

# The influence of metabolic syndrome coexistence on the prognosis of patients with heart failure without atrial fibrillation. Analysis of Polish data from the pilot survey for the ESC Heart Failure Registry

Marcin T. Welnicki<sup>1</sup>, Daniel I. Śliż<sup>1</sup>, Jowita Szeligowska<sup>2</sup>, Wiesława B. Duda-Król<sup>1</sup>, Tomasz Chomiuk<sup>1</sup>, Dominika Dąbrowska<sup>1</sup>, Jarosław Drożdż<sup>3</sup>, Artur J. Mamcarz<sup>1</sup>

<sup>1</sup>3<sup>rd</sup> Department of Internal Diseases and Cardiology, Second Faculty of Medicine, Medical University of Warsaw, Warsaw, Poland

<sup>2</sup>3<sup>rd</sup> Department of Gastroenterology and Internal Diseases, First Faculty of Medicine, Medical University of Warsaw, Warsaw, Poland

<sup>3</sup>Department of Cardiology, Central Clinical Hospital, Medical University, Lodz, Poland

## INTRODUCTION

Chronic heart failure (HF) is one of the most serious challenges of cardiology in the 21<sup>st</sup> century. At present, the prevalence of HF in the general population is estimated at between 1% and 2% [1]. Thus, this condition affects between 6.5 and 10 million Europeans (including 600–700 thousand people in Poland) and over 5 million citizens of the United States [2, 3]. The prognosis is frequently unfavourable and at the same time difficult to assess precisely. The continuous search for factors significantly influencing the prognosis of patients with HF is of considerable importance, especially given the ageing population as well as a clear relationship between age and an increase in incidence of HF [1]. A paradoxical impact of obesity on the prognosis of HF patients has been observed for many years. Obesity increases the risk of HF occurrence, but at the same time, if HF is diagnosed, obesity appears to be a factor improving the prognosis [4–6]. Obesity is seldom an isolated abnormality, more frequently being part of metabolic syndrome (MS) — the coincidence of obesity, hypertension, dyslipidaemia, and carbohydrate metabolism disorders. The importance of MS coexistence for the prognosis of patients with HF remains unclear.

The aim of the study was to analyse the influence of MS on the one-year surveillance of HF patients without atrial fibrillation (AF).

## METHODS

The study was a post hoc analysis of data concerning 893 patients included in the pilot survey for the Heart Failure Registry, carried out in Polish medical centres for the European Society of Cardiology. In this study we presented the results of subgroup analysis of patients without diagnosed AF. For statistical analysis, it was assumed that a patient with MS was a patient with simultaneous occurrence of diabetes, hypertension, and obesity. Detailed information about the methods and limitations of the study are presented in the [Appendix \(see journal website\)](#).

### *Statistical analysis*

The analysis was performed using STATISTICA 12 PL software. The comparative analysis of the survival was performed by log-rank test, showing Kaplan-Meier survival curves and presenting hazard ratio (HR) values. The impact of individual qualitative factors on the survival was assessed by main effect or one-way analysis of variance (ANOVA), and factor interactions were evaluated by ANOVA interaction analysis.

## RESULTS

### *Characteristics of the studied population*

The study group consisted of 893 patients, 339 of whom had no history of any form of AF (men: 223, 69%). The mean

