The role of gender in survival after bilateral internal mammary artery in coronary artery bypass grafting: a propensity score analysis

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Background: The Arterial Revascularization Trial (ART) (1), a randomized controlled trial designed for 10-year comparison between bilateral internal mammary artery (BIMA) and single internal mammary artery (SIMA) coronary artery bypass grafting (CABG), showed no differences regarding survival between those techniques, nevertheless most observational studies supported long-term survival benefit after BIMA (2). Data on females is scarce due to low proportion of females according to the nature of these cohorts. The propensity score (PS) is the probability of some patient being assigned to one intervention conditional on a set of covariates. Different methods using PS have been used for confounding adjustment in observational studies, in way to reduce or eliminate the effects of selection bias (3, 4).

Aim: The aim of our study was to compare long-term survival after coronary artery bypass grafting (CABG) using bilateral internal mammary artery (BIMA) or single internal mammary artery (SIMA) between males and females and using PS techniques (5).

Methods: A single-center retrospective cohort study was conducted using consecutive patients with 2 left-coronary system vessel disease who underwent isolated CABG between 2004 and 2013. All-cause mortality was the primary outcome. Secondary outcomes were early mortality and reoperation due to sternal wound complications (SWC). PS analysis was used to account for selection bias between the studied groups. Gender and BIMA interaction was checked in both univariate and multivariate analysis. Two non-parsimonious multivariate logistic regressions were conducted to

estimate the PS in the overall sample: model 1 using 24 covariates, and model 2 using 24 covariates and 4 interaction terms particularly related to the influence of gender on results. Both models 1 and 2 showed a good discriminative power for BIMA prediction (AUC: 0.887, 95% CI: 0.874 – 0.900; and 0.888, 95% CI: 0.875 – 0.900, respectively). Main effects and interaction analysis were done using inverse probability of treatment weighting (IPW) using stabilized weights and truncation was at 99th percentile threshold. IPW relies on the generation of a synthetic sample in which the distribution of covariates is balanced between treatment groups as a differential amount of information (weight) is taken from each participant depending on the conditional probability of belonging to a treatment group (6). Covariate balance was assessed using absolute standardized mean differences (ASMD), C-statistic (area under receiver operating curve) after weighting and graphical comparisons of the distribution of continuous variables. Both model 1 and 2 presented a C-statistic near to 0.5 (0.54, 95% CI: 0.52-0.57 and 0.55, 95% CI: 0.53-0.58, respectively), suggesting that after IPW it is no longer possible to distinguish the groups, i.e. they are well-balanced. Survival analysis was performed through Kaplan-Meier curves and multivariate cox regression using a robust variance. As a significant interaction between intervention group and gender was found, we performed a subgroup analysis for each gender. In this stratification we used simple PS adjustment due to the smaller sample size of subgroups comparing with overall sample (5).

Results: From 3437 patients undergoing first isolated CABG at our center, 2424 were included in this study: 936 BIMA and 1488 SIMA. Sample baseline characteristics were significantly different between groups: BIMA patients were younger, mostly males, had higher pre-operative haemoglobin level and higher proportion of dyslipidaemia and smoking habits, whereas SIMA patients had more history of neoplasia, diabetes, hypertension, cerebrovascular disease, moderate to severe LV dysfunction, atrial fibrillation, and severe renal function impairment. Females (124 BIMA and 336 SIMA) were older and had higher prevalence of comorbidities than man (812 BIMA and 1152 SIMA).
Median follow-up was 5.5 years (4.6 and 6.2 for BIMA and SIMA, respectively). A lower proportion of BIMA patients died compared with SIMA (9.6% vs. 20.3%, unadjusted HR: 0.61, 95%CI: 0.48-0.77, p<0.001). After IPW adjustment differences were no longer observed (HR: 1.1, 95%CI: 0.68-1.8). In the gender subgroup stratification analysis, females showed worse survival rates for BIMA CABG in the PS covariate-adjusted analysis (HR = 2.00; 95% CI: 1.03–3.89 with SIMA as reference; P = 0.039) whereas no difference was found for males (HR = 0.91; 95% CI: 0.65–1.27). Regarding secondary endpoints SIMA and BIMA CABG showed similar early mortality (1.1%) and risk of re-exploration for bleeding (2.5%). Only 5 patients underwent redo-CABG, 3 in the BIMA CABG group. After IPW, BIMA CABG was associated with a 23% decrease in the need of inotropic support or IABP in the postoperative period while it prolonged mechanical ventilation and increased the rate of reoperation due to infection or SWC (IPW adjusted model OR: 1.74; 95% CI: 1.16–2.60) .

Conclusion: At 5 years of follow-up BIMA and SIMA had similar survival results in the overall sample. However, female gender with BIMA was associated with higher mortality compared to female revascularized with SIMA, which should be further explored (5).

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