Selenium deficiency and the dynamics of changes of thyroid profile in patients with acute myocardial infarction and chronic heart failure

Authors: Magdalena Frączek-Jucha, Małgorzata Kabat, Barbara Szlósarczyk, Urszula Czubek, Jadwiga Nessler, Andrzej Gackowski

Article type: Original article

Received: April 14, 2019.

Accepted: May 6, 2019.

Published online: May 7, 2019.

ISSN: 0022-9032

e-ISSN: 1897-4279

This is an Open Access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives 4.0 International License (CC BY-NC-ND 4.0), allowing third parties to download articles and share them with others, provided the original work is properly cited, not changed in any way, distributed under the same license, and used for noncommercial purposes only. For commercial use, please contact the journal office at kardiologiapolska@ptkardio.pl.
Selenium deficiency and the dynamics of changes of thyroid profile in patients with acute myocardial infarction and chronic heart failure

Frączek-Jucha Magdalena MD\textsuperscript{1,2,3}, Kabat Małgorzata MD\textsuperscript{1,3}, Barbara Szlósarczyk MD\textsuperscript{3}, Czubek Urszula MD\textsuperscript{3}, Nessler Jadwiga MD, PhD, Prof\textsuperscript{1,3}, Gackowski Andrzej MD, PhD\textsuperscript{1,3}

1) Jagiellonian University Medical College, Department of Coronary Disease and Heart Failure, Krakow, Poland
2) Jagiellonian University Medical College, Department of Emergency Medical Care, Krakow, Poland
3) John Paul II Hospital, Department of Coronary Disease and Heart Failure, Krakow, Poland

Brief title: Selenium and thyroid in cardiovascular diseases.

Address for correspondence:
Andrzej Gackowski MD, PhD
Klinika Choroby Wieńcowej i Niewydolności Serca
Krakowski Szpital Specjalistyczny im. Jana Pawła II
ul. Prądnicka 80, 31-202 Kraków
e-mail address: agackowski@gmail.com
phone number: 0048 12 614 22 18
fax number: 0048 12 433 43 76

Conflict of interest: none declared.
ABSTRACT

Background: Selenium (Se) is incorporated in 25 enzymes e.g.: glutathione peroxidase (GPX) (activated by oxidative stress) and deiodinases (converting thyroid hormones). Oxidative stress present in heart failure (HF) and myocardial infarction (MI) might cause Se deficiency and decreased tetraiodothyronine (T4) to triiodothyronine (T3) conversion.

Aims: We sought to evaluate Se levels in Polish patients with MI, HF and healthy volunteers in relation to thyroid hormones.

Methods: The study group consisted of 143 participants: 54 MI patients, 59 patients with decompensated HF, and 30 healthy matched volunteers. Patients underwent echo and laboratory tests on admission and after 5 months.

Results: Se levels were lowered in MI and HF patients in comparison to controls (medians, 65.9 [55.2-76.1] and 59.7 [47.7-70.7] vs. 93.2 [84.2-99.1], p<0.0001).

Se deficiency was very frequent in MI and HF patients, while it was rare in controls [70.37% and 74.58% vs. 10%, p<0.0001]. Patients with MI and HF presented lower free triiodothyronine (fT3) levels and fT3/fT4 ratio comparing to controls (medians, 3.90 [3.60-4.38] and 4.25 [3.57-4.60] vs. 4.92 [4.50-5.27], p <0.0001; and 0.25 [0.23-0.29] and 0.25 [0.21- 0.2] vs. 0.32 [0.29; 0.37], p <0.0001, respectively).

There was a weak to moderate correlation between Se and fT3 and the fT3/fT4 ratio. The fT3/fT4 ratio tended to normalize in MI patients at follow-up, while it remained decreased in HF patients.

Conclusions: Se deficiency is very frequent in Polish MI and HF patients. Thyroid hormones disturbances were more transient in MI patients, while they were more chronic in individuals with HF.

Keywords: myocardial infarction; heart failure; selenium; thyroid hormones
WHAT IS NEW?

The function of deiodinases (enzymes converting thyroid hormones) may be disturbed by oxidative stress accompanying heart failure (HF) or myocardial infarction (MI), because both deiodinases and glutathione peroxidase (an anti-oxidant enzyme) are selenoproteins competing for selenium.

