Archives of Physiology and Biochemistry
The Journal of Metabolic Diseases

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/iarp20

Prognostic value of thiol/disulfide homeostasis in symptomatic patients with heart failure

Haci Mehmet Caliskan, Serkan Sivri, Erdogan Sokmen, Mustafa Celik, Bilal Ilanbey, Sinan Cemgil Ozbek & Burak Celik

To cite this article: Haci Mehmet Caliskan, Serkan Sivri, Erdogan Sokmen, Mustafa Celik, Bilal Ilanbey, Sinan Cemgil Ozbek & Burak Celik (2021) Prognostic value of thiol/disulfide homeostasis in symptomatic patients with heart failure, Archives of Physiology and Biochemistry, 127:5, 462-467, DOI: 10.1080/13813455.2020.1773505

To link to this article: https://doi.org/10.1080/13813455.2020.1773505

ARCHIVES OF PHYSIOLOGY AND BIOCHEMISTRY
2021, VOL. 127, NO. 5, 462–467
https://doi.org/10.1080/13813455.2020.1773505

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Prognostic value of thiol/disulfide homeostasis in symptomatic patients with heart failure

Haci Mehmet Caliskan[a], Serkan Sivri[b], Erdogan Sokmen[b], Mustafa Celik[b], Bilal Ilanbey[c], Sinan Cemgil Ozbek[b] and Burak Celik[a]

[a]Department of Emergency Medicine, Ahi Evran University Training and Research Hospital, Kirsehir, Turkey; [b]Department of Cardiology, Ahi Evran University Training and Research Hospital, Kirsehir, Turkey; [c]Department of Biochemistry, Ahi Evran University Training and Research Hospital, Kirsehir, Turkey

ABSTRACT

We aimed to examine the role of thiol/disulphide homeostasis (TDH) in heart failure and its stages and the prognosis of heart failure. A total of 140 subjects were included in the study. Total and native thiol levels were higher in the control group compared to the patient groups ($p < .001$). While the average disulphide/total thiol ratio was similar in groups 1 and 2, it was found to be significantly lower in the control group compared to other groups and significantly higher in group 3 compared to other groups ($p < .05$). Mean native thiol and total thiol levels were found lower in patients with mortality compared to surviving patients ($p < .001$). In ROC curve analysis, it was determined that the total thiol level had 81.8% sensitivity and 83.1% specificity, and native thiol level had 81.8% sensitivity and 84.3% specificity. We found that TDH was impaired in favour of disulphide in cases of heart failure.

ARTICLE HISTORY
Received 12 April 2020
Revised 14 May 2020
Accepted 19 May 2020
Published online 3 June 2020

KEYWORDS
Heart failure; left ventricular ejection fraction; mortality; thiol/disulphide homeostasis

Introduction

Heart failure (HF) is a disease of high morbidity and mortality, wherein the quality of life becomes disrupted due to the inability of the heart to function properly. While heart failure accounts for about 5% of all admissions to emergency services in the United Kingdom, it is the number one reason for hospitalisation of patients over 65 years of age in the United States (MacCarthy and Shah 2003).

Previous studies reported that oxidative stress played a pivotal role in the pathophysiology of HF and cardiac remodelling (Tsutsui *et al*. 2011). Persistent activation of the sympathetic nervous system in HF settings leads to an increase in the production of reactive oxygen species (ROS), which in turn is associated with deterioration of the status of HF and also with increased mortality due to cardiac arrhythmias (Circu and Aw 2010). ROS are side-products of various cellular metabolisms. In low levels, ROS operate as redox messengers during intracellular signalling and regulations (Burgoyne *et al*. 2012), and they exert detrimental effects by inhibiting protein functions and contributing to cellular death (Circu and Aw 2010). On the other hand, cellular antioxidant systems counteract ROS production, thereby protecting cellular components from damage. However, the balance between ROS and antioxidant systems shifts in favour of increased oxidative stress if ROS production becomes unopposed. In this regard, studies on cell and animal models pointed out the provocative role of oxidative stress in altered gene expression and cellular apoptosis (Sawyer 2011). As an indicator of the status of oxidative stress, dynamic thiol/disulphide homeostasis (TDH) has a significant role in antioxidant protection, signal transduction detoxification, apoptosis, regulation of enzymatic activity and transcription factors, and cellular signalling mechanisms (Erel and Neselioglu 2014).

On the basis of the aforementioned premises, we aimed in the present study to assess TDH among different stages of HF in comparison with healthy subjects, and also to seek a possible prognostic role of TDH in patients with HF.

