

# Long-Term Results of Aortic Valve Replacement with Edwards Prima Plus Stentless Bioprosthesis: Eleven Years' Follow Up

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**Background and aim of the study:** The Edwards Lifesciences Prima Plus stentless valve (ELSV) is a bioprosthesis manufactured from a porcine aortic root. The study aim was to evaluate late clinical outcomes after aortic valve replacement (AVR) with ELSV implanted as a miniroot in patients with aortic valve disease.

**Methods:** Between 1993 and 2004, 318 patients (232 males, 86 females; mean age  $69 \pm 9$  years; range: 37-83 years) underwent AVR with the ELSV. Pre-operatively, 102 patients (32%), 162 (51%) and 54 (17%) were in NYHA classes I/II, III and IV, respectively. Aortic stenosis, aortic regurgitation and combined lesions were present in 124 patients (39%), 114 (36%) and 41 (13%), respectively. Twenty patients (6%) were referred for an acute aortic dissection, 20 (6%) for an aortic root aneurysm, and 139 (44%) had an associated aneurysmal dilatation of the ascending aorta. The ascending aorta was replaced in 159

Stentless porcine aortic valve prostheses have been introduced in clinical practice in order to improve clinical outcomes following aortic valve replacement (AVR), on the basis of their better hemodynamic performance and durability. The Edwards Lifesciences Prima Plus stentless valve (ELSV) is a bioprosthesis which is constructed from a porcine aortic root and reinforced with Dacron fabric. The study aim was to describe early and late clinical outcomes after AVR with the ELSV.

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patients (50%); aortic arch replacement was required in 10 (3%). Coronary artery bypass graft was performed in 86 patients (27%). The follow up was based on clinical data.

**Results:** Operative mortality was 5% ( $n = 17$ ). There were 49 late deaths (5.2%/pt-yr). Valve-related mortality occurred in 10 patients (1%/pt-yr). Actuarial survival at five and 10 years was 78% and 33%, respectively. Actuarial freedom from valve reoperation and structural valve deterioration at 10 years were 100% and 64%. Actuarial freedom from embolic events and endocarditis at 10 years were 84% and 81%, respectively.

**Conclusion:** The ELSV, when implanted as a miniroot, provided good early and long-term results in terms of survival and freedom from major complications.

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## Clinical material and methods

### Patients

Between January 1993 and December 2004, a total of 318 patients underwent AVR with the ELSV at the Division of Cardiac Surgery of San Bortolo Hospital Vicenza, Italy. In all cases the ELSV was implanted using an inclusion cylinder or miniroot technique.

The selection criteria for implantation of an aortic xenograft were: (i) age  $>65$  years; (ii) a contraindication to oral anticoagulation therapy; and (iii) a deliberate request by the patient for a biological valve. The decisions to implant a stented or stentless valve, and which type of stentless bioprosthesis was to be implanted, were ultimately made by the surgeon in a non-randomized fashion. Associated valve or vascular lesions requiring concomitant intervention, reoperation and severity of left ventricular dysfunction were not considered contraindications to the use of a stentless valve.

Senile calcific degeneration represented the most common indication to surgery. The disease was generally severe, as evident from the average NYHA func-

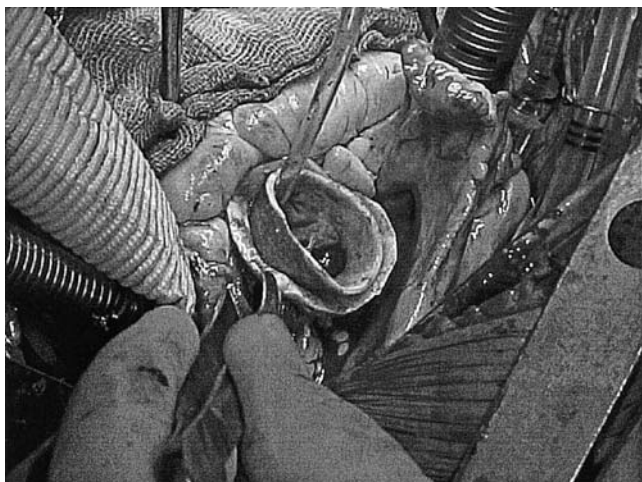


Figure 1: Aortic valve replacement with the ELSV. The prosthesis is implanted with the “miniroot” technique into the native aortic root, the right coronary ostium suture is completed, and the porcine aortic wall has been trimmed before the proximal vascular anastomosis.

