Early and 1-year outcomes of aortic root surgery in patients with Marfan syndrome: A prospective, multicenter, comparative study

Joseph S. Coselli, MD,[a] Irina V. Volguina, PhD,[a] Scott A. LeMaire, MD,[a] Thoralf M. Sundt, MD,[b] Heidi M. Connolly, MD,[c] Elizabeth H. Stephens, MD, PhD,[d] Hartzell V. Schaff, MD,[e] Dianna M. Milewicz, MD, PhD,[f] Luca A. Vricella, MD,[g] Harry C. Dietz, MD,[h] Charles G. Minard, PhD,[i] and D. Craig Miller, MD,[d] on behalf of the Aortic Valve Operative Outcomes in Marfan Patients Study Group

Objective: To compare the 1-year results after aortic valve-sparing (AVS) or valve-replacing (AVR) aortic root replacement from a prospective, international registry of 316 patients with Marfan syndrome (MFS).

Methods: Patients underwent AVS (n = 239, 76%) or AVR (n = 77, 24%) aortic root replacement at 19 participating centers from 2005 to 2010. One-year follow-up data were complete for 312 patients (99%), with imaging findings available for 293 (94%). The time-to-events were compared between groups using Kaplan-Meier curves and Cox proportional hazards models.

Results: Two patients (0.6%)—1 in each group—died within 30 days. No significant differences were found in early major adverse valve-related events (MAVRE; $P = .6$). Two AVS patients required early reoperation for coronary artery complications. The 1-year survival rates were similar in the AVR (97%) and AVS (98%) groups; the procedure type was not significantly associated with any valve-related events. At 1 year and beyond, aortic regurgitation of at least moderate severity (≥2+) was present in 16 patients in the AVS group (7%) but in no patients in the AVR group ($P = .02$). One AVS patient required late AVR.

Conclusions: AVS aortic root replacement was not associated with greater 30-day mortality or morbidity rates than AVR root replacement. At 1 year, no differences were found in survival, valve-related morbidity, or MAVRE between the AVS and AVR groups. Of concern, 7% of AVS patients developed grade ≥2+ aortic regurgitation, emphasizing the importance of 5 to 10 years of follow-up to learn the long-term durability of AVS versus AVR root replacement in patients with MFS. (J Thorac Cardiovasc Surg 2014;147:1758-67)

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In patients with Marfan syndrome (MFS), cardiovascular complications have been the leading cause of mortality and morbidity, including dilatation and dissection of the aortic root and other segments of the thoracic aorta. If untreated, such complications can lead to life-threatening conditions, including aortic valve regurgitation, congestive heart failure, and aortic rupture.[1] The underlying cause of aortic disease involves impaired synthesis, secretion, and deposition of

From the Division of Cardiothoracic Surgery,[a] Michael E. DeBakey Department of Surgery, Baylor College of Medicine, and Department of Cardiovascular Surgery, Texas Heart Institute, Houston, Tex; Division of Cardiac Surgery,[b] Department of Surgery, Massachusetts General Hospital, Boston, Mass; Division of Cardiovascular Diseases,[c] Mayo Clinic, Rochester, Minn; Department of Cardiothoracic Surgery,[d] Stanford University School of Medicine, Stanford, Calif; Division of Cardiovascular Surgery,[e] Department of Surgery, Mayo Clinic, Rochester, Minn; Division of Medical Genetics,[f] Department of Internal Medicine, University of Texas Health Science Center at Houston, Houston, Tex; Division of Cardiac Surgery,[g] Department of Surgery, Johns Hopkins Hospital, Baltimore, Md; McKusick-Nathans Institute of Genetic Medicine and Department of Pediatrics,[h] Johns Hopkins University School of Medicine and Howard Hughes Medical Institute, Baltimore, Md; and Dan L. Duncan Institute for Clinical and Translational Research,[i] Baylor College of Medicine, Houston, Tex.

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Address for reprints: Irina V. Volguina, PhD, Division of Cardiothoracic Surgery, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, One Baylor Plaza, BCM 390, Houston, TX 77584 (E-mail: volguina@bcm.edu).

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Abbreviations and Acronyms

AR = aortic regurgitation
AVR = aortic valve-replacing
AVS = aortic valve-sparing
MAVRE = major adverse valve-related event
MFS = Marfan syndrome
NSVD = nonstructural valve dysfunction
NYHA = New York Heart Association
SVD = structural valve deterioration

the fibrillin-1 protein, resulting from various *FBN1* gene mutations. The aortic root is especially prone to dilatation and dissection.[2] By some estimates, about 80% of adult patients with MFS will have dilated aortic roots.[3]