Materials and methods

Study population

This prospective and cross-sectional study was conducted with patients admitted to the emergency department or cardiology outpatient polyclinics and then hospitalised due to relevant symptoms and signs of HF between February 2018 and March 2019. The Ahi Evran University Medical Faculty's Committee of Ethics approved this study protocol (Date: 26 December 2017; No: 2017–20/235) and the study complied with the Helsinki Declaration. Written informed consent was obtained from the patients for their anonymized information to be published in this article.

A total of 100 consecutive patients who had been admitted to our hospital with physical symptoms and signs of HF were included to form the patient group. Healthy subjects ($n = 40$) without known cardiac pathology and left ventricular ejection fraction (LVEF) of >50% who were admitted to

CONTACT Haci Mehmet Caliskan hmehmet.40@hotmail.com Department of Emergency Medicine, Ahi Evran University Training and Research Hospital, Kervansaray Mah. 2019. Sok. No. 1, Kirsehir 40100, Turkey

cardiology outpatient polyclinics with non-specific symptoms were recruited to the control group. The patient groups were further divided on the basis of LVEF measured by transthoracic echocardiography (TTE) into three subgroups as follows (Ponikowski *et al*. 2016): Group 1, HF patients with preserved LVEF (LVEF >50%, $n = 33$); Group 2, HF patients with mid-range LVEF (LVEF between 40 and 50%, $n = 33$); and, Group 3, HF patients with reduced LVEF (LVEF <40%, $n = 34$). LVEF was >50% in all control subjects in the absence of any other cardiac pathology. Among the exclusion criteria were the presence of acute or chronic infections, autoimmune diseases, cerebrovascular diseases, chronic hepatic and renal failure, severe chronic valvular disease or history of heart valve operation, familial hypercholesterolaemia, malignancy, malnutrition, recent major surgery, use of vitamins or antioxidant medications, oral contraceptive or hormone replacement therapy usage, and smoking. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

The TTEs evaluations of the enrolled patients were performed using a standard TTE device (Vivid S5, GE Vingmed Ultrasound AS, Horten, Norway). The LVEF was calculated using the modified Simpson's rule.

Endpoint

The primary endpoint was accepted to be death due to progressive HF during hospitalisation.

Measurement of biochemical markers

Blood samples were obtained through venipuncture on admission to the emergency department and cardiology outpatient polyclinics. The collected blood samples were centrifuged at $1500 \times g$ for 10 min to separate the serum. Serum was stored at −80 °C until the analysis of thiol/disulphide homeostasis tests.

Routine serum biochemical parameters were measured by using an automated clinical chemistry analyser (Roche Hitachi Cobas c8000 autoanalyzer, Roche Diagnostic Corp., Mannheim, Germany).

TDH parameters were measured through a novel and automated spectrophotometric method by Erel and Neşelioğlu (Erel and Neselioglu 2014). First, native thiol (NT) and total thiol (TT) concentrations were determined, and then disulphide (Ds) concentrations were computed by using the following formula: Ds concentration = (TT concentration − NT concentration)/2. In addition, Ds/TT (%), Ds/TT (%), and NT/TT (%) ratios were determined on the basis of the previously measured NT and TT levels.

Statistical analysis

Data were analysed using IBM SPSS Statistics 21.0 for Windows (IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov test was used to test the normal distribution of data. Continuous variables with normal distribution were expressed as mean ± standard deviation, and continuous variables without normal distribution were expressed as median (min–max). Categorical variables were presented as numbers and percentages. Statistical difference of the numerical variables in LVEF groups was analysed with the ANOVA test (normally distributed numerical variables) and Kruskal–Wallis H test (nonnormally distributed numerical variables). Chi-square and Fisher exact chi-square tests were used in the comparison of categorical variables. Cox regression analysis was performed to identify risk determinants of mortality. Receiver operating characteristic (ROC) curve analysis was used to determine the prediction points of thiol/disulphide homeostasis markers for mortality. In order to determine the predictive value, the point with the highest sensitivity and specificity and the Youden index were selected. Values of $p < .05$ were accepted as significant in the statistical analyses.

Results

Table 1 presents demographic, clinical, and laboratory characteristics of the study population. The groups were similar in terms of demographic variables. There was also no significant difference concerning comorbid conditions such as hypertension, diabetes mellitus, and chronic obstructive pulmonary disease among the groups ($p > .05$). Of all patients admitted with symptoms and signs of HF, 4 patients (12.1%) in group 1, 9 patients (27.3%) in group 2 and 26 patients (76.4%) in group 3 were hospitalised for further treatment (Table 1). As expected, the rate of hospitalisation was greater among HF patients in group 3 compared with those in groups 2 and 1.