tional class; associated lesions requiring associated procedures were present in over 40% of patients. The most common associated lesion was ascending aorta dilatation, which affected 139 patients (44%). The main preoperative clinical features of patients are summarized in Table I.

### Surgical technique and medical management

The ELSV was implanted using the miniroot (inclusion cylinder) technique, as described previously (1,2). The mean cardiopulmonary bypass and cross-clamp times for isolated AVR were  $92 \pm 10$  min and  $60 \pm 10$  min, respectively.

In case of an associated replacement of the ascending aorta, valve inflow rim and coronary ostia sutures were performed first and the proximal vascular anastomosis was performed, after an appropriate trimming, including both patient’s ascending aorta and porcine aortic wall (Fig. 1)

Oral anticoagulation therapy was generally commenced on the first postoperative day, and stopped after two months. Antiplatelet agents were then administered only to patients with associated carotid or coronary artery lesions.

### Follow up

Direct patient follow up clinical assessments were planned at six and 12 months after surgery, and subsequently at 12-month intervals. Patients unable to attend the outpatient clinic were followed up by telephone interview. During each follow up visit, information on the patients’ clinical status was obtained, together with data regarding postoperative complications. The follow up was 100% complete.

### Statistical analysis

Continuous variables were expressed as mean  $\pm$  SD, and categorical variables as percentages. Time-related events were described using Kaplan-Meier survival curves.

## Results

### Operative data

Operations were performed by three surgeons at the authors’ institution. The operative data are summarized in Table II.

### Survival

The mean follow up period was  $35 \pm 30$  months (range: 0 to 143 months). Seventeen perioperative deaths (5%) occurred less than 30 days after surgery. There were 49 late deaths (5.2% per patient-year (pt-yr)). The causes of all deaths are listed in Table III. Actuarial survival at five and 10 years was 78% and 33%, respectively (Fig. 2).

### Late deaths

Valve-related mortality occurred in 10 patients (1%/pt-yr). Actuarial freedom from valve-related mortality at five and 10 years was 94% and 76%, respectively (Fig. 3).

### Non-fatal valve-related events

#### Structural valve deterioration

Structural valve deterioration (SVD) was diagnosed in four patients (0.4%/pt-yr). Two of these patients

Table I: Preoperative patient profile (n = 318).

Parameter	Value
Age (years)*	69 $\pm$ 9 (37-83)
Gender ratio (M:F)	232:86
BSA (m <sup>2</sup> )*	1.74 $\pm$ 0.20 (1.4-2.3)
NYHA class*	2.9 $\pm$ 0.6 (2-4)
I	0 (0)
II	102 (32)
III	162 (51)
IV	54 (17)
Aortic stenosis	124 (39)
Aortic regurgitation	114 (36)
Mixed aortic lesion	41 (13)
Type A dissection	20 (6)
Aortic root aneurysm	20 (6)
Ascending aorta dilatation	139 (44)
CAD	86 (27)
Emergency procedures	20 (6)

\*Values are mean  $\pm$  SD (range).

Values in parentheses are percentages.

BSA: Body surface area; CAD: Coronary artery disease.