Our research revealed that selenium deficiency is very frequent in Polish patients with MI or HF. They also present lower levels of fT3 and the fT3/fT4 ratio. We noticed that thyroid hormones disturbances are transient in acute MI, while they are chronic in HF. There is a mild-to-moderate correlation between selenium and thyroid hormones. Further studies are needed to investigate if selenium deficiency may contribute to the progression of HF. They may create a background for selenium supplementation in HF.
INTRODUCTION

Selenium (Se) is an important micronutrient in human health. It is incorporated in 25 selenoproteins containing selenocysteine at their active center e.g.: glutathione peroxidase (GPX), iodothyronine deiodinases, selenoprotein P, thioredoxin reductase, selenoprotein S and other selenoproteins. Because the health effect of Se is U-shaped, toxic concentrations may be harmful. This is why Se supplementation may be beneficial only in people with low Se status. Dietary Se intake varies worldwide from 7 μg to 4990 μg per day. The mean value in Europe is 40 μg per day and in the USA 93 μg per day (in women) to 134 μg per day (in men). Nutritional products that are rich in selenium are: brazil nuts, offal, seafood, cereals and grains [1-4].

Cardiovascular diseases may be associated with oxidative stress as a consequence of insufficient antioxidant dietary intake and an improper balance between pro-oxidant and anti-oxidant enzymes, leading to an excess of reactive oxygen species [5]. It has been proven that low GPX activity can be used to identify patients at high cardiovascular risk [6,7]. As Se levels correlate positively with enzymatic activity and protein levels of GPX, Se plasma analysis may be used for indirect oxidative stress assessment [8,9]. Insufficiency of GPX and Se may exacerbate endothelial dysfunction, low-density lipoprotein cholesterol oxidation, atherosclerosis, cardiac sensitivity to ischemia and reperfusion, as well as impaired thyroid hormones conversion. These phenomena may contribute to heart failure (HF) development [9-13].

A prospective epidemiological study conducted in Finland revealed that the Se concentration in serum is inversely related to the risk of myocardial infarction (MI) occurrence and cardiovascular death [14]. Another research conducted in New Zealand showed that decreased levels of Se in blood in cigarette smokers is a risk factor for coronary heart disease [15]. Se
deficiency is mentioned in the current European Society of Cardiology Guidelines for the
diagnosis and treatment of acute and chronic HF as a nutritional cause of the disease [16]. Se
deficiency is a possible risk factor for Keshan disease - endemic cardiomyopathy in selenium-
poor areas of China [17]. Even in selenium-rich areas, HF caused by Se deficiency may be a
result of malnutrition occurring in patients with HIV, intestine diseases, parenteral nutrition or
it might occur after bariatric surgery [18-20].

Because selenoproteins (GPX and iodothyronine deiodinases) may compete for Se, oxidative
stress causing Se deficiency may contribute to disturbances of thyroid hormones conversion.
These conditions alone and collectively may affect the cardiovascular system. Lifestyle, diet
and smoking habits differ from country to country and may influence Se levels. To our
knowledge, Se levels were not studied in the context of thyroid function in patients with
cardiovascular diseases in Poland. The main purpose of the study was evaluation of Se levels
in Polish patients with MI, HF and healthy volunteers in relation to thyroid hormones levels.
We also evaluated the clinical course of MI and HF in subgroups with normal or lowered Se
concentrations.

METHODS

Study population

The study protocol (prospective cohort study) was approved by the Ethics Committee. All
procedures performed in studies involving human participants were in accordance with the
ethical standards of the Declaration of Helsinki. From June 2015 to August 2017 we
prospectively evaluated 113 consecutively hospitalized patients and 30 healthy volunteers
who gave written informed consent and fulfilled the inclusion/exclusion criteria:

a) Group MI consisted of patients with acute MI with ST elevation or non-ST elevation,
treated with primary percutaneous coronary intervention [21]. Exclusion criteria were:
previous HF, thyroid disease, treatment with amiodarone, glucocorticosteroids, propranolol), clinical evidence of severe systemic disease (inflammatory, autoimmune, neoplastic disease or chronic renal disease (estimated Glomerular Filtration Rate (eGFR) < 30 mL/min/1.73m²).

b) **Group HF** consisted of patients with decompensation of HF with reduced ejection fraction (HFrEF) [16]. Exclusion criteria were: acute coronary syndrome, thyroid disease, treatment with amiodarone, glucocorticosteroids, propranolol), clinical evidence of severe systemic disease (inflammatory, autoimmune, neoplastic disease or chronic renal disease (eGFR < 30 mL/min/1.73m²).

Patients received optimal guideline-directed medical treatment.

c) **Group C** (control group) was composed of sex and age-matched healthy volunteers with normal electrocardiogram.

Depending on the Se concentration, additional 4 subgroups were distinguished from MI and HF groups: MI-A and HF-A subgroups - patients with Se concentration below the normal values, and MI-B and HF-B subgroups respectively, consisting of the remaining patients without decreased Se levels.

**Biochemical tests**

Single blood samples were collected for thyroid profiles and Se in C group. Serial blood samples were collected in MI and HF groups.

