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Cardiac Surgery

Long-Term Survival Following Coronary Artery Bypass Grafting

Off-Pump Versus On-Pump Strategies

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Objectives This study sought to compare long-term survival after off- and on-pump coronary artery bypass grafting (CABG).

Background Although several large-scale clinical trials have compared the surgical outcomes between off- and on-pump CABG, the long-term survival has not been compared between the 2 surgical strategies in a reasonably sized cohort.

Methods We evaluated long-term survival data in 5,203 patients (age 62.9 ± 9.1 years, 1,340 females) who underwent elective isolated CABG (off-pump: n = 2,333; on-pump: n = 2,870) from 1989 through 2012. Vital statuses were validated using the Korean National Registry of Vital Statistics. Long-term survival was compared with the use of propensity scores and inverse probability weighting to adjust selection bias.

Results Patients undergoing on-pump CABG had a higher number of distal anastomoses than those undergoing off-pump CABG (3.7 ± 1.2 vs. 3.0 ± 1.1; $p < 0.001$). Survival data were complete in 5,167 patients (99.3%), with a median follow-up duration of 6.4 years (interquartile range: 3.7 to 10.5 years; maximum 23.1 years). During follow-up, 1,181 patients (22.7%) died. After adjustment, both groups of patients showed a similar risk of death at 30 days (odds ratio: 0.70; 95% confidence interval [CI]: 0.35 to 1.40; $p = 0.31$) and up to 1 year (hazard ratio [HR]: 1.11; 95% CI: 0.74 to 1.65; $p = 0.62$). For overall mortality, however, patients undergoing off-pump CABG were at a significantly higher risk of death (HR: 1.43; 95% CI: 1.19 to 1.71; $p < 0.0001$) compared with those undergoing on-pump CABG. In subgroup analyses, on-pump CABG conferred survival benefits in most demographic, clinical, and anatomic subgroups compared with off-pump CABG.

Conclusions In patients undergoing elective isolated CABG, on-pump strategy conferred a long-term survival advantage compared with off-pump strategy. (J Am Coll Cardiol 2014;63:2280–8) © 2014 by the American College of Cardiology Foundation

After the revival of the off-pump technique for coronary artery bypass grafting (CABG) in the early 1990s, a number of observational studies had shown the potential benefits of off-pump CABG over on-pump surgery. These benefits included superior neurocognitive outcomes, preservation of renal function, and reduction in surgical bleeding and transfusion-related complications (1–5). The enthusiasm for off-pump technique consequently followed, especially in eastern Asian countries: more than 60% of CABG is being conducted with the off-pump technique in South Korea and in Japan (6,7).

Recently, large-scale, prospective randomized trials have been conducted that showed trends toward reduced risks of early surgical complications with off-pump CABG, but these early benefits failed to prove to be significant in longer-term follow-up (8–10). Moreover, off-pump CABG had shown worse outcomes in terms of graft patency and the requirement for coronary reintervention compared with conventional on-pump CABG up to 1 year after surgery (10,11). To date, results of randomized trials are limited to within 1 year of surgery; therefore, the long-term comparative data regarding clinical outcomes between the 2 strategies are currently unavailable. Considering that the benefits of CABG most likely appear throughout a long-term period, the 2 operative strategies for CABG need to be compared using long-term follow-up data in a reasonably sized cohort to allow adequate statistical power.

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In this study, we sought to compare long-term survival after off- and on-pump CABG under adequate statistical risk adjustments through a large institutional database linked with the National Population Registry of the Korea National Statistical Office.

Methods

Patients. All patients undergoing cardiac surgery are prospectively registered in our institution's database, which records baseline patient characteristics, detailed information on surgery, and perioperative outcomes (12). A total of 6,658 patients who underwent CABG between April 1989 and April 2012 were identified, and of them, we excluded patients who underwent concomitant valvular or aortic surgery (n = 1,123) and those who had emergent or urgent surgeries (n = 332), thus including patients who underwent isolated elective CABG only. Finally, 5,203 patients who met the enrollment criteria formed the study population; of these, 2,333 patients (44.8%) underwent off-pump CABG whereas 2,570 (55.2%) underwent on-pump CABG. Patients who were initially intended to undergo off-pump CABG but were converted to on-pump CABG intraoperatively (n = 46, 0.9% of all patients, 2% of off-pump patients) were regarded as having underwent off-pump CABG for the purposes of the intension-to-treat analyses.

