The influence of bilateral internal mammary arteries on short- and long-term outcomes: A propensity score matching in accordance with current recommendations

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Objectives: We undertook a single-center, 12 years outcomes analysis of the influence of bilateral internal mammary arteries (BIMA) over single internal mammary artery (SIMA) on short-term outcomes and long-term outcomes by means of propensity score matching technique in accordance to current recommendations.

Methods: A propensity score was generated for each patient from a multivariable logistic regression model based on 20 pretreatment covariates. The study population consisted of 4195 patients undergoing coronary artery bypass graft procedure using SIMA (n = 3445; 78.3%) or BIMA (n = 750; 21.7%). A total of 750 matching sets were derived.

Results: The BIMA group was associated with an increased rate of superficial sternal wound infection (5.6% vs 1.7%; $P = .0001$) but the incidence of deep sternal wound infection was comparable between the 2 groups, at 2.1% and 1.5% in BIMA and SIMA groups, respectively ($P = .43$). With regard to other postoperative complications the 2 groups were comparable. Operative mortality rate did not significantly differ between the 2 groups, at 0.7% and 1.2% in the BIMA and SIMA groups, respectively ($P = .28$). After a mean follow-up time of 4.8 ± 3.2 years, BIMA use was associated with a significantly lower risk for late mortality (hazard ratio, 0.61; 95% confidence interval 0.38-0.97; $P = .03$) and need for repeat revascularization (hazard ratio, 0.75; 95% confidence interval, 0.53-0.96; $P = .03$).

Conclusions: When compared with SIMA grafting, BIMA use did not increase operative morbidity and mortality and was associated with a better long-term survival. (J Thorac Cardiovasc Surg 2014;148:2699-705)

The use of bilateral internal mammary arteries (BIMA) compared with single internal mammary artery (SIMA) use has been proposed to improve late survival in patients undergoing coronary artery bypass graft (CABG) procedure.[1] This survival advantage from BIMA use is currently supported by several observational cohort studies[2] because the only randomized controlled trial to date evaluating long-term survival and freedom from reintervention from BIMA is still ongoing.[3] However observational studies often have several methodologic flaws that limit the usefulness of their conclusions.[4]

Propensity score (PS) matching, which creates groups of patients who have similar pretreatment characteristics when treatment assignment is not random, has emerged as the most effective statistical method to reduce bias in treatment comparisons in observational studies.[5-7] With regard to BIMA use, only 4 out of 27 observational studies included in a recent systematic review[2] using PS matching demonstrated a survival benefit from BIMA.[8-11] Moreover surgeons continue to be reluctant to use BIMA routinely because concerns still exist regarding the detrimental effect of this strategy on operative outcomes,[12] including the increased risk for sternal wound complications.[13] Therefore there is an urgent need for additional well-conducted studies to validate the safety and efficacy of BIMA grafting and enhance its universal adoption.

Recently general recommendations have been proposed in conducting PS matching.[5-7] We undertook a single-center, 12 years outcomes analysis using the PS matching technique in accordance with current recommendations to evaluate the influence of BIMA over SIMA on short- and long-term outcomes.

METHODS

Study Population

The study was conducted in accordance with the principles of the Declaration of Helsinki. The local ethics committee approved the study, and the requirement for individual patient consent was waived. We retrospectively analyzed prospectively collected data from an institutional surgical database (Dendrite Clinical Systems, Ltd, Oxford, UK) from April 2001 to May 2013. The database captures detailed information on a wide

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Abbreviations and Acronyms

BIMA = bilateral internal mammary arteries
CABG = coronary artery bypass graft
DWSI = deep sternal wound infection
LAD = left anterior descending
LVEF = left ventricular ejection fraction
PCI = percutaneous coronary intervention
PS = propensity score
PVD = peripheral vascular disease
SIMA = single internal mammary artery
SSWI = superficial sternal wound infection
SVG = saphenous vein grafts

range of preoperative, intraoperative, and hospital postoperative variables (including complications and mortality) for all patients undergoing CABG in our institution. The data is collected and reported in accordance with the Society for Cardiothoracic Surgery in Great Britain & Ireland database criteria. The database is maintained by a team of full-time clinical information analysts who are responsible for continuous prospective data collection as part of a continuous audit process. Data collection is validated regularly. Information about death from any cause is regularly obtained from the General Register Office approximately 1 week after the event and data on repeat revascularization is collected from a national surgical and interventional database.

