The prognostic impact of concomitant coronary artery bypass grafting during aortic valve surgery: Implications for revascularization in the transcatheter era

Nassir M. Thalji, MBChB,[a] Rakesh M. Suri, MD, DPhil,[a] Richard C. Daly, MD,[a] Kevin L. Greason, MD,[a] Joseph A. Dearani, MD,[a] John M. Stulak, MD,[a] Lyle D. Joyce, MD,[a] Harold M. Burkhart, MD,[a] Alberto Pochettino, MD,[a] Zhuo Li, MSc,[b] Robert L. Frye, MD,[c] and Hartzell V. Schaff, MD[a]

Objective: Clinicians may give greater consideration to medical management versus coronary artery bypass grafting (CABG) for coronary artery disease (CAD) at the time of aortic valve intervention. We evaluated the prognostic impact of revascularization strategy during aortic valve replacement (AVR).

Methods: We studied 1308 consecutive patients with significant CAD (≥50% stenosis) undergoing AVR with or with out CABG between 2001 and 2010. Late mortality and its determinants were analyzed using multivariable Cox models.

Results: Patients undergoing CABG (n = 1043; 18%) had more frequent angina (50% vs 26%; $P < .001$), left ventricular dysfunction (22% vs 14%; $P = .003$), advanced (>70% stenosis) CAD (85% vs 48%; $P < .001$), and incidence of triple-vessel/left-main CAD (44% vs 8%; $P < .001$). Whereas operative mortality was comparable between patients undergoing AVR plus CABG versus isolated AVR (2.9% vs 3.0%; $P = .90$), 5-year (72% vs 64%) and 8-year (50% vs 39%) survival was higher following CABG ($P = .007$). Adjusting for older age (hazard ratio [HR], 1.28 per 5 years), female sex (HR, 1.23), peripheral vascular disease (HR, 1.71), New York Heart Association functional class III to IV (HR, 1.48), and diabetes (HR, 1.50) concomitant CABG at AVR reduced late mortality risk by more than one-third (HR, 0.62, 95% confidence interval, 0.49-0.79; $P < .001$). CABG continued to confer a survival advantage in patients with moderate (50%-70%) (HR, 0.62; $P = .02$) and severe (>70%) CAD (HR, 0.62; $P = .002$).

Conclusions: In patients undergoing AVR with coexistent CAD, concomitant CABG reduces risk of late death by more than one-third, without augmenting operative mortality. This survival advantage persists in moderate (50% to 70%) and severe (>70%) CAD. These findings underline the prognostic importance of revascularization in this population and should influence decisions regarding revascularization strategy in patients undergoing transcatheter valve therapy. (J Thorac Cardiovasc Surg 2015;149:451-60)

See related commentary on pages 460-1.

Supplemental material is available online.

Coronary artery disease (CAD) is identified in almost half of patients undergoing aortic valve replacement (AVR),[1,2] and—if left unmanaged—may negatively impact early and late postoperative outcomes.[3,4] Previous iterations of the American Heart Association/American College of Cardiology (AHA/ACC) guidelines considered coronary artery bypass grafting (CABG) indicated (class I) for "significant" CAD (>70% stenosis) at time of aortic valve replacement (AVR), and reasonable (class IIa) in patients with "moderate" CAD (50%-70% stenosis)

From the Division of Cardiovascular Surgery,[a] Department of Biomedical Statistics and Informatics,[b] and Division of Cardiovascular Diseases,[c] Mayo Clinic, Rochester, Minn.

Supported by the Division of Cardiovascular Surgery of the Mayo Clinic.

Disclosures: The Division of Cardiovascular Surgery at the Mayo Clinic has research relationships with Edwards Life sciences, Medtronic, and St Jude Medical. Rakesh M. Suri is the national principal investigator for the Food and Drug Administration trial of the Sorin Perceval valve, a member of the steering committee of the St Jude Portico trial, a member of the clinical selection committee for the Abbott Coapt trial, and site principal investigator for the Edwards Partner II trial. Richard C. Daly serves on the advisory board of Neochord, Inc. None of the disclosures pertain to the current investigation. The other authors have nothing to disclose with regard to commercial support.

Read at the 94th Annual Meeting of The American Association for Thoracic Surgery, Toronto, Ontario, Canada, April 26-30, 2014.

Received for publication April 28, 2014; revisions received Aug 17, 2014; accepted for publication Aug 20, 2014.; available ahead of print Oct 11, 2014.

Address for reprints: Rakesh M. Suri, MD, DPhil, Division of Cardiovascular Surgery, Mayo Clinic College of Medicine; 200 First St, SW, Rochester, MN 55905 (E-mail: suri.rakesh@mayo.edu).