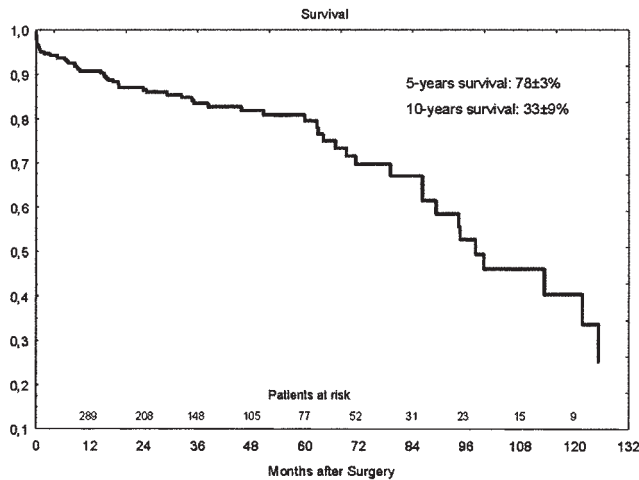


Figure 2: Actuarial patient survival.

died before reoperation, the diagnosis being made at autopsy, where one leaflet tear and one leaflet prolapse were found. The other two patients underwent clinical and echocardiographic assessment which showed primary valve failure with significant regurgitation and increased NYHA class. These two patients are currently awaiting reoperation. The actuarial freedom from SVD was 100% at five years and 64% at 10 years after surgery (Fig. 4). No signs of calcific degeneration were noted in any patient.

#### Valve reoperation

No reoperations were performed during the follow up period.

#### Embolic events

Thromboembolic events occurred in nine patients (1%/pt-yr); these included six neuroembolic events and three peripheral embolic events. Actuarial freedom from thromboembolism at 10 years was 84% (Fig. 5).

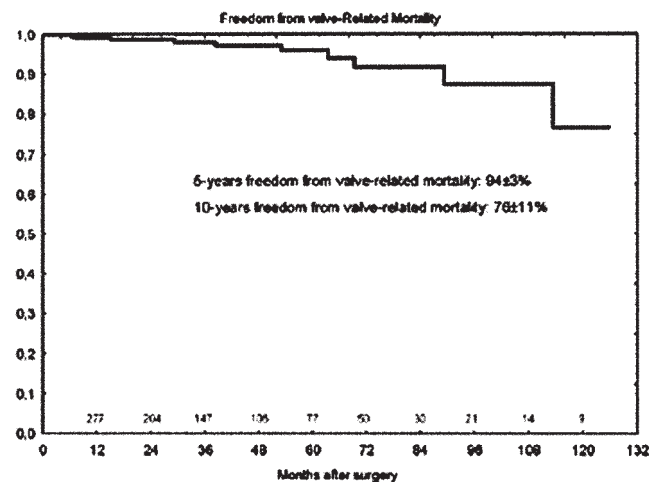


Figure 3: Freedom from valve-related mortality.

Table II: Operative variables of patients.

Parameter	Value
Stentless valve (n)	
21 mm	14
23 mm	106
25 mm	88
27 mm	82
29 mm	28
Aortic cross-clamp time (min)*	
AVR alone	60 ± 10 (50-120)
AVR + AAR	98 ± 25 (73-182)
AVR + AAR + CABG	122 ± 16 (106-187)
AVR + AAR + ARCH	136 ± 15 (120-191)
Cardiopulmonary bypass time (min)*	
AVR alone	92 ± 10 (70-110)
AVR + AAR	212 ± 94 (132-256)
AVR + AAR + CABG	245 ± 98 (167-356)
AVR + AAR + ARCH	240 ± 105 (123-389)
Associated procedures	
CABG	86 (27)
Mitral valve replacement/repair	13 (4)
Ascending aorta replacement	159 (50)
Aortic arch replacement	10 (3)
CABG + mitral valve operation	3 (0.9)

\*Values are mean ± SD (range).

Values in parentheses are percentages.

AAR: Ascending aorta replacement; ARCH: Aortic arch replacement; AVR: Aortic valve replacement; CABG: Coronary artery bypass grafting.

Table III: Causes of death.

Cause of death	Patients (n)
<i>Early deaths</i>	
Acute myocardial infarction	2 (11)
Multiple organ failure	5 (29)
Sepsis	1 (6)
Pulmonary insufficiency	3 (18)
Splanchnic infarction	3 (18)
Stroke	3 (18)
<i>Late deaths</i>	
Valve-related	10 (20)
SVD (degenerative calcification)	2 (4)
Prosthesis thrombosis	1 (2)
Hemorrhage	4 (8)
Endocarditis	3 (6)
Cardiac-related	11 (22)
Congestive heart failure	4 (8)
Myocardial infarction	5 (10)
Sudden arrhythmia	2 (4)
Non-cardiac	19 (39)
Unknown	9 (19)

Values in parentheses are percentages of all deaths.