Patients included in the final analysis met the following criteria: first-time isolated CABG, ≥2 grafts received, and surgical strategies included single left internal mammary artery to left anterior descending (LAD) artery and additional saphenous vein grafts (SVG) for non-LAD targets (SIMA group) or BIMA with or without additional SVG (BIMA group). Internal mammary arteries were harvested as pedicled or skeletonized conduit according to surgeon preference. Antibiotic prophylaxis included 2 g cefazolin administrated intravenously between 20 to 30 minutes after the induction of anesthesia, followed by 1 g every 8 hours for 24 hours. For all interventions lasting >3 hours, a new dose of 1 g cefazolin was administered. All patients had strict blood glucose control according to a unique intravenous insulin therapy protocol. The target blood glucose was 100 to 139 mg/dL (5.5-7.7 mmol/L). Blood glucose monitoring began upon the arrival of the patient to the operating room. Blood glucose measurements were taken hourly during the intraoperative period and after admission to our intensive care unit until a stable blood glucose level within the blood glucose target range was achieved. Blood glucose was then checked every 3 hours. Depending on the patient's clinical condition, oral intakes were initiated as soon as possible postoperatively. Intravenous insulin therapy was replaced by subcutaneous insulin when either oral feeding was initiated or 2 days postoperatively.

Pretreatment Variables and Study End Point

The effect of BIMA was adjusted for the following 20 pretreatment variables: age, female gender, New York Heart Association functional class III to IV, prior myocardial infarction prior percutaneous coronary intervention (PCI), diabetes mellitus, current smoking, chronic obstructive pulmonary disease, cerebrovascular accident, peripheral vascular disease (PVD), history of atrial fibrillation, number of vessels diseased, left main stem disease, left ventricular ejection fraction (LVEF) <50%, renal impairment defined as a serum creatinine >200 mmol/L, obesity defined as body mass index ≥30, urgent/emergent indication, preoperative use of intra-aortic balloon pump, surgery performed by a resident physician, and the use of cardiopulmonary bypass.

The short-term outcomes investigated were the incidence of superficial sternal wound infection (SSWI) and deep sternal wound infection (DSWI) as defined by the Centers for Disease Control and Prevention,[14] postoperative cerebrovascular accident, need for renal replacement therapy, reintubation for acute respiratory failure, reexploration for bleeding, postoperative atrial fibrillation, and operative mortality (within 30 days).

Long-term outcomes investigated were all-cause late mortality and need for repeat revascularization, including PCI and/or redo CABG. All-cause death is considered the most robust and unbiased index because no adjudication is required, thus avoiding inaccurate or biased documentation and clinical assessments.[15]

Statistical Analysis

The authors adhered to guidelines[16] for reporting observational studies. For baseline characteristics, variables are summarized as mean for continuous variables and proportion for categorical variables.

Multiple imputation using bootstrapping-based expectation-maximization algorithm was used to address missing data.[17] To control for measured potential confounders in the data set, PS was generated for each patient from a multivariable logistic regression model based on 20 pretreatment covariates as independent variables with treatment type (BIMA vs SIMA) as a binary dependent variable.[18] The resulting propensity score represented the probability of a patient undergoing CABG with BIMA grafting. Pairs of patients receiving BIMA and SIMA were derived using greedy 1:1 matching with a calliper of width of 0.2 standard deviation of the logit of the PS.[7] The quality of the match was assessed by comparing selected pretreatment variables in the PS-matched patient using the standardized mean difference, by which an absolute standardized difference >10% is suggested to represent meaningful covariate imbalance.[6] Analytic methods for the estimation of the treatment effect in the matched sample included McNemar's test to compare proportions. Kaplan-Meier survival curves between treated and untreated subjects in the matched sample were compared using a test described by Klein and Moeschberger.[6,19]

R version 3.1.0 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis.

RESULTS

The study population consisted of 4195 patients undergoing CABG using SIMA (n = 3445; 78.3%) or BIMA (n = 750; 21.7%). In the BIMA group, the right internal mammary artery was used as in situ graft to the LAD in 456 cases. Among those, the left internal mammary artery was used as in situ graft to the circumflex territory. A total of 165 patients had the right internal mammary artery grafted as in situ conduit to the circumflex territory through the transverse sinus. The right internal mammary artery was used as Y graft to the circumflex territory in 90 cases and as free graft to the right coronary artery in 39 cases. In the BIMA group, BIMAs were harvested as pedicled conduits in 299 out of 750 patients (40%) and as skeletonized conduits in the remaining 451 out of 750 patients (60%). In the SIMA group, skeletonized technique was used in 1293 out of 3445 patients (37.5%).

Missing Data

The fraction missing ranged from 0% (age) to 0.8% (body mass index). Pattern of missingness in the data were 44 and rows after listwise deletion were 3977. Rows after imputation were 4195.