

Abstract

Background. Cardiogenic shock (CS) initially complicates acute myocardial infarction (AMI) in approximately seven percent of patients. According to available data, the morbidity of AMI initially complicated by cardiogenic shock (CS-AMI) is in the range of 40-60%, which is ten times the short-term mortality of AMI without this initial complication.

Objective. To analyze and define independent predictors of prognosis in patients with acute myocardial infarction initially complicated by cardiogenic shock.

Methods. We designed a retrospective cohort data analysis by merging 3 national registries- the National Registry of Reimbursed Health Services, the Database of Death Records, and the National Registry of Cardiovascular Operations and Interventions, which are part of the National Health Information System in the Czech Republic. In cooperation with the Institute of Health Information and Statistics of the Czech Republic, a complex analysis was developed to provide an overview of all CS-AMI patients in the Czech Republic over a 5-year period.

Results. The initial data set included 50,745 patients with AMI from 2016-2020 (58.2% with ST-elevation myocardial infarction and 41.8 % with non-ST-elevation myocardial infarction), of whom 2,822 had CS-AMI. Data from patients with available information on 30-day mortality (N = 2,693) were used for analysis. On average, 56.7 % of patients with CS-AMI required cardiopulmonary resuscitation (both out-of-hospital and in-hospital), 67.1% required mechanical ventilation, and 53.5% required both. The hazard ratio for 30-day mortality of AMI patients with CS vs. AMI patients without CS based on survival analysis is 15.25 (95% CI 14.24 - 16.33). Univariate logistic regression identified female sex (OR 1.23), age (OR 1.04 for each additional year), chronic kidney disease (OR 1.67), diabetes mellitus (OR 1.68), resuscitation (OR 1.23), mechanical ventilation (OR 1.35), multivessel disease (OR 1.79), left main disease (OR 1.42), and delay of more than 8 hours from symptom onset to revascularization (OR 1.48) as factors with the highest predictive value for 30-day mortality. Although mortality was

numerically higher in the fall and winter months compared with the summer months (54.2% vs. 45.8% and 51.45% vs. 48.55%, $p = 0.02$) and during the weekend vs. during the workweek (51.45% vs. 48.55%, $p < 0.01$), the predictive role of these factors was not confirmed in either univariate or multivariate analysis.

Multivariate logistic regression showed that age (>80 years), diabetes mellitus, cardiopulmonary resuscitation, mechanical ventilation, multivessel disease, and left main disease were independent factors with the highest predictive value for 30-day mortality.

In the next analysis, we focused on significant left main disease as a predictor of mortality in patients with CS-AMI. The initial dataset included 48,881 patients with AMI hospitalized in the Czech Republic during a 5-year period (2017-2021). Pre-existing significant left-sided valvular heart disease (VHD) was diagnosed in 1,445 patients (3.0%), significant mitral regurgitation (MR) in 510 patients (35.3%), and significant aortic stenosis (AS) in 869 patients (60.1%). Patients with VHD had worse baseline characteristics, a history of ischemic heart disease, a more complicated hospital course with a higher Killip class, a lower left ventricular ejection fraction, and more comorbidities. Angiographically, patients with VHD had more frequent left main stenosis, less severe coronary artery stenosis and TIMI 3 flow before PCI, and less frequent stent implantation. Patients with VHD had significantly higher 7-day (10.1% vs. 4.5%, $p < 0.01$), 30-day (16.0% vs. 7.0%, $p < 0.01$) and 1-year mortality (28.7 vs. 12.7, $p < 0.01$) compared to patients without VHD. AS was associated with a high risk of short-term (OR 1.80; 95% CI 1.51 - 2.13) and long-term (OR 1.63; 95% CI 1.47 - 1.81) mortality, $p < 0.01$ for both. MR did not significantly increase the risk of 30-day mortality, but remained independently associated with long-term all-cause mortality (OR 1.21; 95% CI 1.04 - 1.40, $p < 0.01$).

AMI is the most common cause of OHCA. In left-sided valvular heart disease, the outcome of resuscitation may be worse because of obstruction of the outflow tract in aortic stenosis or high

regurgitant flow in mitral regurgitation, which prevents adequate blood flow to the aorta and increases myocardial oxygen demand. Therefore, we analyzed a group of patients with AMI complicated by out-of-hospital cardiac arrest (AMI-OHCA), N=4,414, of whom 1.8% (N=80) had pre-existing AS and 1.1% (N=47) had MR. Patients with AMI-OHCA were divided into three groups: those who died during OHCA (N = 238), those who were admitted after OHCA on mechanical ventilation (N = 3,255), and those who were spontaneously ventilating on admission (N = 921). Multivariate analysis showed that AS was not a significant risk factor for the use of mechanical ventilation in AMI-OHCA patients (OR 1.61; 95% CI 0.83 - 3.09, $p = 0.16$), but was a significant risk factor for pre-hospital mortality in AMI-OHCA patients (OR 3.4; 95% CI 1.20 - 9.58, $p = 0.02$). In addition, in-hospital, 30-day, and long-term prognosis of patients with AMI-OHCA was adversely affected by AS (OR 2.47; 95% CI 1.38 - 4.41), (OR 2.83; 95% CI 1.61 - 4.95), and (OR 1.81; 95% CI 1.38 - 2.38) vs. non-VHD, respectively, $p < 0.01$ for all.

Cardiogenic shock results in centralization of the circulation and splanchnic hypoperfusion, which may be associated with impaired absorption from the gastrointestinal tract, slower metabolization to active forms, and overall delayed and attenuated effects of oral drugs. The use of an active form of an antiplatelet drug is expected to increase the likelihood of rapid and successful reperfusion in this patient population. These premises led to the design of a multicenter, randomized, double-blind academic trial, Dual Antiplatelet Treatment of Patients with Acute Myocardial Infarction in Cardiogenic Shock (DAPT - SHOCK AMI), initiated by Prof. MOŽOVSKÁ. It is the largest non-commercial study testing pharmacotherapeutic management of patients with cardiogenic shock complicating acute myocardial infarction. The study also includes a registry of patients with CS-AMI who could not be included in the study due to the presence of an exclusion criterion. Analysis of study and registry data, including

dynamic monitoring of laboratory parameters during annual follow-up, will provide material for the study of new predictors of prognosis in patients with CS-AMI.

Conclusion. Significant aortic stenosis is an independent predictor of more severe heart failure and greater need for mechanical ventilation in AMI, has a significant adverse effect on patient survival after OHCA, and is a significant risk factor for both pre-hospital and long-term mortality. Patients with AS should therefore be carefully screened for coronary artery disease and antithrombotic treatment should be considered. Shortly after AMI, it is important to assess the progression of aortic stenosis and the need for earlier aortic valve intervention.

Early and successful revascularization is an important modifiable predictor of CS-AMI. Early revascularization in the infarct-related artery and microcirculatory perfusion are critical for survival in patients with CS-AMI. Modifying the current recommendations for adjuvant antithrombotic therapy may improve the success of reperfusion and thereby contribute to improving the prognosis of CS-AMI patients. The DAPT-SHOCK-AMI trial will contribute to the optimization of adjuvant antiplatelet therapy and thereby potentially improve the prognosis of patients with CS-AMI.