Among routine blood parameters, the white blood cell (WBC) count was greater in all HF patients compared to the controls; however, pairwise comparison of WBC counts among the 3 HF subgroups was similar. C-reactive protein was higher ($p = .004$) and haemoglobin was lower ($p = .08$) in group 3 compared with groups 1 and 2 and the controls. Other blood parameters were similar among the groups ($p > .05$) (Table 1).

As for TDH, the control group had the highest mean NT and TT levels, whereas group 3 had the lowest TT level (381.4 ± 57.5 μmol/L vs. 267.1 ± 76.1 μmol/L, $p < .001$ and 423.6 ± 56.6 μmol/L vs. 305.8 ± 83.9 μmol/L, $p < .001$, respectively). On the other hand, groups 1 and 2 displayed no significant differences between each other regarding TT and NT ($p > .05$). Ds levels were similar among the study groups ($p > .05$). The NT/TT ratio was lowest in group 3 compared to groups 1 and 2 and the control group; however, pairwise comparison for the same ratio did not show significant differences among groups 1 and 2 and the controls. Among all groups, Ds/NT and Ds/TT ratios were the greatest in group 3 and the lowest in the controls (6.3 ± 1.9 vs. 4.5 ± 1.0, $p < .001$ and 7.3 ± 2.3 vs. 5.0 ± 1.2, $p < .001$, respectively). Patients in group 3 had the lowest mean TT, mean NT, and NT/TT, but the highest mean Ds/TT and Ds/NT ratios.

Out of 100 patients admitted to the emergency department with relevant symptomology for HF, 11 (11%) died of further deterioration of HF during hospitalisation, 10 of

Table 1. Demographic and biochemical characteristics of HF patients group 1, 2 and 3, and the control group.

Variables	Control group ($n = 40$)	Group 1, LVEF >50% ($n = 33$)	Group 2, LVEF = 40–50% ($n = 33$)	Group 3, LVEF <40% ($n = 34$)	p-Value
Age, years	64.2 ± 6.9	68 ± 10.3	66.9 ± 10.2	69.4 ± 14	.181
Male gender, n (%)	29 (72.5)	24 (72.7)	26 (78.8)	22 (64.7)	.655
BMI, kg/m^2	27.3 ± 4.1	27.4 ± 4.7	28 ± 5.4	27.1 ± 5	.888
Hypertension, n (%)	14 (35.0)	13 (39.4)	12 (36.4)	13 (38.2)	.985
Diabetes mellitus, n (%)	14 (35.0)	13 (39.4)	11 (33.3)	13 (38.2)	.961
COPD, n (%)	6 (15.0)	4 (12.1)	5 (15.2)	8 (23.5)	.677
Hospitalisation, n (%)					
Discharge		29 (87.9)	24 (72.7)	8 (23.5)	<.001*
Hospitalisation		4 (12.1)	9 (27.3)	26 (76.4)	
Hospitalisation duration, days			1 (1–19)	**3 (1–54)**	<.001*
Mortalite, n (%)					
Alive		33 (100.0)	32 (97.0)	24 (70.6)	<.001*
Exitus			1 (3.0)	10 (29.4)	
Hb, g/dL	13.4 ± 1.7	13.2 ± 1.9	13.8 ± 2.1	**12.3 ± 1.8**	.008*
WBC, 10^3	**6 (3.4–8.9)**	7.4 (4.5–12.5)	7.8 (2.4–12.8)	7.7 (3.2–22.5)	<.001*
Platelets, 10^3	276.2 ± 49.8	257.3 ± 70.8	238.9 ± 71.5	241.2 ± 87.3	.086
Glucose, mg/dL	102.5 (87–315)	127 (81–311)	124 (87–333)	124 (75–455)	.432
C-RP, mg/dL	0.5 (0.1–8.7)	0.7 (0.1–9.8)	0.4 (0.1–7)	**2 (0.1–13.6)**	.004*
eGFR, mL/min	74.9 ± 17.9	67.5 ± 21.6	72.6 ± 21.1	70.0 ± 24	.487
ALT, U/L	17.5 (9–45)	14 (6–26)	17 (6–83)	**21 (5–62)**	.041*
AST, U/L	**27.5 (16–49)**	18 (10–37)	20 (11–52)	19 (5–43)	<.001*
Native thiol, μmol/L	**381.4 ± 57.5**	330.9 ± 55.4	327.3 ± 75.1	**267.1 ± 76.1**	<.001*
Total thiol, μmol/L	**423.6 ± 56.6**	367.9 ± 57.3	365 ± 81.4	**305.8 ± 83.9**	<.001*
Disulphide, μmol/L	18.8 ± 3.5	18.7 ± 4.1	19.1 ± 4.8	19.1 ± 6.0	.981
Native thiol/total thiol (%)	89.9 ± 3.4	89.8 ± 2.3	89.6 ± 2.3	**87.2 ± 4.1**	<.001*
Disulphide/native thiol (%)	4.8 ± 1.0	5.1 ± 1.2	5.3 ± 1.2	**6.3 ± 1.9**	<.001*
Disulphide/total thiol (%)	5.2 ± 1.2	5.8 ± 1.5	5.9 ± 1.4	**7.3 ± 2.3**	<.001*