On the 1st and 3rd days of hospitalization and on the follow-up visit the patients had the following laboratory tests performed: thyroid stimulating hormone (TSH) (electrochemiluminescent immunoassay [ECLIA] method), free tetraiodothyronine (fT4), free triiodothyronine (fT3) (ECLIA method). Then, the fT3/fT4 ratio was calculated. Reverse triiodothyronine (rT3) (radioisotope method) was determined on the 3rd day of hospitalization.
Laboratory reference values were: TSH (0.27 – 4.2 µIU/mL), fT3 (3.10 – 6.80 pmol/L), fT4 (12.0-22.0 pmol/L), rT3 (0.09-0.35 ng/mL).

N-terminal pro B-type Natriuretic Peptide (NT-proBNP) (ECLIA method) levels were analyzed on the 1st and 3rd days of hospitalization and on the follow-up. The reference value for NT-proBNP was < 125.0 pg/mL. Inflammatory markers: high sensitivity C-reactive protein (hsCRP) (immunoturbidimetric method) and white blood count (WBC) (Hydro Dynamic Focusing flow cytometry method) were performed on the 1st and 3rd days.

Creatinine levels (Jaffé Gen.2 method, rate blanked, compensated) and eGFR/CKD-EPI/ were assessed at admission.

Serum levels of high sensitivity troponin T (hsTnT), creatinine kinase MB (CK-MB) and creatinine kinase (CK) (ECLIA method) in group MI were measured at admission and every 6 hours during the first 24 hours. Normal values were: hsTnT (<0,014 ng/mL), CK-MB (0-24 U/L), CK (0-190 U/L).

Biochemical tests were performed with the use of Roche Diagnostics GmbH (Mannheim, Germany) kits. Full Blood Count was performed with the use of Sysmex Corporation (Kobe, Japan) kits.

Samples for selenium levels in serum were taken on the 3rd day of hospitalization using the Vacutainer system. After collection, blood samples were left to clot for 30 minutes and were centrifuged afterwards (1300G, 12 minutes). Serum samples were frozen at -80°C (-112°F).

On the day of analysis, samples were centrifuged (5000G, 5 minutes). Analyses were carried out using inductively coupled plasma mass spectrometry. Se determination was performed on an inductively coupled plasma mass spectrometer NexION 350D (PerkinElmer, Shelton, USA). The spectrometer was equipped with a dynamic reaction cell operating with high purity methane. It was calibrated using an external calibration technique. Calibration standards were prepared from 10 µg/mL Multi-Element Calibration Standard 3.
coefficients for calibration curves were always greater than 0.999. The analysis protocol assumed 100-fold dilution of serum in a reagent blank. The reagent blank consisted of 10 mL of 65% Suprapur Grade nitric acid (Merck, Germany), 0.20 mL of Triton X-100 (PerkinElmer, USA) filled to the mark of a 1 liter flask with class I deionized water (Merck Millipore). Germanium isotope - Ge$^{74}$ was set as an internal standard.

The quality of Se determination was checked with the use of reference material Clincheck Plasmonorm Serum Trace Elements Level 1. Se reference levels were established in the group of 2500 women and 1600 men from Polish population.

Reference values of selenium in the local laboratory were as follows: females <50 years old (75.0 - 85.0 µg/L), females >50 years old (65.0 - 75.0 µg/L), males <60 years old (85.0 - 95.0 µg/L), males >60 years old (70.0 - 90.0 µg/L).

**Echocardiographic assessment**

A transthoracic echocardiographic evaluation of the left ventricle was performed during hospitalization and on the follow-up visit (Philips IE33, Amsterdam, The Netherlands) by the same echocardiographer and reviewed and confirmed blindly by another echocardiographer. The following parameters were analyzed: left ventricle end-diastolic diameter and volume (LVEDD, LVEDV), left ventricle ejection fraction (LVEF), the left ventricle filling profile, E/E’ index, tricuspid annular plane systolic excursion (TAPSE) and right ventricle systolic pressure (RVSP).

**Study end-points**

Major adverse cardiovascular events (MACE) in MI and HF groups included: resuscitated cardiac arrest, cardiovascular death, re-hospitalization for heart failure decompensation requiring intravenous diuretics and/or catecholamines, evidence of ventricular tachycardia, severe sinus bradycardia or atrioventricular blocks.
Each of the events was analyzed during the hospital stay and during the follow-up of 154.0 (132.8;168.8) days in MI group and 144.0 (123.0;161.0) days in HF group. The occurrence of the composite endpoint of the above adverse events was also analyzed.