The decision to perform off- or on-pump CABG was influenced by several demographic (diabetes, renal function) and clinical (coronary lesion category, cardiac functions) risk profiles and years of surgery, but was finally at the discretion of the attending surgeon; the authors of this study had different attitudes regarding the use of cardiopulmonary bypass (CPB) during CABG.

This study was approved by our institutional Ethics Committee/Review Board, and the board waived the requirement for informed patient consent due to the retrospective nature of the study.

Surgical procedures and medication. Most patients (96.6%) were operated on through a median sternotomy, whereas some of the patients receiving single- or double-vessel off-pump CABG (n = 177, 3.4%) were operated on through mini-thoracotomy approaches. Internal thoracic arteries (ITAs) were dissected in either a pedicled or skeletonized fashion according to the surgeon preferences. All saphenous grafts were harvested by the open technique. The pedicled radial artery was harvested with the use of a harmonic scalpel or electrocautery in an open fashion. To prevent arterial graft spasm after harvesting, a vasodilatory cocktail was applied topically and injected intraluminally. In cases of on-pump CABG, intermittent, antegrade blood cardioplegic infusion (22°C to 32°C) was the principal strategy for myocardial protection during aortic cross clamping. The left ITA was used to bypass the left anterior descending artery whenever possible. Choices of conduits and their configurations for other coronary territories were determined on the basis of conduit availability, number of distal targets, the target territory (right coronary vs. left circumflex territories), and the surgeon's preference.

Statin medications and aspirin were routinely prescribed to all of the patients starting from postoperative day 1 or 2 and were continued indefinitely, if not contraindicated, through the 6-month interval outpatient clinic visits. The dose of statin medication was adjusted for a target low-density lipoprotein level of <100 mg/dl.

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CI = confidence interval
CPB = cardiopulmonary bypass
HR = hazard ratio
IPTW = inverse-probability-of-treatment weighting
ITA = internal thoracic artery
LV = left ventricular

Study endpoints. The primary endpoint was defined as all-cause mortality, because it is the most robust and unbiased index, requiring no adjudication to avoid inaccurate or biased documentation and clinical assessments (13). For validation of complete follow-up data regarding mortality, information about vital status was obtained through November 30, 2012, from the National Population Registry of the Korea National Statistical Office through the use of a unique personal identification number.

Statistical analysis. Categorical variables, presented as frequencies and percentages, were compared using the chi-square or Fisher exact test. Continuous variables, expressed as mean ± SD or median with range, were compared using the Student unpaired *t* test or the Mann-Whitney *U* test, as appropriate. Survival curves were constructed using Kaplan-Meier estimates and compared with the log-rank test.

To reduce the effect of treatment selection bias and potential confounding, we adjusted for differences in baseline characteristics by weighted Cox proportional-hazards regression models with inverse-probability-of-treatment weighting (IPTW) (14,15). With that technique, weights for patients receiving off-pump CABG were the inverse of the propensity score, and weights for patients receiving on-pump CABG were the inverse of 1 − propensity score. The propensity score is the probability given baseline variables that any patient in either group would be selected for receiving off-pump CABG. The propensity scores were estimated without regard to outcomes by multiple logistic regression analysis. A full nonparsimonious model was developed that included variables shown in Table 1. Model discrimination was assessed with C-statistics (C = 0.869), and model calibration was assessed with Hosmer-Lemeshow statistics (p = 0.497). The results of IPTW were verified by those of propensity score matching. The propensity score–matched pairs were created by matching between off- and on-pump CABG subjects on the logit of the propensity score using calipers of width equal to 0.2 of the SD of the logit of the propensity score (16). After propensity score matching, we examined the similarity of off- and on-pump CABG subjects in the propensity score–matched sample by calculating SDs for each of the baseline variables listed in

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