SVD: Structural valve deterioration.

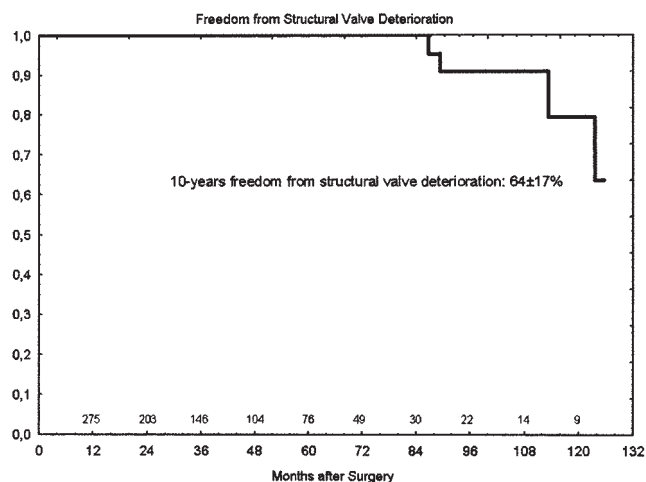


Figure 4: Freedom from structural valve deterioration.

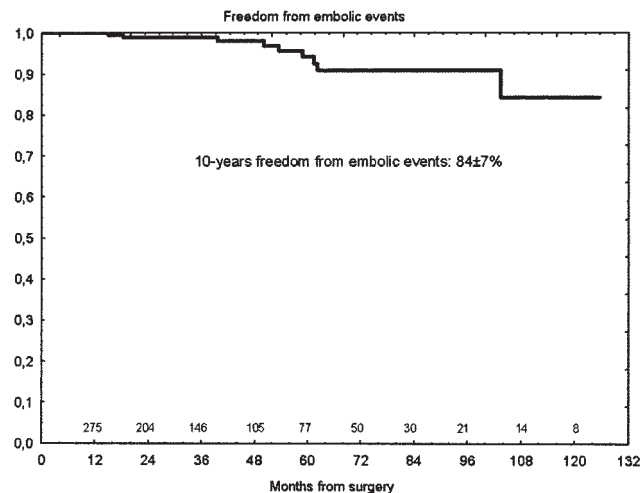


Figure 5: Freedom from embolic events.

### Endocarditis

Bacterial endocarditis occurred in six patients (0.6%/pt-yr). There were three deaths from bacterial endocarditis before reoperation, and no reoperations. Actuarial freedom from bacterial endocarditis at 10 years was 81%.

### Late NYHA classification

A significant clinical improvement was observed in all survivors, with 95% currently in NYHA functional class I.

## Discussion

Although stentless aortic xenografts were introduced into clinical practice over a decade ago, the use of a stentless bioprosthesis for AVR was first reported by Binet and colleagues (3) during the 1960s. The observation that freehand aortic homografts showed longer durability than stent-mounted homografts (4) stimulated the revival of stentless porcine xenografts (5,6). Renewed interest in stentless xenografts was also stimulated by David et al. (7), who demonstrated an improved hemodynamic performance when compared to stented valves. In theory, the absence of a stent, thereby reducing mechanical stress on the leaflets and distributing it uniformly to the aortic wall, should lead to better valve durability.

Nevertheless, stentless bioprostheses have shown extreme versatility when used in a number of complex clinical settings, including small aortic annulus, ascending aorta aneurysm, aortic root disease, endocarditis with annular abscess, and left ventricular dysfunction (8).

The management of aortic root and ascending aorta dilatation in patients with aortic valve disease represents a therapeutic challenge, and many surgeons con-

sider this pathology as an exclusion criterion for stentless bioprosthesis implantation (9).

