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Impact of Classic and Paradoxical Low Flow on Survival After Aortic Valve Replacement for Severe Aortic Stenosis

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ABSTRACT

BACKGROUND Low flow (LF) can occur with reduced (classic) or preserved (paradoxical) left ventricular ejection fraction (LVEF).

OBJECTIVES The objective of this study was to compare outcomes of patients with low ejection fraction (LEF), paradoxical low flow (PLF), and normal flow (NF) after aortic valve replacement (AVR).

METHODS We examined 1,154 patients with severe aortic stenosis (AS) who underwent AVR with or without coronary artery bypass grafting.

RESULTS Among these patients, 206 (18%) had LEF as defined by LVEF of <50%; 319 (28%) had PLF as defined by LVEF of ≥50% but stroke volume indexed to body surface area (SVi) of ≤35 ml · m^{-2}; and 629 (54%) had NF, as defined by LVEF of ≥50% and SVi of >35 ml · m^2. Aortic valve area was lower in low flow/LVEF groups (LEF: 0.71 ± 0.20 cm^2 and PLF: 0.65 ± 0.23 cm^2 vs. NF: 0.77 ± 0.18 cm^2; $p < 0.001$). The 30-day mortality was higher ($p < 0.001$) in LEF and PLF groups than in the NF group (6.3% and 6.3% vs. 1.8%, respectively). SVi and PLF group were independent predictors of operative mortality (odds ratio [OR]: 1.18, $p < 0.05$; and OR: 2.97, $p = 0.004$; respectively). At 5 years after AVR, overall survival was 72 ± 4% in LEF group, 81 ± 2% in PLF group, and 85 ± 2% in NF group ($p < 0.0001$).

CONCLUSIONS Patients with LEF or PLF AS have a higher operative risk, but pre-operative risk score accounted only for LEF and lower LVEF. Patients with LEF had the worst survival outcome, whereas patients with PLF and normal flow had similar survival rates after AVR. As a major predictor of perioperative mortality, SVi should be integrated in AS patients' pre-operative evaluation. (J Am Coll Cardiol 2015;65:645–53) © 2015 by the American College of Cardiology Foundation.

Low flow in aortic stenosis (AS) can occur with reduced or preserved left ventricular ejection fraction (LVEF), which are named classic and paradoxical low flow, respectively. Because the transvalvular pressure gradient is highly flow dependent, these clinical conditions are often associated with low gradient, which adds complexity to the assessment of stenosis severity and therapeutic decision making. According to current American College of Cardiology/American Heart Association (ACC/AHA) guidelines (1), aortic valve replacement (AVR) should be considered (Class I or IIa) in symptomatic patients with low ejection fraction (LEF) or paradoxical low flow (PLF), low-gradient AS, if the presence of severe stenosis can be confirmed. Low flow, as documented by reduced stroke volume index (SVi), has been shown to be an independent predictor of mortality following transcatheter aortic valve replacement, regardless of LVEF (2,3), but little is known about the impact of flow status after surgical AVR (4–6). Thus, the primary objective of this study was to compare the outcomes of patients with LEF, PLF, and normal flow (NF) after AVR. The secondary objective was to

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ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

AVR = aortic valve replacement

CABG = coronary artery bypass graft

LEF = low ejection fraction

LV = left ventricular

LVEF = left ventricular ejection fraction

NF = normal flow

NYHA = New York Heart Association

PLF = paradoxical low flow

SVi = stroke volume index

compare perioperative outcomes among patients with LEF, PLF, and NF AS.

METHODS

STUDY POPULATION. Among 1,984 consecutive patients who underwent AVR with or without coronary artery bypass graft (CABG) as their first open-heart surgery in our institution between 2002 and 2010, we included 1,154 patients with calcific severe AS (as defined by a mean gradient ≥40 mm Hg, a peak aortic jet velocity ≥4 m · s^{1}, an aortic valve area ≤1.0 cm^2, or an indexed aortic valve area ≤0.6 cm^2 · m^{-2}) (Figure 1). Data were prospectively collected and stored in an electronic database.

SEE PAGE 654

Patients for whom primary indication for AVR was aortic insufficiency or CABG and patients with an incomplete echocardiographic evaluation in the 3 months before AVR were excluded.