Categorical variables were expressed as numbers (%). Numerical variables were expressed as mean ± standard deviation or median (min–max). Bold characters indicate differences between groups.
BMI: body-mass index; COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; ICU: intensive care unit; CS: cardiology service; Hb: haemoglobin; WBC: white blood cell; C-RP: C-reactive protein; GFR: glomerular filtration rate; ALT: alanine aminotransferase; AST: aspartate aminotransferase.
*$p < .05$ shows statistical significance.

whom were included in group 3 and 1 of whom was among the patients in group 2.

The NT, TT, and Ds levels were significantly lower for in-hospital mortality among the HF patients (respectively 216.4 ± 51.2 vs. 319.3 ± 69.6, $p < .001$; 248.6 ± 61.1 vs. 357.9 ± 73.7, $p < .001$; 15.5 ± 4.8 vs. 19.4 ± 5.3, $p = .031$; Table 2). A decrease of 1 μmol/L in NT, TT, and Ds levels increases the risk of mortality by 1.02 (1/0.98) fold, 1.02 (1/0.98) fold, and 1.19 (1/0.84) fold, respectively (respectively HR: 0.98, $p < .001$; HR: 0.98, $p < .001$; HR: 0.84; $p = .031$).

ROC curve analysis was conducted to define the diagnostic cut-offs of NT, TT, Ds, and NT/TT for in-hospital mortality in HF patients, which yielded a cut-off value of ≤244 μmol/L for NT with 81.8% sensitivity and 84.3% specificity (AUC: 0.877, 95% CI: 0.796–0.934, $p < .001$), a cut-off value of ≤288 μmol/L for TT with 81.8% sensitivity and 83.1% specificity (AUC: 0.871, 95% CI: 0.789–0.930, $p < .001$), a cut-off value of ≤14 μmol/L for Ds with 54.5% sensitivity and 85.4% specificity (AUC: 0.719, 95% CI: 0.620–0.804, $p = .018$), and a cut-off value of ≤89.7 for NT/TT with 90.9% sensitivity and 49.4% specificity (AUC: 0.713, 95% CI: 0.614–0.799, $p = .004$) (Figure 1). NT and TT levels were found to exhibit similar diagnostic performance in predicting mortality. However, they were found to have superior diagnostic performance compared to Ds and NT/TT levels. Meanwhile, Ds and NT/TT levels were found to exhibit similar diagnostic performance in predicting mortality. According to these cut-off values, in-hospital mortality risk is shown in Figure 2.

Discussion

In this study, we found a statistically significant difference regarding the parameters of TDH between HF patients and the controls. In brief, it was observed that progression in the stages of HF resulted in a decrease in TT and NT levels and NT/TT ratio, but an increase in Ds/NT and Ds/TT ratios. Much more importantly, decreases in the TT, NT, and Ds levels were found to be associated with in-hospital all-cause mortality.

In their study, Grieve and Shah (2003) demonstrated an increase in the levels of oxidative stress markers similar to those found in our study in the setting of HF, and they stated that the increase correlated with the seriousness of myocardial functional disruption and hence the stage of HF. Previous evidence suggested abnormalities in TDH as an important factor in the etiopathogenesis of various disease conditions, such as hypertension (Ates *et al*. 2016), coronary artery ectasia (Kiziltunc *et al*. 2016), acute myocardial infarction (Kavakli *et al*. 2018), diabetes mellitus (Gulpamuk *et al*. 2018), rheumatoid arthritis (Tetik *et al*. 2010), cancer (Prabhu *et al*. 2014), acute kidney failure (Yavuz Otal *et al*. 2018), chronic asthma (Nar Rukiye 2018), and obstructive sleep

Table 2. Comparison of the subgroups of HF patients with and without in-hospital death.