Before the introduction of aortic valve and ascending aorta replacement by Bentall and DeBono[4] in 1968, followed by the advent of aortic valve-sparing (AVS) aortic root replacement (remodeling technique of Yacoub and colleagues[5] in 1979 and the reimplantation procedure of David and Feindel[6] in 1988), the life expectancy of most patients with MFS did not exceed 40 years.[7] Numerous modifications were subsequently introduced, including a recently developed computer-modeled custom external aortic root support device.[8] The hope was that lifelong anticoagulation (mandatory after an aortic valve-replacing [AVR] procedure using a mechanical valve) could be avoided if the valve were preserved[6,9]; however, the potential for valve deterioration and the need for reoperation was unknown. Although many single-center analyses have reported mid-term success after AVS root replacement using the David and Feindel reimplantation technique, the native valve durability remains unclear because of limited follow-up durations, retrospective designs, single-center reporting, and insufficient sample sizes. A recent meta-analysis by Benedetto and colleagues[10] provided more insight; however, the results were concerning in that patients with MFS had a substantially greater risk of reoperation after an AVS procedure than after an AVR procedure.

This first prospective, multicenter, international registry study—Aortic Valve Operative Outcomes in Marfan Patients—was initiated to provide contemporary data regarding the clinical outcomes of AVS versus AVR aortic root replacement. We report the 1-year results for 316 patients with MFS who were enrolled in this registry.

METHODS

Study Design and Patient Recruitment

Patient enrollment continued from March 2005 until November 2010, when the enrollment target of 316 patients was reached. The Data Coordinating Center with 4 Study Cores coordinated the efforts of the 19 participating study centers (see the "Acknowledgment" section). After the preliminary analysis,[11] the target sample size was increased from 250 to 316 patients to allow detection of a 2.3-fold difference between the AVR and AVS groups in the risk of valve-related complications.[12]

The enrolled patients had confirmed MFS, had undergone AVS or AVR aortic root replacement, and were available for follow-up. No limitations regarding age, gender, previous cardiovascular intervention, or surgery acuity were included. The type of surgical repair was dependent on the patient's clinical situation and surgeon and patient preference. Using the 1996 Ghent nosology,[13] the Marfan Diagnostic Core (Johns Hopkins) confirmed the MFS diagnosis clinically for all patients.

Each participating institution's institutional review board or ethics committee approved the study protocol. Each patient gave written informed consent. The protected health information was coded. The funding agencies outside of Baylor College of Medicine had no role in data interpretation.

Data Collection and Definitions

The data collection and definitions had been previously described in detail.[11] The clinical data were collected preoperatively, at discharge, and 6, 12, 24, and 36 months postoperatively. Echocardiograms were obtained at the same times if possible or whenever available otherwise and were analyzed by the Imaging Core (Mayo Clinic). When digital images were not available, the echocardiographic reports were substituted. The 1-year follow-up period extended from 274 to 457 postoperative days (12 ± 3 months). The AVS and AVR groups were formed according to the initial operation performed; the AVS procedures were classified according to the definitions suggested by Miller.[14]

Valve-related morbidity and mortality were initially defined according to the 1996 American Association for Thoracic Surgery and Society of Thoracic Surgeons guidelines.[15] Valve-related complications included structural valvular deterioration (SVD), nonstructural valve dysfunction (NSVD), valve thrombosis, embolism, and bleeding. The consequences of morbid events were defined as reoperation on the aortic valve, valve-related mortality, sudden unexplained death, cardiac death, death from any cause, and permanent valve-related impairment. The 2008 revision of the American Association for Thoracic Surgery, Society of Thoracic Surgeons, and European Association for Cardio-Thoracic Surgery valve-reporting guidelines[16] introduced an updated composite indicator to capture all types of valve-related events—major adverse valve-related events (MAVRE)—which we used as a primary endpoint. The MAVRE variable was defined as all-inclusive valve-related morbidity and mortality and the need for permanent pacemaker or defibrillator implantation within 14 days of valve intervention.

The patients were categorized as having SVD or NSVD if they had echocardiographic aortic regurgitation (AR) grade $\geq$2+ or a decline by $\geq$1 New York Heart Association (NYHA) functional class caused by impairment of the operated valve, pursuant to the 2008 guidelines.[16] (This method of categorization violated the guidelines in that AR grade 1+ was not considered NSVD; see the justification in the "Discussion" section). Conversion from AVS to AVR surgery or from 1 type of AVR to another during the same operation was considered to indicate NSVD. Bleeding was classified as a valve-related event if it occurred after hospital discharge and caused death, hospitalization, or permanent injury or necessitated transfusion, regardless of whether the patient was taking anticoagulant or antiplatelet drugs. Early postoperative bleeding events, such as mediastinal hemorrhage requiring re-exploration, were recorded separately and were not categorized as valve-related complications. The definitions of non–valve-related cardiac, pulmonary, and renal complications have been described previously.[11]

Patients and Operations

Of the 375 consecutively screened patients who had a tentative MFS diagnosis, needed aortic root replacement, and agreed to participate in the present study, 316 (84%) met the inclusion criteria and were enrolled at 19 participating centers (Table E1). The 59 excluded patients included 54 who did not meet the Ghent criteria and 5 who had undergone isolated valve replacement instead of root replacement. The types of aortic root