ECHOCARDIOGRAPHY. Doppler echocardiographic measurements included LV dimensions according to recommendations of the American Society of Echocardiography: LVEF calculated by the biplane Simpson method, the peak aortic jet velocity, the peak and mean transvalvular pressure gradients obtained with the use of the modified Bernoulli equation, and the aortic valve area obtained with the use of the standard continuity equation (7). Doppler echocardiographic measurement of LV outflow tract stroke volume was corroborated by the 2-dimensional (2D) volumetric method.

Our population was divided into 3 groups depending on the values of LVEF and SVi: the NF group, defined as LVEF ≥50% and SVi >35 ml · m^{-2}; the PLF group, defined as LVEF ≥50% and SVi ≤35 ml · m^{-2}; and the LEF group, defined as LVEF <50%.

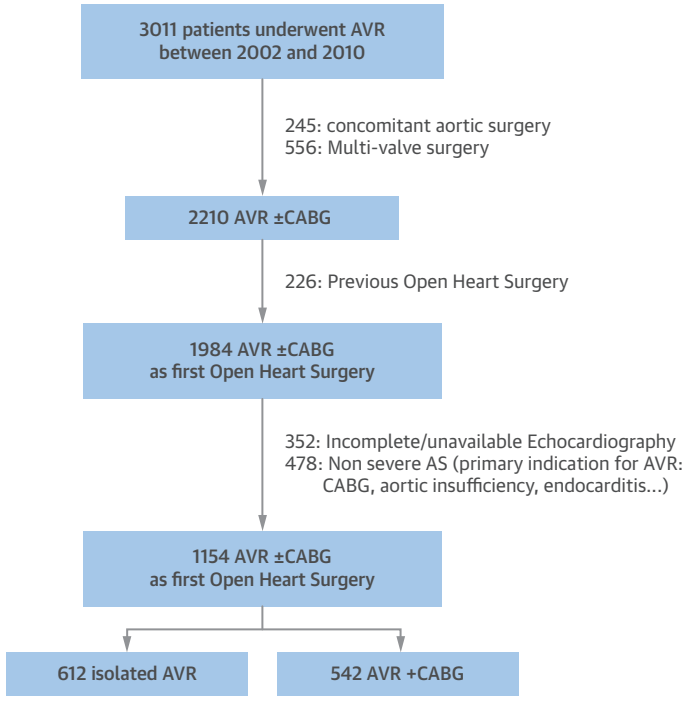
CORONARY ANGIOGRAPHY. All patients underwent coronary angiography as part of the pre-operative evaluation. The severity of coronary artery disease was assessed by angiographic Duke myocardial jeopardy score, which expresses how many of the 6 coronary arterial segments are jeopardized by significant (>70% estimated luminal area reduction) stenoses (8). Two points are added to the score for each jeopardized segment.

STUDY ENDPOINTS. Primary endpoints for this study were 30-day mortality and long-term mortality. Secondary endpoints were: 1) perioperative major cardiovascular nonfatal events consisting of atrial fibrillation/flutter, ventricular tachycardia/fibrillation, cardiac arrest, low output syndrome, acute cardiac failure, intra-aortic balloon pump application, multiorgan failure and ischemic event; 2) perioperative noncardiac, nonfatal events consisting of respiratory intubation (intubation time period longer than 48 h and reintubation), renal (hemodialysis/filtration and increase in blood level rate of creatinine higher than 100 μmol · l^{-1}), and neurological (stroke and transient ischemic accident) events; 3) length of time of vasotrope/inotrope use; 4) intensive care unit length of stay; and 5) hospital length of stay.

Perioperative events and deaths were prospectively collected. Late mortality data were retrospectively obtained from Quebec Institute of Statistics. To maximize the interrogation of the central Quebec Institute of Statistics database, a list with multiple demographics (including first and last names, dates of birth, and social security numbers) and a delay of 1 year between interrogation and closing follow-up dates were used.

STATISTICAL ANALYSIS. Results are mean ± SD or percentages. For continuous variables, differences between groups were analyzed with the use of 1-way ANOVA, followed by the Tukey post-hoc test for

FIGURE 1 Study Flow Chart



AVR = aortic valve replacement; AS = aortic stenosis; CABG = coronary artery bypass graft.