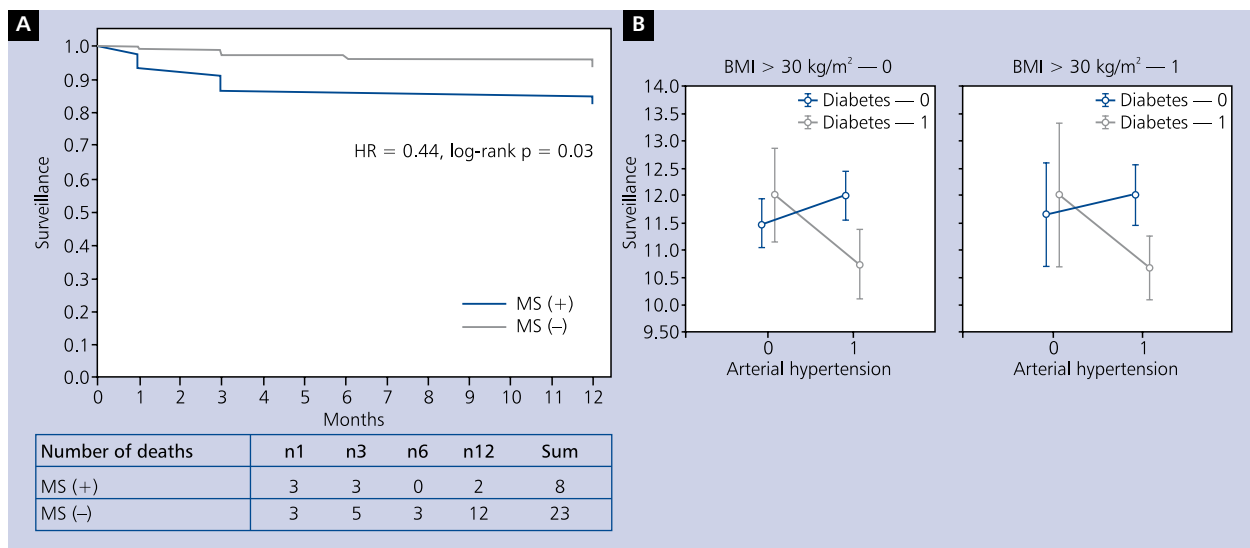
---

#### Address for correspondence:

Marcin T. Welnicki, MD, 3<sup>rd</sup> Department of Internal Diseases and Cardiology, Second Faculty of Medicine, Medical University of Warsaw, ul. Solec 93, 00–382 Warszawa, Poland, e-mail: welnicki.marcin@gmail.com

Received: 17.01.2018 Accepted: 22.01.2018

Kardiologia Polska Copyright © Polish Cardiac Society 2018



**Figure 1.** The influence of the coexistence of metabolic syndrome (MS) on the surveillance of patients with heart failure without atrial fibrillation; **A.** Kaplan-Meier survival curve for the study group with or without MS; HR — hazard ratio; n1, n3, n6, n12 — number of deaths in the first, third, sixth, and twelfth month of the follow-up study, respectively (explanation in the text); **B.** Coexistence of hypertension and diabetes negatively affects the survival of patients ( $p = 0.002$  for interaction between hypertension and diabetes). Negative interaction effects are observed in patients with and in patients without obesity; MS (-) — without metabolic syndrome; MS (+) — with coexisting metabolic syndrome; BMI — body mass index

age of the study population was  $63.6 \pm 13.5$  years, mean blood pressure was  $133.4 \pm 28.9/79.8 \pm 15.8$  mmHg, mean heart rate  $78.7 \pm 17.4$  bpm, left ventricular ejection fraction  $40.2\% \pm 13.9$ , and mean body mass index (BMI)  $28.4 \pm 5.3$  kg/m<sup>2</sup>. As far as comorbidities are concerned, 61% ( $n = 208$ ) of the group had previously diagnosed coronary artery disease, 54% ( $n = 187$ ) were previously hospitalised due to HF, and approximately 63% of patients received antihypertensive treatment. Diabetes was diagnosed in 33% ( $n = 114$ ), arterial hypertension in 62% ( $n = 212$ ), BMI > 30 kg/m<sup>2</sup> in 36% ( $n = 121$ ), dyslipidaemia in 75% ( $n = 255$ ), and MS in 13% ( $n = 45$ ) of patients.

### Survival analysis

During the 12-month follow-up study, 7.8% of patients without and 17.8% of patients with MS died (HR 0.44; log-rank test  $p = 0.03$ ). The Kaplan-Meier survival curve depending on the coexistence of MS is presented in Figure 1A. Interaction ANOVA analysis demonstrated that the adverse influence of MS on the prognosis of HF patients without AF was caused by the coexistence of hypertension and diabetes ( $p < 0.002$  for interaction). The negative prognostic effect of the coexistence of these two conditions was independent of obesity (lack of the obesity paradox), as shown in Figure 1B.