**Statistical analysis**

Categorical variables are presented as numbers and percentages. Continuous variables are expressed as mean ± standard deviations (SD) or median and interquartile ranges (IQR). Normality was assessed by the Shapiro-Wilk test. The equality of variances was assessed using the Levene’s test. Differences between groups were compared using the Student’s or Welch’s t-test depending on the equality of variances for normally distributed variables. The Mann-Whitney U-test was used for non-normally distributed continuous variables. Categorical variables were compared by the Pearson’s chi-squared test or the Fisher’s exact test if 20% of cells had an expected count of less than 5. For two paired data samples, the paired Student’s t-test was used if differences between pairs were normally distributed, and the Wilcoxon signed-rank was used if they were not normally distributed. For more than two measurements the repeated measures ANOVA was used. Post hoc analyses for independent samples were made using the Tukey-Kramer HSD or the Steel-Dwass method, for paired samples, p-values were adjusted using the Bonferroni correction. The coefficient correlation that measures dependence between variables was calculated using the Pearson’s test or the Spearman’s rank correlation coefficient depending on normality. Statistical analyses were performed with JMP®, Version 14.0.0 (SAS Institute INC., Cary, NC, USA) and using R, Version 3.4.1 (R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. Vienna, Austria, 2017). A p-value less than 0.05 was considered as statistically significant.
RESULTS

Characteristics of MI and HF groups and comparison of subgroups according to Se concentration are presented in Table 1 and Table 2.

There was no difference between MI-A and MI-B groups according to age, sex, body mass index (BMI), MI type, culprit coronary artery and occurrence of hypertension, diabetes mellitus, dyslipidemia and smoking. In addition, subgroups did not differ according to laboratory tests: hsTnT, CKMB, CK, NT-proBNP, hsCRP, eGFR, TSH, thyroid hormones as well as all analyzed echocardiographic parameters. We noticed increased WBC on the 3rd day in subgroup MI-A in comparison to subgroup MI-B.

We demonstrated that patients from subgroup HF-A in comparison to patients from subgroup HF-B presented: higher rT3 levels and a higher number of patients with a restrictive mitral filling pattern. There was no difference between groups HF-A and HF-B according to age, sex, BMI, occurrence of hypertension, diabetes mellitus, dyslipidemia, smoking and HF etiology. Subgroup HF-A did not differ from subgroup HF-B according to laboratory tests: NT-proBNP, hsCRP, WBC, eGFR, TSH, fT3, fT4, the fT3/fT4 ratio as well as all remaining echocardiographic parameters.

We did not find more frequent occurrence of individual MACE (p>0.05 for each predefined end point) nor for the composite endpoint of all adverse events (p>0.05) in MI-A and HF-A subgroups in comparison to MI-B and HF-B subgroups.

Comparison of MI, HF and C groups is presented in Table 3. There was no difference regarding age and sex. The studied groups differed with respect to BMI and blood pressure. The prevalence of Se deficiency was present in the majority of participants from MI and HF groups. Conversely, Se deficiency was found in the minority of participants in the control group. In addition, Se levels were lower in both MI and HF groups in comparison to the controls (Table 3, Figure 1).
Differences existed between study groups in TSH, fT3, fT4 and the fT3/fT4 ratio (Table 3, Figure 2). There were differences in evolution of fT3 levels and fT3/fT4 ratio in both MI and HF groups (Figure 3). There was also a dynamic change of TSH during the acute phase of MI and its normalization during a follow-up (Figure 3).

Correlation analysis between Se, TSH and TH is presented in Table 4 and Figure 4. There were weak correlations between Se, fT3 and fT4. Moderate correlations were found between Se and fT3/fT4 ratio.

We did not find correlations between selenium and clinical variables such as: LVEF, hsT, CK, CKMB, NT-proBNP, creatinine, WBC, hsCRP.

**DISCUSSION**

Our research revealed that Se levels were significantly lowered in both patients with MI and chronic HF in comparison to healthy controls. Results of former research available in literature were inconclusive. De Lorgeril et al. demonstrated that dietary intake and blood levels of Se were lowered in French patients with chronic HF [22]. Also, Kosar et al. of Turkey demonstrated that both dilated idiopathic and ischemic cardiomyopathy were associated with lower Se levels [23]. Conversely, another study conducted by Ghaemian et al. of northern Iran did not support these results [24]. Lower Se concentrations were previously found in patients with myocardial infarction [15, 25-27]. Discrepancies found in various studies might have been caused by differences in Se intake in distinctive geographical areas. The Mediterranean diet in the northern Iran is rich in Se. This is possibly the reason why both HF patients and healthy controls in their study had high Se levels [22,24].

In our research we did not find correlations between Se and clinical variables reflecting disease severity. Previously, Se levels were found to be positively correlated with serum CK activity, serum myoglobin and maximum troponin levels [25,28,29]. Another research
revealed that Se may play a role in the clinical severity of HF (assessed by peak exercise oxygen consumption) [22], rather than in the degree of left ventricular dysfunction [22-24]. However, the results are inconclusive because some previous researches found a positive correlation between Se and the LVEF in HF, and coronary artery disease [30-32,28]. Nevertheless, sample sizes of the above study groups were very limited.

