Editorial

# Reperfusion in women with STEMI: a date not to be late!

## Reperfusão em mulheres com IAMCST: um encontro para não chegar atrasado!

"You may delay, but time will not"
*Benjamin Franklin*

Results from large studies investigating clinical outcomes following ST-elevation myocardial infarction (STEMI) have suggested that outcomes are worse in women in comparison to men,[1] regardless of the reperfusion strategy employed. The majority of these observations, however, have been based upon results from large clinical trials in which women have only made up 20 to 30% of the total study population.[2-4] A number of explanations have been postulated for the worse outcomes in women, including older mean age at presentation, several comorbidities, more extended coronary artery disease, late presentation, and delays in diagnosis.[5,6] Nonetheless, specific independent predictors for poor response to reperfusion therapy and therefore clinical outcomes in women are poorly defined; moreover, following multivariable adjustment for baseline confounders, in several studies mortality was not statistically different between men and women.[7]

In this issue of the Revista Brasileira de Cardiologia Invasiva, Sousa et al. reported the results of a retrospective analysis of 327 women presenting with STEMI treated with thrombolysis as first-line treatment.[8] They reported clinical outcomes of women who achieved successful reperfusion following lysis compared to those who did not and required rescue angioplasty. Additionally, they attempted to identify independent predictors for lysis failure in this patient group. Out of the total cohort of 1,261 patients in the registry, 327 (26%) were women and were treated with thrombolysis and early catheterization following successful reperfusion (n = 206) or rescue angioplasty for failed lysis (n = 121). There were no differences in baseline characteristics between groups, which included women with a large percentage of cardiovascular risk factors, such as smoking history, dyslipidemia, and hypertension. A few general observations should be made. Firstly, in women presenting with STEMI who cannot be treated with the gold standard treatment of primary angioplasty in a timely manner, the administration of contemporary thrombolysis regimens is safe, with only one occurrence of hemorrhagic stroke in each group reported in this patient cohort. Secondly, this representative "all-comer" population demonstrated that, in support of previous observations,[3] lysis failed in approximately one-third of women presenting with STEMI, resulting in clinical outcomes that were significantly worse (in-hospital mortality 22% vs. in 2.5%; $p < 0.001$), supporting the practice of transferring patients to angioplasty-capable centers following administration of lysis to facilitate emergency rescue angioplasty if required. Finally, as expected, patients who failed lysis had lower prevalence of post-percutaneous coronary intervention (PCI) Thrombolysis in Myocardial Infarction (TIMI) flow 2 or 3 and post-PCI myocardial blush 2 or 3, with subsequent significantly worse ejection fraction and higher incidence of heart failure when compared to patients that achieved successful reperfusion. Specifically, with regards to predicting lysis failure, the authors identified pain-to-needle time greater than 3 hours, Zwolle Risk Score (which includes ischaemic time as contributing component), and presence of renal dysfunction as independent predictors in women, in support of findings applicable to the population as a whole.

However, it is necessary to consider that some limitations apply to this study. First, as in every retrospective analysis, the findings are subject to confounder bias. Second, the small sample size of the study population, and therefore low statistical power, precludes an adequate multivariable adjustment and detection of other covariates independently associated with the need for rescue PCI. Third, important procedural and angiographic variables, such as antiplatelet and anticoagulant treatment, arterial access site, infarct location, and culprit artery characteristics were not reported, therefore limiting the interpretation of the severely impaired outcomes associated with rescue PCI.

Notwithstanding these limitations, the present study underscores the importance of "time" in the current STEMI practice in a female Brazilian population. Both pain-to-needle time and Zwolle Risk Score were strong predictors of lysis failure in women. Previous data suggest that every minute of delay in treatment of patients with STEMI has a significant effect on mortality after both thrombolytic and primary PCI reperfusion.[9] Female gender has been constantly associated with delayed presentation, reperfusion, and undertreatment.[7,10,11] Moreover, STEMI in women demonstrated to be associated with worse outcomes when compared with males. Several distinct mechanisms might explain the greater effect of STEMI on mortality in women: (i) the higher risk for bleeding complications, whose subsequent impact on morbidity and mortality has been well described;[12] (ii) a more adverse clinical risk profile at baseline when compared with males;[1] and (iii) the greater burden of myocardial injury and necrosis with secondary higher risk of negative myocardial remodelling and death for heart failure when compared with males.[13] A substudy from the HORIZONS-AMI (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction) trial reported higher in-hospital, 30-day, and 3-year major adverse cardiac events (MACE) and bleeding in women compared with men after STEMI.[12] However, in that study, after multivariable adjustment for baseline and procedural confounders, there were no differences in mortality between genders.[12] Stronger evidence has been also provided by a large gender-based meta-analysis that included over 18,000 women and reported higher in-hospital and

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1 year mortality in women after STEMI.[14] The multiplicative effect between STEMI and female gender on mortality might therefore be further independently accentuated by presentation delay.

With these data in mind, how can we improve women's cardiovascular health and early recognition and prognosis of acute myocardial infarction? A first step would be a community-based action to increase the awareness of the prevalence, incidence, and importance of cardiovascular diseases among the female population through patient education, public health initiatives, and efforts in promote cardiovascular research in women.[11] Cardiovascular disease in women are often underdiagnosed and undertreated.[11] The study of Sousa et al. suggests the presence of this issue in a Brazilian population.[8] A collaboration to uniformly change the perception, at a physician- and patient-level, is therefore of paramount importance in order to improve cardiovascular women's health.

## Conflicts of interest

Drs. Giustino, Ruparelia and Chieffo declare no conflicts of interest. Dr. Mehran has received institutional research grant support from The Medicines Company, Bristol-Myers Squibb, Sanofi Aventis, Lilly, Daiichi Sankyo, Regado Biosciences, and STENTYS; is a consultant for Abbott Vascular, AstraZeneca, Boston Scientific, Covidien, CSL Behring, Janssen Pharmaceuticals, Merck, and Sanofi Aventis; and has equity in and is a shareholder of Endothelix, Inc.

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**Gennaro Giustino[a,1], Neil Ruparelia[b,1], Roxana Mehran[a], Alaide Chieffo[b,*]**

[a] *The Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA*
[b] *San Raffaele Scientific Institute, Interventional Cardiology Unit, Milan, Italy*

[1]The first two authors equally contributed to the manuscript.

*Corresponding author: Alaide Chieffo, San Raffaele Scientific Institute – Interventional Cardiology Unit – Via Olgettina 60, Milan, Italy.
*E-mail*: chieffo.alaide@hsr.com (Chieffo A.).