	Survival		Univariable cox regression		
Variables	Alive ($n = 89$)	Exitus ($n = 11$)	HR	95% CI	p-Value
Age, years	68.0 ± 11.1	68.8 ± 15.5	1.01	0.96–1.06	.815
Male gender, n (%)	65 (73.0)	7 (63.6)	0.60	0.17–2.04	.408
BMI, kg/m^2	27.7 ± 5	25.8 ± 4.7	0.92	0.79–1.07	.284
Hypertension, n (%)	33 (37.1)	5 (45.5)	1.41	0.43–4.64	.567
Diabetes mellitus, n (%)	32 (36.0)	5 (45.5)	1.50	0.46–4.90	.506
COPD, n (%)	13 (14.6)	4 (36.4)	3.08	0.90–10.53	.073
Hb, g/dL	13.4 ± 1.9	11.0 ± 1.6	0.56	0.40–0.78	.001*
WBC, 10^3	7.9 (2.4–15.1)	5.2 (3.6–22.5)	0.97	0.76–1.24	.814
Platelets, 10^3	247.8 ± 76.2	229 ± 82.4	0.99	0.98–1.01	.495
Glucose, mg/dL	126 (75–455)	118 (85–243)	0.99	0.98–1.01	.753
C-RP, mg/dL	0.6 (0–9.8)	2.4 (0–13.6)	1.27	1.07–1.50	.006*
eGFR, mL/min	70.3 ± 21.5	68.4 ± 20.3	0.99	0.97–1.02	.723
ALT, U/L	17 (5–83)	17 (6–39)	0.99	0.94–1.04	.990
AST, U/L	18 (9–52)	19 (5–42)	0.98	0.93–1.06	.743
Native thiol, μmol/L	319.3 ± 69.6	216.4 ± 51.2	0.98	0.97–0.99	<.001*
Total thiol, μmol/L	357.9 ± 73.7	248.6 ± 61.1	0.98	0.97–0.99	<.001*
Disulphide, μmol/L	19.4 ± 5.3	15.5 ± 4.8	0.84	0.72–0.98	.031*
Native thiol/total thiol (%)	89.0 ± 3.2	87.2 ± 3.2	0.90	0.81–0.99	.050*
Disulphide/native thiol ratio (%)	5.5 ± 1.5	6.2 ± 0.8	1.19	0.94–1.51	.147
Disulphide/total thiol ratio (%)	6.3 ± 2.2	7.1 ± 1.2	1.11	0.95–1.30	.198

Categorical variables were expressed as numbers (%). Numerical variables were expressed as mean ± standard deviation or median (min–max).
BMI: body-mass index; COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; ICU: intensive care unit; CS: cardiology service; Hb: haemoglobin; WBC: white blood cell; C-RP: C-reactive protein; GFR: glomerular filtration rate; ALT: alanine aminotransferase; AST: aspartate aminotransferase: HR: hazard ratio; CI: confidence intervals.
*$p < .05$ shows statistical significance.