The presented findings suggest that Se levels may be lowered in both acute and chronic cardiac disorders. Further studies are needed because it is not clear whether Se deficiency contributes to disease progression or a marker of its severity only. In addition, data about Se supplementation and its possible positive influence on clinical variables are very limited and not focused on Se alone; instead they consider many micronutrients taken together. It is also important that in studies of Se supplementation, baseline and target Se levels were not clearly defined, although it is known that Se overdosing may be harmful [33-35].

There is growing evidence that oxidative stress and thyroid function are significant factors in HF development, while GPX correlate with Se. We sought to check the relationship between Se and thyroid hormones. We found only weak correlations between Se and thyroid hormone levels, while the correlation between Se and fT3/fT4 ratio was moderate. It would be of interest to investigate the causality of this relationship.

Our results showed differences in thyroid profiles between groups. Patients with MI and HF presented lower levels of fT3 in comparison to the controls. Patients with MI presented dynamic changes of TSH and fT3 in the first 3 days of hospitalization. Similar findings came from the research performed by Friberg et al. who demonstrated that there was a rapid down-regulation of thyroid hormones in acute MI [36]. The low T3 syndrome and the decreased fT3/fT4 ratio was previously shown to be a prognostic predictor of death in patients with heart diseases [37,38]. Our data indicate that there is a difference in T4 to T3 conversion between acute and chronic conditions.
Additionally, there was no difference in the fT3/fT4 ratio between the MI group and the control group on follow-up. However, a lowered fT3/fT4 ratio was still present in the HF group in comparison to the control group. The results suggest that changes of the fT3/fT4 ratio are more dynamic and transient in MI in comparison to the more chronic condition of HF.

Although we were able to find articles considering Se deficiency and thyroid hormones disturbances in HF and MI patients, there is a lack of studies involving both conditions together. Lima et al. did not find connections between Se and thyroid hormones and concluded that hypothyroidism is possibly linked with severity of HF but not micronutrients [39]. However, in our research not only we demonstrated lowered Se levels and disturbed thyroid hormones in study groups, but we also found a correlation between them. Perhaps there is a dependence between these phenomena. In our opinion, further research focused on Se levels, selenium-dependent enzymes and their influence on the course of cardiovascular diseases, especially HF is needed.

**CONCLUSIONS**

Se levels in both acute MI and HF patients are lower when compared to healthy volunteers. Se deficiency is very frequent in acute MI and both acute and chronic HF. The correlation between Se and thyroid hormones was found to be weak to moderate. Further research on Se deficiency in relation to oxidative stress markers and thyroid hormone conversion disturbances in cardiovascular diseases is needed, particularly in HF patients. The potential role of Se deficiency in the progression of HF should also be studied to verify if there is a background for possible benefits of Se supplementation.
STUDY LIMITATIONS

Enrolling patients and performing the research in the decompensated heart failure or acute MI with strict entry criteria is difficult. As a result, the sample size of the study was limited. We mainly sought to evaluate the selenium and thyroid status in both groups comparing to controls and the study sample was not calculated to perform hard end-points analysis. This is why the value of clinical events rate assessment is limited. The control group was selected to meet similar demographics as the study groups, however the BMI median in the control group was above the normal range and it is a disadvantage of our research. The study was intended to show a real-life group of patients with HF and MI. This is why we did not exclude smokers although smoking may influence the Se levels. For the same reason we did not exclude smokers from the control group to have it comparable.

ACKNOWLEDGMENTS

This work was supported by Jagiellonian University Medical College statutory funds [grant number K/ZDS/005640.

REFERENCES:


### Table 1. Characteristics of whole MI group and of its subgroups according to Se concentration.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group MI (n=54)</th>
<th>Subgroup MI-A Se below normal values (n=38)</th>
<th>Subgroup MI-B normal Se values (n=16)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Se (3 day), µg/L</td>
<td>66.73 (±14.56)</td>
<td>60.24 (±10.93)</td>
<td>82.13 (±9.72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, years</td>
<td>60.41 (±8.91)</td>
<td>60.11 (±9.55)</td>
<td>61.13 (±7.38)</td>
<td>0.7047</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>47 (87.04%)</td>
<td>34 (89.47%)</td>
<td>13 (81.25%)</td>
<td>0.4105</td>
</tr>
<tr>
<td>BMI, (kg/m²)</td>
<td>26.2 (24.8;30.8)</td>
<td>26.7 (24.4;30.6)</td>
<td>26.2 (24.8;32.3)</td>
<td>0.7565</td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STEMI</td>
<td>41 (75.93%)</td>
<td>27 (71.05%)</td>
<td>14 (87.50%)</td>
<td>0.3006</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>13 (24.07%)</td>
<td>11 (28.95%)</td>
<td>2 (12.50%)</td>
<td></td>
</tr>
<tr>
<td>hsTnT (max), ng/mL</td>
<td>4.09 (0.96;6.30)</td>
<td>4.09 (0.94;5.62)</td>
<td>3.50 (0.90;6.81)</td>
<td>0.9095</td>
</tr>
<tr>
<td>TSH (1 day), µIU/mL</td>
<td>1.12 (0.72;1.59)</td>
<td>1.11 (0.74;1.54)</td>
<td>1.13 (0.64;1.72)</td>
<td>0.8721</td>
</tr>
<tr>
<td>fT3 (1 day), pmol/L</td>
<td>4.21 (3.86;4.71)</td>
<td>4.30 (3.90;4.82)</td>
<td>3.90 (3.77;4.38)</td>
<td>0.2077</td>
</tr>
<tr>
<td>fT4 (1 day), pmol/L</td>
<td>15.96 (±2.27)</td>
<td>16.00 (±2.47)</td>
<td>15.85 (±1.77)</td>
<td>0.8163</td>
</tr>
<tr>
<td>fT3/fT4 ratio (1 day)</td>
<td>0.26 (0.24;0.30)</td>
<td>0.26 (0.23;0.30)</td>
<td>0.26 (0.24;0.30)</td>
<td>0.7317</td>
</tr>
<tr>
<td>rT3 (3 day), ng/mL</td>
<td>0.20 (0.13;0.28)</td>
<td>0.22 (0.14;0.28)</td>
<td>0.18 (0.12;0.21)</td>
<td>0.1406</td>
</tr>
<tr>
<td>NT-proBNP (3 day), pg/mL</td>
<td>809.0 (385.5;1385.6)</td>
<td>809.0 (460.3;1489.5)</td>
<td>667.5 (106.5;1263.5)</td>
<td>0.2888</td>
</tr>
<tr>
<td>hsCRP (1 day), mg/L</td>
<td>6.98 (3.17;12.38)</td>
<td>6.68 (2.40;11.88)</td>
<td>7.86 (4.97;13.65)</td>
<td>0.3533</td>
</tr>
<tr>
<td>WBC (1 day), 10³/L</td>
<td>11.41 (±3.24)</td>
<td>11.52 (±3.79)</td>
<td>1.17 (±1.28)</td>
<td>0.6164</td>
</tr>
<tr>
<td>WBC (3 day), 10³/L</td>
<td>8.87 (±2.35)</td>
<td>9.36 (±2.41)</td>
<td>7.69 (±1.73)</td>
<td>0.0153</td>
</tr>
<tr>
<td>eGFR/CKD-EPI/ (1 day)</td>
<td>78.06 (±16.72)</td>
<td>79.61 (±17.32)</td>
<td>74.38 (±15.08)</td>
<td>0.2984</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>111.50 (92.75;143.50)</td>
<td>114.50 (92.75;148.00)</td>
<td>105.50 (91.65;145.00)</td>
<td>0.4207</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>52.63 (±10.31)</td>
<td>52.08 (±11.12)</td>
<td>53.94 (±8.27)</td>
<td>0.5505</td>
</tr>
</tbody>
</table>

