Pol-tako — the first, nationwide Polish multicenter analysis of patients with takotsubo syndrome

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INTRODUCTION
Takotsubo syndrome (TTS) was initially described by Hikaru Sato in Japan in 1990 [1]. The first case involving Polish population was published in The Polish Heart Journal in 2006 [2]. One of the largest TTS registries in the world, Inter-TAK registry, is coordinated by researchers from University Heart Center at University Hospital in Zurich [3]. Takotsubo syndrome is diagnosed in between 1 and 3% of patients with suspicion of myocardial infarction [4]. It’s pathophysiology is currently not fully understood, but the association with stress is apparent [5]. Acute stress, either emotional or physical, is a factor preceding about 50% of all episodes of TTS. Chronic stress, (e.g. depression, neoplastic disease) increases the risk of a TTS episode. During the 2019 SARS-CoV-2 pandemic, unprecedented social distancing measures were introduced. This resulted in a sudden and significant reduction in social interaction by encouraging people to stay at home, closing schools and recreation facilities, and introducing work at home as commonplace. This introduced a strong stress factor.

AIMS
The aim of this study is to describe and discuss population characteristics of Polish patients hospitalised due to TTS as well as a clinical presentation and prognosis of patients with TTS before and during the COVID-19 pandemic.

METHODS
The data (Pol-tako, ClinicalTrials.gov identifier, NC 04634487) will be collected both retrospectively and prospectively. It’s retrospective arm will include ten Polish cardiological centers experienced in treating TTS. The prospective arm will include cardiological centers which have around the clock catheterisation laboratories and dedicated COVID-19 centers. Patients concurrently hospitalised with TTS and COVID-19 will be included in the analysis. We have estimated that each center will include between fifty and three hundred patients and so, anticipate that we will gather a total number of 2000 cases.

The anonymised database will include demographical and clinical characteristics, introduced treatment, laboratory results, electrocardiograms, echocardiography, coronary imaging tests and short term in-hospital prognosis (Table 1).
Based on the collected information, we will evaluate the clinical characteristics of patients with TTS and their prognosis among the Polish population. We will prepare a comparison of individuals hospitalised before and during the COVID-19 pandemic and will compare patients with and without coexisting SARS-CoV-2 infection.

The Ethics Committee of the Medical University of Warsaw granted consent to conduct this study. Due to the collection of data in a completely anonymous manner there is no need to obtain consent of the study. Patients will not undergo any additional intervention and will be treated according to current recommendations.

The registry received patronage from the Association of Heart Failure and Association of Cardiovascular Intervention of the Polish Society of Cardiology.

**Statistical analysis**

Normally distributed continuous variables will be presented as mean values and standard deviations. Ordinal variables and non-normally distributed continuous variables will be presented as median values and interquartile ranges (IQR). Categorical data will be presented as a number of patients and percentages. The Fisher’s exact test and the Mann-Whitney U test will be used for categorical and continuous variables respectively. To determine the risk factors of endpoint (cardiogenic shock and death) occurrence, univariate and multivariate logistic regression will be applied. The factors that will be included to the univariate analysis will be demographic parameters, comorbidities, laboratory values, ECG, echocardiographic parameters and clinical course.

$P$ value less than 0.05 will be considered significant. All tests are two-tailed. All statistical analyses will be performed using SAS software version 9.4 (SAS Institute Inc. Cary, North Carolina, United States).

**RESULTS AND DISCUSSION**

Multiple criteria for TTS diagnosis, based on registries and observational studies, have been published. These were proposed a.o. by researchers from Mayo Clinic, Japanese Research Committee for Idiopathic Cardiomyopathy, The Johns Hopkins Hospital, Heart Failure Association of the European Society of Cardiology and scientists from InterTAK registry [5–9]. Polish patients were included only in the InterTAK registry, but constituted less than 10% of the study population.

To date, interesting results have been published involving single-center experience regarding markers used in TTS diagnosis, inter-sex differences, application of GRACE scale and poor
prognosis of patients with chronic kidney disease or low body mass index (BMI) [10–14]. It would, however, be extremely valuable to verify these results for large scale population. According to early global reports, the incidence of TTS has been significantly higher in patients admitted with acute coronary syndrome symptoms during the COVID-19 pandemic compared to the pre-pandemic era. Social isolation can account for multiple psychological disturbances including stress, anxiety, depression, insomnia, anger, frustration, irritability and boredom. These could have long lasting consequences even after lock-down or quarantine termination. The occurrence or intensification of emotional stress may be related to uncertainty and concerns about the future, compounded by systematic and alarming news (daily reports of infections and deaths). The increase in TTS incidence during COVID-19 may be linked to concern over the virus infection and it’s consequences but also to psychological, social and economic factors that have been part of the reaction to the pandemic. There have been a few cases of TTS with coexisting Covid-19 described and published, however, the mechanism of myocardium injury in these patients is still unknown.

Proposed mechanism of COVID-19 induced cardiac injury is the destruction of ACE2 receptors, surge in catecholamines due to the acute viral illness, severe hypoxia, and the associated acute respiratory distress syndrome observed in moderate-to-severe COVID-19 infections or cytokine storm [15].

We hope that Pol-tako may be a valuable source of knowledge in this area.

REFERENCES


Table 1. Data collected in the Pol-tako registry

<table>
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<tr>
<th>Baseline characteristic</th>
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<td>5th day</td>
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