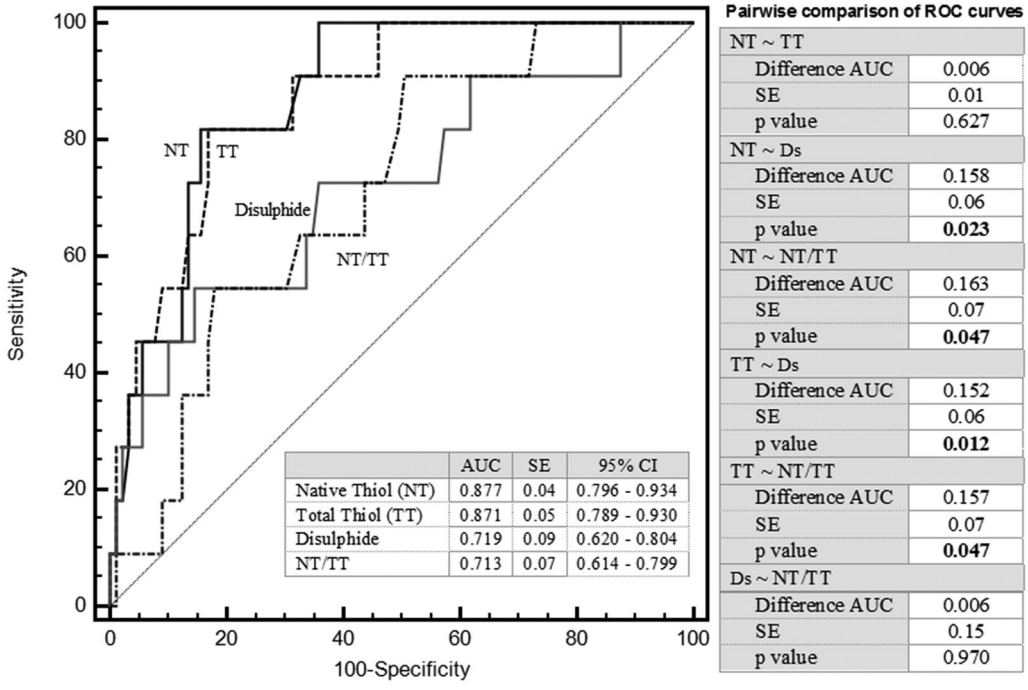

Figure 1. ROC curve analysis of thiol/disulphide homeostasis parameters for the prediction of in-hospital mortality.

apnoea (Dinc *et al*. 2017). To the best of our knowledge, however, there is no study comparing the dynamics of TDH in HF patients stratified according to LVEF as lower-LVEF, mid-range LVEF, and higher LVEF and demonstrating prognostic cut-off values for in-hospital mortality. Accordingly, ours is the first such study.

When found in excessive amounts, ROS can readily lead to cellular dysfunction, protein and lipid peroxidation, and DNA harm, thereby giving way to cellular damage and death, which has been held responsible in the etiopathogenesis of a variety of cardiovascular disease states. Oxidative stress proves much more important when it comes to the pathological cardiac remodelling underlying the emergence and progression of HF (Xu *et al*. 1997). To give a simple example, ROS can directly impair contractile function by modifying the proteins of paramount importance in the process of excitation–contraction coupling. Moreover, ROS operate through activation of a congeries of hypertrophy signalling kinases and transcription factors, and thereby the modulation of cell death. They also act through inducing the proliferation of cardiac fibroblasts and boosting the secretion of matrix metalloproteinases, which in turn activates another cascade of