Table 1. footnote: Depending on data distribution mean ± SD or median (Q1;Q3) was given. Abbreviations: BMI – body mass index; eGFR - estimated Glomerular Filtration Rate; fT4 – free triiodothyronine; fT3 - free triiodothyronine; group MI – myocardial infarction group; hsCRP - high sensitivity C-reactive protein; hsTnT - high sensitivity troponin T; LVEDV - left ventricle end-diastolic volume; LVEF - left ventricle ejection fraction; NSTEMI – acute myocardial infarction non-ST elevation; NT- proBNP – N-terminal pro B-type Natriuretic Peptide; rT3 - reverse triiodothyronine; Se – selenium; subgroup MI-A – myocardial infarction subgroup with Se below normal values, subgroup MI-B – myocardial infarction subgroup with normal Se values; STEMI – acute myocardial infarction with ST elevation; TSH - thyroid stimulating hormone; WBC - white blood count.
Table 2. Characteristics of whole HF group and of its subgroups according to Se concentration.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group HF (n=59)</th>
<th>Group HF-A Se below normal values (n =44)</th>
<th>Group HF-B normal Se values (n=15)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Se (3 day), µg/L</td>
<td>59.74 (47.73;70.66)</td>
<td>52.17 (45.01;60.43)</td>
<td>81.08 (74.85;86.80)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, years</td>
<td>65.0 (59.0;74.0)</td>
<td>64.0 (56.25;73.25)</td>
<td>67.00 (62.0;77.0)</td>
<td>0.1914</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>48 (81.36%)</td>
<td>38 (86.36%)</td>
<td>10 (66.67%)</td>
<td>0.1260</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.4 (25.5;32.3)</td>
<td>28.9 (25.6;33.3)</td>
<td>28.1 (24.9;31.0)</td>
<td>0.3544</td>
</tr>
<tr>
<td>TSH (1 day), µIU/mL</td>
<td>1.54 (0.93;2.05)</td>
<td>1.52 (0.91;2.16)</td>
<td>1.56 (1.06;2.01)</td>
<td>0.9030</td>
</tr>
<tr>
<td>rT3 (1 day), pmol/L</td>
<td>4.16 (+0.94)</td>
<td>4.05 (+0.89)</td>
<td>4.51 (+1.01)</td>
<td>0.0990</td>
</tr>
<tr>
<td>rT4 (1 day), pmol/L</td>
<td>17.95 (+2.98)</td>
<td>17.70 (+2.77)</td>
<td>18.66 (+3.53)</td>
<td>0.2885</td>
</tr>
<tr>
<td>rT3/rT4 ratio (1 day)</td>
<td>0.24 (+0.06)</td>
<td>0.23 (+0.06)</td>
<td>0.24 (+0.06)</td>
<td>0.4858</td>
</tr>
<tr>
<td>rT3 (3 day), ng/mL</td>
<td>0.21 (+0.09)</td>
<td>0.23 (+0.09)</td>
<td>0.17 (+0.08)</td>
<td>0.0335</td>
</tr>
<tr>
<td>NT-proBNP (1 day), pg/mL</td>
<td>3478.0 (1888; 6837)</td>
<td>2989.5 (1870; 7011)</td>
<td>4029.0 (1909; 5922)</td>
<td>0.8755</td>
</tr>
<tr>
<td>hsCRP (1 day), mg/L</td>
<td>4.77 (1.90;9.83)</td>
<td>6.73 (1.93;10.29)</td>
<td>2.75 (1.62;7.10)</td>
<td>0.2038</td>
</tr>
<tr>
<td>WBC (1 day), 10^3</td>
<td>7.81 (6.05;9.45)</td>
<td>8.02 (6.01;9.41)</td>
<td>7.40 (6.32;9.45)</td>
<td>0.9931</td>
</tr>
<tr>
<td>eGFR/CKD-EPI/ (1 day)</td>
<td>65.90 (+18.92)</td>
<td>64.40 (+17.73)</td>
<td>70.20 (+22.06)</td>
<td>0.3104</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>234.47 (+86.11)</td>
<td>230.43 (+81.77)</td>
<td>246.33 (+99.93)</td>
<td>0.5415</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>23.96 (+7.92)</td>
<td>24.36 (+8.00)</td>
<td>22.80 (+7.81)</td>
<td>0.5146</td>
</tr>
<tr>
<td>Number of patients with</td>
<td>18 (52.94%)</td>
<td>15 (65.22%)</td>
<td>3 (27.27%)</td>
<td>0.0381</td>
</tr>
</tbody>
</table>

