A. Hashim, R.C. Hoogeveen, C.R. Ayers, W. Sun, D.K. McGuire, C.M. Ballantyne, J.A. de Lemos, Age- and sex-dependent upper reference limits for the high-sensitivity cardiac troponin T assay, J. Am. Coll. Cardiol. 63 (2014) 1441–1448.

[19] F. Olivieri, R. Galeazzi, D. Giavarina, R. Testa, A.M. Abbatecola, A. Ceka, P. Tamburrini, F. Busco, R. Lazzarini, D. Monti, C. Franceschi, A.D. Procopio, R. Antonicelli, Aged-related increase of high sensitive Troponin T and its implication in acute myocardial infarction diagnosis of elderly patients, Mech. Ageing Dev. 133 (2012) 300–305.

[20] P. Bahrmann, H.J. Heppner, M. Christ, T. Bertsch, C. Sieber, Early detection of non-ST-elevation myocardial infarction in geriatric patients by a new high-sensitive cardiac troponin T assay, Aging Clin. Exp. Res. 24 (2012) 290–294.

[21] M.J. Zaman, K. Vrotsou, G.S. Chu, H.M. May, P.K. Myint, A high incidental rise in cardiac troponin I carries a higher mortality risk in older patients than in those with a diagnosed acute coronary syndrome, Age Ageing 40 (2011) 122–125.

[22] A. Carro, J.C. Kaski, Myocardial infarction in the elderly, Aging Dis 2 (2011) 116–137.

[23] M. Covino, B. Simeoni, M. Montalto, F. Burzotta, F. Buccelletti, L. Carbone, A. Gallo, N. Gentiloni Silveri, Reduced performance of Troponin T for acute coronary syndromes diagnosis in the elderly and very elderly patients: a retrospective study of 2688 patients, Eur. Rev. Med. Pharmacol. Sci. 16 (Suppl. 1) (2012) 8–15.

[24] T. Zeller, F. Ojeda, F.J. Brunner, P. Peitsmeyer, T. Munzel, H. Binder, N. Pfeiffer, M. Michal, P.S. Wild, S. Blankenberg, K.J. Lackner, High-sensitivity cardiac troponin I in the general population—defining reference populations for the determination of the 99th percentile in the Gutenberg Health Study, Clin. Chem. Lab. Med. 53 (2015) 699–706.

[25] I.G. Webb, S.T. Yam, R. Cooke, A. Aitken, P.D. Larsen, S.A. Harding, Elevated baseline cardiac troponin levels in the elderly - another variable to consider? Heart Lung Circ 24 (2015) 142–148.

[26] J. Gravning, E.T. Askevold, S.H. Nymo, T. Ueland, J. Wikstrand, J.J. McMurray, P. Aukrust, L. Gullestad, J. Kjekshus, Group CS, Prognostic effect of high-sensitive troponin T assessment in elderly patients with chronic heart failure: results from the CORONA trial, Circ Heart Fail 7 (2014) 96–103.

[27] T.P. Noeller, S.W. Meldon, W.F. Peacock, C.L. Emerman, E.S. McErlean, F. Vanlente, S.E. Nissen, Troponin T in elders with suspected acute coronary syndromes, Am. J. Emerg. Med. 21 (2003) 293–297.