## DISCUSSION

The significance of MS in assessing the prognosis of patients with HF remains a difficult and controversial issue. We experi-

ence the obesity paradox described in the introduction and at the same time, also in a paradoxical context, the lack of clinical benefit from intensive treatment of dyslipidaemia. It may be assumed that hypertension and diabetes become the crucial elements of MS in this context. The existing research on this matter provides conflicting information. Tamariz et al. [7] showed that the coexistence of MS (defined by the National Cholesterol Education Programme — Adult Treatment Panel III criteria) was associated with a 50% increase in the relative risk of death [7]. Yoon et al. [8], however, observed lower mortality in patients with MS than in patients without MS (4.9% vs. 8.3%,  $p < 0.001$ ). By contrast, Tadaki et al. [9] observed a 28% (HR 1.28, 95% confidence interval 1.06–1.54,  $p = 0.011$ ) increased risk of death or cardiovascular event in the case of coexisting HF and MS, but only in men. Perrone-Filardi et al. [10] observed comparable survival in patients without MS and diabetes and in those with MS and coexisting diabetes. They indicated that the influence of MS on a prognosis may be related to whether the method used implies the presence of diabetes as a sine qua non condition for diagnosing MS [10]. Furthermore, Yamauchi et al. [11] demonstrated that the occurrence of a new AF episode in patients with HF significantly increases mortality risk.

Based on these and other studies, it can be assumed that the negative impact of AF on the prognosis of patients with HF has been confirmed [12]. In light of the abovementioned studies, the definition of MS used in the present study, and the fact that it separately analysed patients without AF, allows

us to obtain new data on the impact of MS on the prognosis of patients with HF.

Similarly to the study by Perrone-Filardi et al. [10], and in contrast to the study by Tamariz et al. [7], in the presented analysis obesity was a sine qua non condition for MS. In turn, as opposed to the study by Perrone-Filardi et al. [10], diabetes was also a prerequisite for the diagnosis of MS. In our study, as far as patients without AF were concerned, coexistence of MS was related to a 56% higher relative risk of death. This observation remains consistent with the previously presented results of the studies by Tamariz et al. [7] and Tadaki et al. [9], but simultaneously appears to contradict the results of Perrone-Filardi et al. [10]. Interaction analysis, however, showed that the negative impact of MS on the survival of HF patients without AF resulted primarily from the coexistence of diabetes and hypertension. This is, in fact, consistent with the observations of Italian researchers, and, at the same time, provides additional information on the importance of coexisting diabetes for the prognosis of patients with HF. The negative impact of diabetes and hypertension is so strong that it can eliminate the phenomenon of the obesity paradox. It is worth noting that the negative influence of MS on the survival of patients in this group was independent of sex in the study population.

In conclusion, the coexistence of MS worsens the prognosis of HF patients without AF. The worsening of the prognosis is primarily caused by the coexistence of diabetes and hypertension, and the occurrence of obesity has no influence on the prognosis (lack of the obesity paradox).