Table 2. footnote: Depending on data distribution mean ± SD or median (Q1;Q3) was given. Abbreviations: group HF – heart failure group; subgroup HF-A – heart failure subgroup with Se below normal values, subgroup HF-B – heart failure subgroup with normal Se values. Remaining abbreviations — see Table 1.
Table 3. Comparison of MI, HF and C group.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group MI n= 54</th>
<th>Group HF n= 59</th>
<th>Group C n= 30</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>61.0 (53.8; 67.3)</td>
<td>65.0 (59.0; 74.0)</td>
<td>61.5 (57.5; 68.8)</td>
<td>0.0837</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>47 (87.04%)</td>
<td>48 (81.36%)</td>
<td>25 (83.33%)</td>
<td>0.7104</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>33 (61.11%)</td>
<td>21 (35.59%)</td>
<td>8 (27.59%)</td>
<td>0.0035 α,β</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.2 (24.8; 30.79)</td>
<td>28.4 (25.5; 32.3)</td>
<td>30.1 (27.4; 34.8)</td>
<td>0.0127 β</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>153.0 (137.0; 167.3)</td>
<td>123 (111; 138)</td>
<td>140.5 (123; 155)</td>
<td>&lt;0.0001 α,β</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>91.9 (±13.1)</td>
<td>80.8 (±15.0)</td>
<td>84.1 (±13.3)</td>
<td>0.0002 α,β</td>
</tr>
<tr>
<td>Se, µg/L</td>
<td>65.9 (55.2; 76.1)</td>
<td>59.7 (47.7; 70.6)</td>
<td>93.2 (84.2; 99.1)</td>
<td>&lt;0.0001 β,χ</td>
</tr>
<tr>
<td>Se deficiency, n (%)</td>
<td>38 (70.37%)</td>
<td>44 (74.58%)</td>
<td>3 (10.00%)</td>
<td>&lt;0.0001 β,χ</td>
</tr>
<tr>
<td>1st day TSH, µIU/mL</td>
<td>1.12 (0.72; 1.59)</td>
<td>1.54 (0.93; 2.05)</td>
<td>1.08 (0.68; 1.80)</td>
<td>0.0101 α,χ</td>
</tr>
<tr>
<td>fT3, pmol/L</td>
<td>4.21 (±0.69)</td>
<td>4.16 (±0.94)</td>
<td>4.99 (±0.66)</td>
<td>&lt;0.0001 β,χ</td>
</tr>
<tr>
<td>fT4, pmol/L</td>
<td>15.96 (±2.27)</td>
<td>17.95 (±2.98)</td>
<td>15.31 (±1.91)</td>
<td>&lt;0.0001 α,χ</td>
</tr>
<tr>
<td>fT3/fT4 ratio</td>
<td>0.27 (±0.04)</td>
<td>0.24 (±0.06)</td>
<td>0.33 (±0.05)</td>
<td>&lt;0.0001 α,β,χ</td>
</tr>
<tr>
<td>3rd day TSH, µIU/mL</td>
<td>2.23 (1.20; 3.11)</td>
<td>1.60 (1.16; 2.03)</td>
<td>1.08 (0.68; 1.80)</td>
<td>0.0002 β,χ</td>
</tr>
<tr>
<td>fT3, pmol/L</td>
<td>3.90 (3.60; 4.38)</td>
<td>4.25 (3.57; 4.60)</td>
<td>4.92 (4.50; 5.27)</td>
<td>&lt;0.0001 β,χ</td>
</tr>
<tr>
<td>fT4, pmol/L</td>
<td>5.33 (±2.07)</td>
<td>17.40 (±2.57)</td>
<td>15.31 (±1.91)</td>
<td>&lt;0.0001 α,χ</td>
</tr>
<tr>
<td>fT3/fT4 ratio</td>
<td>0.25 (0.23; 0.29)</td>
<td>0.25 (0.21; 0.28)</td>
<td>0.32 (0.29; 0.37)</td>
<td>&lt;0.0001 β,χ</td>
</tr>
<tr>
<td>follow-up TSH, µIU/mL</td>
<td>1.21 (0.95; 1.66)</td>
<td>1.48 (1.08; 2.10)</td>
<td>1.08 (0.68; 1.80)</td>
<td>0.0470</td>
</tr>
<tr>
<td>fT3, pmol/L</td>
<td>4.99 (4.50; 5.28)</td>
<td>4.66 (4.10; 4.96)</td>
<td>4.92 (4.50; 5.27)</td>
<td>0.0312</td>
</tr>
<tr>
<td>fT4, pmol/L</td>
<td>16.35 (±2.60)</td>
<td>17.41 (±2.66)</td>
<td>15.31 (±1.91)</td>
<td>0.0021 χ</td>
</tr>
<tr>
<td>fT3/fT4 ratio</td>
<td>0.31 (±0.06)</td>
<td>0.27 (±0.05)</td>
<td>0.33 (±0.05)</td>
<td>0.0001 α,χ</td>
</tr>
<tr>
<td>Low T3 prevalence, n (%)</td>
<td>7 (12.96%)</td>
<td>9 (15.25%)</td>
<td>0 (0.00%)</td>
<td>0.0849</td>
</tr>
</tbody>
</table>

Table 3. footnote: Depending on data distribution mean ± SD or median (Q1;Q3) was given. Abbreviations: DBP – diastolic blood pressure; SBP – systolic blood pressure. Remaining abbreviations - see Table 1/Figure 1. α - p<0.05 between group MI and HF, β - p<0.05 between group MI and C; χ - p<0.05 between group HF and C.
Table 4. Correlations between Se, TSH and TH.

<table>
<thead>
<tr>
<th>Variable</th>
<th>by variable</th>
<th>Correlation</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Se</td>
<td>TSH</td>
<td>-0.1427</td>
<td>0.0902</td>
</tr>
<tr>
<td>Se</td>
<td>fT3</td>
<td>0.3900</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Se</td>
<td>fT4</td>
<td>-0.2136</td>
<td>0.0104</td>
</tr>
<tr>
<td>Se</td>
<td>fT3/fT4</td>
<td>0.4294</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 4 footnote: Abbreviations — see Table 1 legend.
Figure 1. Se plasma levels in MI and HF patients in comparison to controls. Medians (Q1;Q3) – see Table 3. Group C – control group; Group HF – heart failure group, Group MI – myocardial infarction group.
Figure 2. TSH, fT3 levels and fT3/fT4 ratio in MI and HF patients in comparison to controls.
Medians (Q1;Q3) – see Table 3. Abbreviations — see Table 1/Figure 1.
Figure 3. Changes of TSH, fT3 and fT3/fT4 ratio in time in MI and HF groups.

Mean ± SD or medians (Q1;Q3) – see Table 3. Abbreviations — see Table 1/Figure 1.

* p<0.05; ** p>0.05.
Figure 4. Correlation between Se, fT3 and fT3/fT4 ratio. Abbreviations - see Table 1/Figure 1.