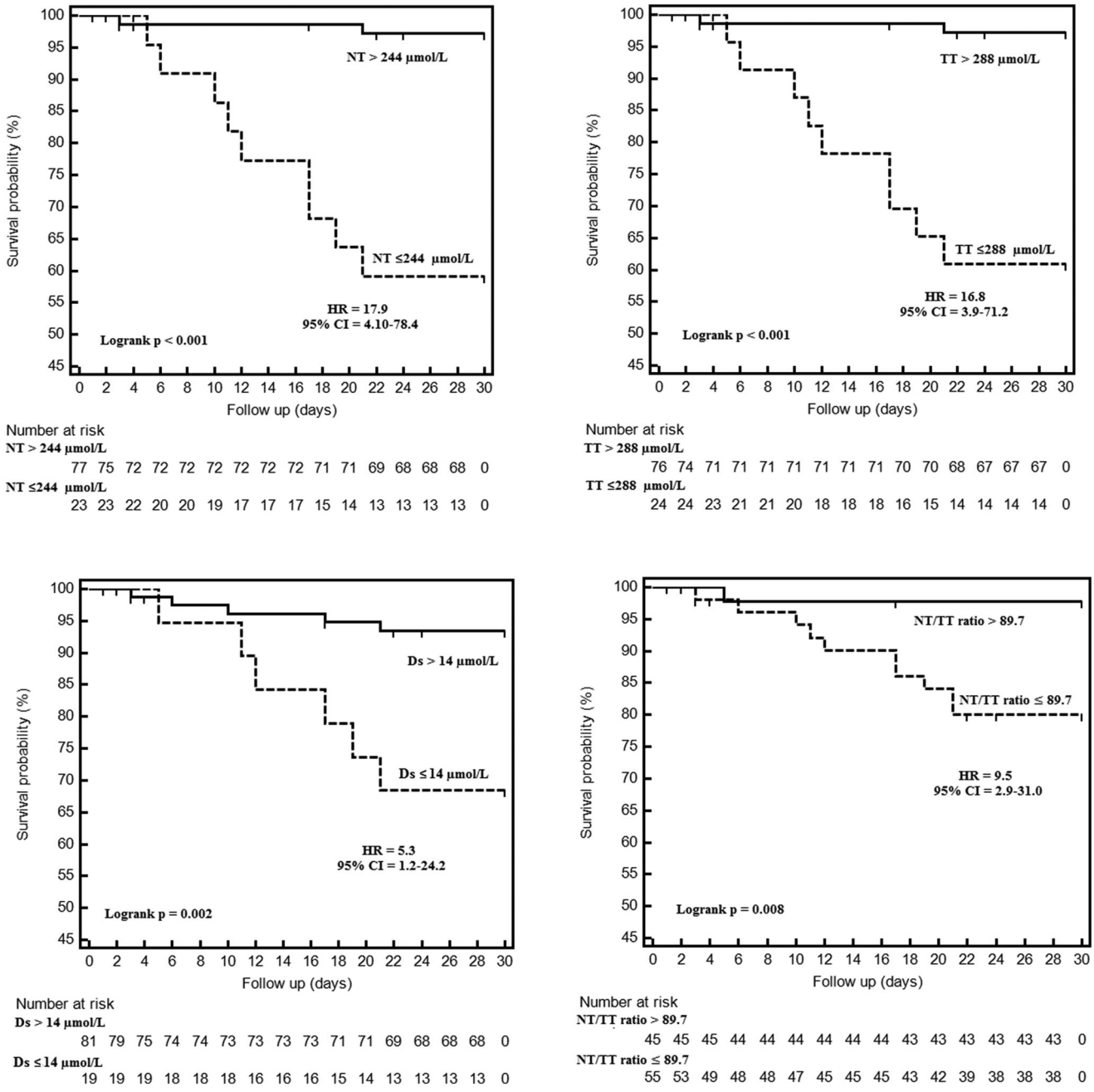

Figure 2. Mortality risk according to the cut-off values of thiol/disulphide homeostasis parameters.

extracellular matrix remodelling processes. All these events are responsible for the development and progression of maladaptive remodelling and failure of the myocardium (Tsutsui *et al*. 2011). In addition, ROS are also implicated in Ca^{+2} transition into the myocytes via activation of Na/Ca^{+2} exchanger protein, thus modulating the excitation–contraction coupling and causing intracellular Ca^{+} overload (Xu *et al*. 1997).

Two previous studies reported that oxidative stress caused a congeries of modulations responsible for the progression of HF, such as cellular hypertrophy, modifications in gene expressions, and cellular apoptosis (Siwik *et al*. 1999, Kwon *et al*. 2003). In another study conducted in 2017, oxidative stress was widespread in the myocardium of HF patients and correlated with the level of left ventricular dysfunction (Munzel *et al*. 2017). Kundi *et al*. (2015) demonstrated a progressive increase in TT and NT as LVEF increased. Similarly, our study revealed a decrease in TT and NT as LVEF deteriorated, hence pointing out a close link between different stages of HF and oxidative stress.

In a recent study on TDH by Sivri *et al*. (2017), TT and NT were found to be low in the absence of a significant change in the Ds levels of patients with the acute coronary syndrome. In our study, the Ds level slightly increased in the subgroup with low LVEF, which, however, did not reach a statistical level of significance. Although it was mentioned in two previous studies on acute coronary syndromes (Kundi *et al*. 2015, Kavakli *et al*. 2018) that Ds levels were subjected to a decrease together with a decrease in TT and NT levels,

Ds levels in our study did not change significantly among varying HF stages. In this regard, our findings are more compatible with the findings of Sivri *et al*. (2017).

Topuz *et al*. (2016) assessed the prognostic significance of TT and NT in subjects with acute pulmonary thromboembolism and found a decreased serum level of TT and NT but increased Ds levels in the patients with high Pulmonary Embolism Severity Index (PESI). The PESI is an index that indicates bodily hemodynamic worsening and right ventricular pressure impingement. Similar to their findings, HF patients with LVEF of <40% (group 3) in our study were characterised with more severe worsening in cardiovascular hemodynamics, and it would be plausible to expect more in-hospital mortality and lower serum levels of TT and NT in such a patient group. Our study findings seem consistent with the findings of Topuz *et al*. (2016) in that the mean Ds level was also elevated, albeit statistically nonsignificant, and TT and NT levels were decreased in the HF group with LVEF of <40%.

Our study should be assessed together with some limitations. First and most importantly, our study is a single-center study with a relatively small patient cohort.

Conclusions

The parameters of TDH differ significantly among symptomatic HF patients with different LVEFs. More specifically, a decrease in TT and NT levels was found to be associated with lower LVEF and higher in-hospital mortality in symptomatic HF patients. On the basis of our findings, we suggest that TDH parameters may be used as prognostic markers in HF patients. However, further prospective studies with larger cohorts are warranted to affirm our findings.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This study received funding from Ahi Evran University Scientific Research Committee (Grant number: TIP.A4.19.013).

References

Ates, I., *et al*., 2016. Dynamic thiol/disulphide homeostasis in patients with newly diagnosed primary hypertension. *Journal of the American society of hypertension*, 10 (2), 159–166.

