

Both sexes should be treated equally: sex difference in patients with ischemic heart failure undergoing surgical revascularization

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Provenance: This is an invited Editorial commissioned by the Section Editor Raffaele Giordano (Department of Advanced Biomedical Sciences, Adult and Pediatric Cardiac Surgery, University of Naples Federico II, Naples, Italy).

Comment on: Piña IL, Zheng Q, She L, *et al.* Sex Difference in Patients With Ischemic Heart Failure Undergoing Surgical Revascularization: Results From the STICH Trial (Surgical Treatment for Ischemic Heart Failure). *Circulation* 2018;137:771-80.

Submitted Jul 09, 2018. Accepted for publication Jul 23, 2018.

doi: 10.21037/jtd.2018.08.26

View this article at: <http://dx.doi.org/10.21037/jtd.2018.08.26>

We read with the interest the work of Piña *et al.* (1). STICH trial (2) is the first and for long time remains only randomized trial to compare CABG plus medical therapy for heart failure (HF) versus medical therapy for HF only in patients with severe left ventricular dysfunction (EF \leq 35%, for inclusion criteria see below). Data for this randomised trial is collected from 99 centers of 22 countries, which means on average one expects 12 patients collected from every center, and on average 55 patients from every country. This makes us think that there should be some wide range of variability when it concerns quality of the data collection, protocol application, practical application of inclusion and exclusion criteria. It is well known that coronary artery disease (CAD) is a leading cause of death and HF is the leading cause of hospitalisation in woman >65 years old (3,4).

After 2,000's female patients (with a mean age of 70) counted for only 2% of total world population (around 140 million; The World Bank Data interactive site: <https://data.worldbank.org/>). Fifteen million in Europe (5) and 6 million (6) in the United States only have HF, with most common cause is a CAD (7) and complications from it, HF when come to example.

From the landmark clinical trials' results that from starting 70's it is recommended to perform CABG for relieving symptoms of angina, particularly among high risk patients (8) but excluded patients with severe left ventricular dysfunction by that time. The STICH trial (2) addressed this problem few years ago and concluded for 'no significant difference between groups with respect of primary end

point (rate of death for any cause); rate for cardiovascular death or hospitalisation was lower in CABG group'. However, the authors did not underline the sex differences in that original paper. Female sex, as matter of fact, considered as a risk factor for CABG and poor prognostic variable for perioperative risk evaluation scores, for example EuroSCORE [mainly used in Europe (9,10)] and many others [for example STS Score (Society of Thoracic Surgeons site: <http://riskcalc.sts.org/stswebriskcalc/#>) (11)].

Piña *et al.* (1) conducted study using STICH trial data with longer follow up (median around 10 years). Authors selected two groups dividing them by gender. By the original trail design the inclusion criteria were (12):

- (I) man;
- (II) women not of childbearing potential;
- (III) age \geq 18 years old;
- (IV) LVEF \leq 0.35 measured by means of contrast magnetic resonance ventriculography, gated SPECT ventriculography, echocardiography, or contrast ventriculography within 3 months of trial entry;
- (V) CAD suitable for revascularization.

It is not difficult to point out that there could be some bias on female patients inclusion in to this trial. In fact, authors elaborate on their limitations section underline that probably the design of STICH trial could have made the investigations to enroll less 'sick' women and left out more symptomatics out from the inclusion to trial. Ignoring this bias Piña *et al.* (1) analysed the data without using

valid statistical technique (e.g., propensity score matching) in order to loosen the bias although it is not possible to remove after all. Even after considering all the limitations still this paper and analysis of the contemporary data is valuable. Take home message here is that the sex should not be the bias for addressing female patients to CABG. Moreover, it seems that even when female patients clinically are worse candidate are over-performing in the follow up having less all-cause and cardiovascular mortality. In our opinion for the future elaboration on this topic with available data should be analysed in more statistically complex and appropriate manner.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Cite this article as: Margaryan R, Murzi M. Both sexes should be treated equally: sex difference in patients with ischemic heart failure undergoing surgical revascularization. *J Thorac Dis* 2018;10(Suppl 26):S3153-S3154. doi: 10.21037/jtd.2018.08.26