0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2014.08.073

Abbreviations and Acronyms

ACC	= American College of Cardiology
AHA	= American Heart Association
AS	= aortic stenosis
AVR	= aortic valve replacement
CABG	= coronary artery bypass grafting
CAD	= coronary artery disease
LAD	= left anterior descending
LCX	= left circumflex
NYHA	= New York Heart Association
RCA	= right coronary artery

(level of evidence: C).[5] Recently updated recommendations have reclassified CABG at time of AVR for >70% stenosis from a class I to a class IIa indication, whereas altogether deemphasizing the role of coronary revascularization in those with 50% to 70% stenosis.[6] Recent randomized trials in patients with stable CAD have not demonstrated an advantage for revascularization over medical management in minimizing risk of myocardial infarction or death, except in patients with the most extensive (ie, triple-vessel) CAD. Considered alongside the revised guidelines for management of aortic valve disease, this may lead to the proposal that patients with less extensive and/or less severe CAD may be best served by conservative coronary management at AVR.[7,8]

The optimal management of CAD at the time of valve intervention has been met with further uncertainty in light of the growing availability of minimally invasive and transcatheter platforms for AVR. Specifically, clinicians may give greater consideration to medical therapy versus CABG for the management of underlying CAD at aortic valve intervention. We therefore evaluated patients undergoing surgical AVR with or without CABG, all of whom had diagnoses of coexistent aortic stenosis (AS) and CAD at index surgery. We sought to determine the survival effect of the decision to perform concomitant CABG at the time of AVR, in contemporary practice and in patients with various distributions and severities of CAD, testing the null hypothesis that the addition of CABG is prognostically neutral.

METHODS

Study Subjects

We evaluated all patients older than age 18 years who underwent surgical AVR for AS with or without concomitant CABG, between January 1, 2001, and December 31, 2010, and in whom there was evidence of significant CAD on preoperative coronary angiography. Exclusion criteria were prior sternotomy, active endocarditis, at least moderate aortic insufficiency, and concomitant major procedures other than CABG (ie, thoracic aortic surgery and mitral valve repair). A total of 1308 patients met enrollment criteria and were divided into 2 groups according to whether concomitant CABG was performed at the time of AVR (n = 1043 CABG vs n = 265 no CABG). Enrollment was limited to patients operated on up to December 31, 2010, to allow the opportunity for at least 3 years of follow-up in all patients, thus permitting us to more definitively comment upon the impact of concomitant CABG at AVR on long-term patient prognosis. The Mayo Clinic Institutional Review Board approved our study. Valid informed consent was obtained for all patients.

Clinical Data

Patient demographics, symptoms, medical/surgical history, cardiac status, and perioperative outcomes were derived from the Division of Cardiovascular Surgery database, and by review of medical records. Echocardiographic data was abstracted from the Division of Cardiovascular Diseases echocardiography database. Variable definitions were in accordance with criteria set forth by the Society of Thoracic Surgeons national database. Follow-up data were obtained from review of medical records, postal questionnaires, electronic Accurint database (www.Accurint.com), and death certificates. The primary end point was late all-cause mortality.

Coronary Angiograms and Coronary Artery Disease

Preoperative coronary angiograms within 6 months of surgery were available from the Division of Cardiovascular Disease Catheterization database and by review of medical records. CAD burden was evaluated according to percent luminal stenosis documented at the time of angiography. In keeping with ACC/AHA guidelines, significant CAD was defined as ≥50% luminal stenosis of any major epicardial coronary vessels, including side branches.[5] In subset analyses, severe CAD was considered >70% stenosis in at least 1 coronary vessel/branch, and moderate CAD defined as no more than 50% to 70% stenosis in any coronary vessel/branch. Proximal CAD was defined as ≥50% stenosis in the left main artery or the proximal one-third of the left anterior descending (LAD) artery, left circumflex (LCX) artery, or right coronary artery (RCA). All other coronary lesions were considered nonproximal disease.

Statistical Analysis

Continuous variables were summarized by means ± standard deviation or medians and interquartile range and compared between groups using the Student t test or Wilcoxon rank-sum test where appropriate. Categorical variables were summarized as counts and percentages and compared using the χ^2 test or Fisher exact test where appropriate.

Long-term follow-up was calculated from time of surgery to death or last follow-up. Survival was estimated by Kaplan-Meier methods with patients censored at last known follow-up. The log-rank test compared overall survival between patients undergoing isolated AVR versus AVR with CABG. To examine the effect of performing CABG in managing various degrees and distributions of CAD at AVR, further survival curves were generated after stratifying patients into groups of moderate or severe CAD; proximal or nonproximal CAD; single-vessel, double-vessel, or triple-vessel/left main CAD; and among patients with single-vessel disease, LAD, LCX, or RCA disease.

Univariate and multivariate Cox proportional hazards models were used to identify predictors of late all-cause mortality in all patients. Parameters considered for selection were determined a priori and included age, female sex, New York Heart Association (NYHA) functional class III to IV, family history of CAD, smoking history, obesity (ie, body mass index ≥ 30), history of cerebrovascular accident, diabetes, hypercholesterolemia, hypertension, prior myocardial infarction, peripheral vascular disease, previous percutaneous coronary intervention, ejection fraction <50%, aortic valve area, mean aortic valve gradient, percent coronary stenosis (ie, 50% to 70% or >70%), distribution of CAD (ie, single-vessel, double-vessel, or triple-vessel/left main CAD), proximity of CAD (ie, proximal or nonproximal), surgical era (ie, 2001-2004, 2005-2007, or 2008-2010), surgical status (ie, elective or urgent/emergent), and