**Conflict of interest:** none declared

### References

1. Ponikowski P, Voors A, Anker S, et al. Wytyczne ESC dotyczące diagnostyki i leczenia ostrej i przewlekłej niewydolności serca w 2016 roku. [2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure]. *Kardiologia Pol.* 2016; 74(10): 1037–1147, doi: [10.5603/kp.2016.0141](https://doi.org/10.5603/kp.2016.0141).
2. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. *Circulation.* 2013; 127(1): e6–e245, doi: [10.1161/CIR.0b013e31828124ad](https://doi.org/10.1161/CIR.0b013e31828124ad), indexed in Pubmed: [23239837](https://pubmed.ncbi.nlm.nih.gov/23239837/).
3. Rywik TM, Kołodziej P, Targoński R, et al. Characteristics of the heart failure population in Poland: ZOPAN, a multicentre national programme. *Kardiologia Pol.* 2011; 69(1): 24–31, indexed in Pubmed: [21267960](https://pubmed.ncbi.nlm.nih.gov/21267960/).
4. Wang J, Sarnola K, Ruotsalainen S, et al. The metabolic syndrome predicts incident congestive heart failure: a 20-year follow-up study of elderly Finns. *Atherosclerosis.* 2010; 210(1): 237–242, doi: [10.1016/j.atherosclerosis.2009.10.042](https://doi.org/10.1016/j.atherosclerosis.2009.10.042), indexed in Pubmed: [19945701](https://pubmed.ncbi.nlm.nih.gov/19945701/).
5. Curtis JP, Selter JG, Wang Y, et al. The obesity paradox: body mass index and outcomes in patients with heart failure. *Arch Intern Med.* 2005; 165(1): 55–61, doi: [10.1001/archinte.165.1.55](https://doi.org/10.1001/archinte.165.1.55), indexed in Pubmed: [15642875](https://pubmed.ncbi.nlm.nih.gov/15642875/).
6. Oreopoulos A, Padwal R, Kalantar-Zadeh K, et al. Body mass index and mortality in heart failure: a meta-analysis. *Am Heart J.* 2008; 156(1): 13–22, doi: [10.1016/j.ahj.2008.02.014](https://doi.org/10.1016/j.ahj.2008.02.014), indexed in Pubmed: [18585492](https://pubmed.ncbi.nlm.nih.gov/18585492/).
7. Tamariz L, Hassan B, Palacio A, et al. Metabolic syndrome increases mortality in heart failure. *Clin Cardiol.* 2009; 32(6): 327–331, doi: [10.1002/clc.20496](https://doi.org/10.1002/clc.20496), indexed in Pubmed: [19569069](https://pubmed.ncbi.nlm.nih.gov/19569069/).
8. Yoon HJ, Ahn Y, Kim KH, et al. Korea HF Registry. The prognostic implication of metabolic syndrome in patients with heart failure. *Korean Circ J.* 2013; 43(2): 87–92, doi: [10.4070/kcj.2013.43.2.87](https://doi.org/10.4070/kcj.2013.43.2.87), indexed in Pubmed: [23508725](https://pubmed.ncbi.nlm.nih.gov/23508725/).
9. Tadaki S, Sakata Y, Miura Y, et al. Prognostic Impacts of Metabolic Syndrome in Patients With Chronic Heart Failure. A Multicenter Prospective Cohort Study. *Circ J.* 2016; 80(3): 677–688, doi: [10.1253/circj.cj-15-0942](https://doi.org/10.1253/circj.cj-15-0942).
10. Perrone-Filardi P, Savarese G, Scarano M, et al. Prognostic impact of metabolic syndrome in patients with chronic heart failure: data from GISSI-HF trial. *Int J Cardiol.* 2015; 178: 85–90, doi: [10.1016/j.ijcard.2014.10.094](https://doi.org/10.1016/j.ijcard.2014.10.094), indexed in Pubmed: [25464226](https://pubmed.ncbi.nlm.nih.gov/25464226/).
11. Yamauchi T, Sakata Y, Miura M, et al. CHART-2 Investigators. Prognostic Impact of New-Onset Atrial Fibrillation in Patients With Chronic Heart Failure: A Report From the CHART-2 Study. *Circ J.* 2016; 80(1): 157–167, doi: [10.1253/circj.CJ-15-0783](https://doi.org/10.1253/circj.CJ-15-0783), indexed in Pubmed: [26639067](https://pubmed.ncbi.nlm.nih.gov/26639067/).
12. Patel NJ, Patel A, Agnihotri K, et al. Prognostic impact of atrial fibrillation on clinical outcomes of acute coronary syndromes, heart failure and chronic kidney disease. *World J Cardiol.* 2015; 7(7): 397–403, doi: [10.4330/wjc.v7.i7.397](https://doi.org/10.4330/wjc.v7.i7.397), indexed in Pubmed: [26225200](https://pubmed.ncbi.nlm.nih.gov/26225200/).

**Cite this article as:** Wełnicki MT, Śliż DI, Szeligowska J, et al. The influence of metabolic syndrome coexistence on the prognosis of patients with heart failure without atrial fibrillation. Analysis of Polish data from the pilot survey for the ESC Heart Failure Registry. *Kardiologia Pol.* 2018; 76(4): 794–796, doi: [10.5603/KP.2018.0077](https://doi.org/10.5603/KP.2018.0077).