Burgoyne, J.R., *et al*., 2012. Redox signaling in cardiac physiology and pathology. *Circulation research*, 111 (8), 1091–1106.

Circu, M.L. and Aw, T.Y., 2010. Reactive oxygen species, cellular redox systems, and apoptosis. *Free radical biology & medicine*, 48 (6), 749–762.

Dinc, M.E., *et al*., 2017. Thiol/disulfide homeostasis as a novel indicator of oxidative stress in obstructive sleep apnea patients. *The laryngoscope*, 127 (7), E244–E250.

Erel, O. and Neselioglu, S., 2014. A novel and automated assay for thiol/disulphide homeostasis. *Clinical biochemistry*, 47 (18), 326–332.

Grieve, D.J. and Shah, A.M., 2003. Oxidative stress in heart failure. More than just damage. *European Heart Journal*, 24 (24), 2161–2163.

Gulpamuk, B., *et al*., 2018. The significance of thiol/disulfide homeostasis and ischemia-modified albumin levels to assess the oxidative stress in patients with different stages of diabetes mellitus. *Scandinavian journal of clinical and laboratory investigation*, 78 (1–2), 136–142.

Kavakli, H.S., *et al*., 2018. Thiol disulphide homeostasis in patients with acute myocardial infarction (AMI). *Journal Pakistan medical association*, 68 (11), 1631–1635.

Kiziltunc, E., *et al*., 2016. Plasma thiols and thiol-disulfide homeostasis in patients with isolated coronary artery ectasia. *Atherosclerosis*, 253, 209–213.

Kundi, H., *et al*., 2015. A novel oxidative stress marker in acute myocardial infarction; thiol/disulphide homeostasis. *The American Journal of Emergency Medicine*, 33 (11), 1567–1571.

Kwon, S.H., *et al*., 2003. H_2O_2 regulates cardiac myocyte phenotype via concentration-dependent activation of distinct kinase pathways. *Journal of molecular and cellular cardiology*, 35 (6), 615–621.

MacCarthy, P.A. and Shah, A.M., 2003. Oxidative stress and heart failure. *Coronary artery disease*, 14 (2), 109–113.

Munzel, T., *et al*., 2017. Impact of oxidative stress on the heart and vasculature: part 2 of a 3-part series. *Journal of the American college of cardiology*, 70 (2), 212–229.

Nar Rukiye, Ç., 2018. Assessment of dynamic thiol/disulfide homeostasis in patients with asthma. *Journal of laboratory medicine*, 42 (3), 99–104.

Ponikowski, P., *et al*., 2016. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *European heart journal*, 37 (27), 2129–2200.

Prabhu, A., *et al*., 2014. Cysteine catabolism: a novel metabolic pathway contributing to glioblastoma growth. *Cancer research*, 74 (3), 787–796.

Sawyer, D.B., 2011. Oxidative stress in heart failure: what are we missing? *The American journal of the medical sciences*, 342 (2), 120–124.

Sivri, S., *et al*., 2017. Dynamic thiol/disulphide homeostasis and its prognostic value in patients with non-ST elevation-acute coronary syndromes. *Kardiologia polska*, 76 (2), 426–432.

Siwik, D.A., *et al*., 1999. Inhibition of copper-zinc superoxide dismutase induces cell growth, hypertrophic phenotype, and apoptosis in neonatal rat cardiac myocytes in vitro. *Circulation research*, 85 (2), 147–153.

Tetik, S., *et al*., 2010. Determination of oxidant stress in plasma of rheumatoid arthritis and primary osteoarthritis patients. *Indian journal of biochemistry and biophysics*, 47 (6), 353–358.

Topuz, M., *et al*., 2016. The prognostic importance of thiol/disulfide homeostasis in patients with acute pulmonary thromboembolism. *The American journal of emergency medicine*, 34 (12), 2315–2319.

Tsutsui, H., Kinugawa, S., and Matsushima, S., 2011. Oxidative stress and heart failure. *American journal of physiology. Heart and circulatory physiology*, 301 (6), H2181–H2190.

Xu, K.Y., Zweier, J.L., and Becker, L.C., 1997. Hydroxyl radical inhibits sarcoplasmic reticulum Ca(2+)-ATPase function by direct attack on the ATP binding site. *Circulation research*, 80 (1), 76–81.

Yavuz Otal, S.D., *et al*., 2018. Acute renal failure and thiol-disulfide homeostasis. *Journal of nephrology & therapeutics*, 8 (3). doi:10.4172/2161-0959.1000312