Sex-specific differences in total ischemic time coincide with similar cardiovascular outcome in patients with acute coronary syndrome: a Swiss multicentre cohort study

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Funding Acknowledgement: Type of funding sources: Other. Main funding source(s): Swiss National Science Foundation - SNFFoundation for Cardiovascular Research - Zurich Heart House

Background: Previous studies showed prolonged patient and system delay in female patients with acute coronary syndromes (ACS) which is thought to be a major driver of discrepancies in their cardiovascular (CV) outcomes. Indeed, timely management is particularly important in patients with ST-segment elevation myocardial infarction (STEMI), as increased total ischemic time augments infarct size and relates to poor CV survival. However, contemporary evidence on sex-specific differences in ACS management and discrepancies in outcomes is limited and controversial.

Purpose: We sought to systematically investigate whether a sex-gap in symptom-to-door (STD), door-to-balloon (DTB)/door-to-PCI (DTP) time exists in a prospective ACS cohort and if such differences translate into different rates of major adverse cardiovascular events (MACE) at one year.

Methods: From 2009 to 2019, 4'930 ACS patients with a main diagnosis of NSTEMI (43.3%), STEMI (53.3%) or unstable angina (3.4%) were enrolled in the multicentre, prospective SPUM-ACS study of which 4'671 completed follow-up at one year. STD, DTB and DTP time was analyzed. The primary endpoint, a composite measure of all-cause death, nonfatal myocardial infarction, nonfatal stroke and ischemia-driven revascularization, was adjudicated by an independent clinical endpoint committee. Kaplan-Meier and multivariate-adjusted Cox proportional hazard regression models were used for time-to-event analyses.

Results: A total of 1'019 (20.7%) women and 3'911 (79.3%) men with a main diagnosis of ACS were included in the study. At presentation, women were older (69.6±12.0 vs. 62.2±12.1 years, $P<0.001$), more likely to have impaired renal function (median, 81.2 vs. 89.2 ml/min/1.73m^2, $P<0.001$) and a history of hypertension (63.9% vs. 54.3%, $P<0.001$). STD time was significantly higher in female STEMI (median, 3.2 vs. 2.5 hours, $P<0.001$) and NSTEMI patients (median, 7.0 vs. 5.0 hours, P=0.015). Importantly, DTB time did not differ between sexes in STEMI patients (1.0 vs. 1.0 hour, P=0.430). Similarly, DTP time of female NSTEMI patients was comparable to males (4.3 vs. 4.4 hours, P=0.855). In the entire cohort, female ACS patients did not show a higher occurrence of the primary endpoint at one year (crude HR 0.86, 95% CI 0.72–1.04; adjusted HR 0.83, 95% CI, 0.66–1.05). In a multivariate-adjusted subgroup analysis, neither female STEMI (adjusted HR 0.82, 95% CI 0.59–1.15) nor NSTEMI patients (adjusted HR 0.87, 95% CI 0.61–1.24) showed higher hazards for the primary endpoint compared to male patients.

Conclusions: Women with a main diagnosis of STEMI show considerably higher prehospital delay, thus prolonged total ischemic time which is mainly driven by increased STD time. Intriguingly, this does not translate into higher rates of MACE compared to men at one year. Women with ACS may particularly benefit from measures aimed at reducing prehospital delay, as this may further improve long-term prognosis after the acute event.