The ELSV, when implanted as a miniroot, has the advantage of treating aortic valve and aortic root disease simultaneously. This valve has been available for clinical use since 1991 (10), the present authors having used it only for isolated AVR with the miniroot (inclusion cylinder) technique. This limitation was due to early concerns about the hemodynamic performance of the device when implanted in the subcoronary position, as high transaortic gradients were recorded shortly after surgery. It appears that these hemodynamic findings may at least in part be explained by the peculiar anatomic characteristics of the porcine aortic root, which has a right coronary ostium that is higher than the human counterpart for the presence of a muscle shelf. When suturing the inferior rim of the prosthetic right coronary ostium below the patient's right coronary ostium, the polyester fabric is able to bend inward, creating a fixed obstacle in the left ventricular outflow tract at the valvular level. Implanting an excessively large prosthesis may potentiate this effect. Bortolotti et al. reported two patients in whom the ELSV was explanted intraoperatively for this reason (11), while Westaby et al. (12) described a similar mechanism with the Medtronic Freestyle stentless valve. In order to overcome this complication, alternative implantation techniques have been proposed, such as clockwise rotation of the prosthesis so that the polyester cloth corresponds to the non-coronary sinus, its use as a complete root replacement, or as a miniroot implantation. In the present authors' experience, the miniroot implantation method was safe, reproducible and effective, and not influenced by any variability of the aortic root diameter. Furthermore, this technique does not significantly increase operative time when compared to other more conventional techniques. It is also associated with a

very low incidence of bleeding complications, and it may be easily applied in case of emergency situations such as acute type A aortic dissection.

Actuarial survival in the present study at 10 years was 33%; although this value appeared low, account must be taken of the patients' preoperative characteristics, with the mean age being almost 70 years and more than 50% of patients undergoing combined procedures due to high-risk co-morbidities. Consequently, these patients might be considered to constitute a moderately high-risk group.

Freedom from primary valve failure was 100% at five years after surgery, and 64% at 10 years. Based on the Kaplan-Meier curve, freedom from SVD fell from 100% to 64% in only three years; however, this might be explained by the small number of patients at risk and did not appear to indicate a critical time-point of the prosthesis.

### Study limitations

As with all retrospective studies, the present study had intrinsic limitations. Notably, patient and prosthesis selection was not conducted in a randomized fashion, and data relating to effective orifice area and left ventricular mass regression were unavailable. A further limitation was the small number of patients examined at late follow up, which may have led to an underestimation of the number of primary valve failures. Nonetheless, no worsening occurred of either NYHA class or general clinical conditions requiring valve functional assessment by echocardiography.

*In conclusion*, the authors' experience with AVR, whether isolated or associated with ascending aorta replacement, showed that the ELSV, when implanted with the miniroot (inclusion cylinder) technique, provided good clinical results. Based on these findings, the ELSV is considered the bioprosthesis of choice when combined AVR and replacement of the ascending aorta is required, especially in elderly patients. Three questions remain, however, after long-term follow up: (i) whether these prostheses will degenerate; (ii) will the porcine aortic wall calcify; and (iii) will a redo operation be more complicated and present a higher risk for the patient?

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### Meeting discussion

**MR. JOHN R. PEPPER** (London, UK): You had 12 patients with a paravalvular leak, which is rather uncommon with a stentless valve.

**DR. AUGUSTO D'ONOFRIO** (Vicenza, Italy): These patients were identified at the start of the study, so perhaps the data were influenced by our learning curve at that time.

**DR. FRANCIS D. FERDINAND** (Wynnewood, PA, USA): So the patients with paravalvular leak have not been explanted?

**DR. D'ONOFRIO**: The regurgitation was not significant.

**DR. FERDINAND**: Did you have one patient with valve thrombosis?

**DR. D'ONOFRIO**: Yes, but those data were not clear

**DR. ROBERT FRATER** (Bronx, New York, USA): In relation to your last comment, the FDA's OPCs include a defined rate of thrombosis for tissue valves - I thought it would be zero, but it is not.

**MR. PEPPER**: Yes, that's a good point.