

# Early Results after Aortic Valve Replacement Using Last Generation Bioprosthetic Aortic Valve

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## ABSTRACT

**Introduction:** Few data are available about the newest generation surgical bioprosthesis. We aimed to evaluate early clinical and hemodynamic outcomes after using the INSPIRIS RESILIA aortic valve (Edwards Lifesciences, Irvine, California, USA).

**Methods:** Between July 2018 and April 2021, 80 patients underwent aortic valve replacement receiving the INSPIRIS RESILIA aortic valve at our institution. Primary outcomes were the composite of early mortality, stroke, and myocardial infarction. Secondary outcomes were hemodynamic performances of the valve, paravalvular leakage, and new pacemaker implantation.

**Results:** The mean age of the study population was  $60.6 \pm 8.3$  years. The mean Society of Thoracic Surgery-Predicted Risk of Mortality score was  $2.9 \pm 1.7\%$ . In 43.7% of the patients, concomitant surgery was performed. The in-hospital mortality, all-stroke, and myocardial infarction rates were 2.5%, 1.2%, and 1.2%, respectively. No valve was explanted and no redo was performed. The mean postoperative transprosthetic gradient at discharge was  $10.2 \pm 4.1$  mm Hg. There was no need for new pacemaker implantation. We registered only two cases with minimal (trace) paravalvular leakage.

**Conclusion:** The use of the INSPIRIS RESILIA aortic valve in a young, low-risk population is safe and associated with very good early clinical and hemodynamic outcomes.

## INTRODUCTION

The advancement of the transcatheter aortic valve replacement (TAVR) in recent years has led to fundamental changes, regarding the practice of treatment of the aortic stenosis. The utility of this method has been expanded to low-risk patients [Mack 2019]. The noninvasive nature of this method has shown very good results also in patients with degenerated bioprostheses, with foregone aortic valve replacement

(AVR) as a valve-in-valve procedure. Even with better outcomes as the surgical redo procedures [Malik 2020]. This evolvement is changing increasingly the paradigm of the use of bioprosthetic valves over mechanical prostheses also in younger patients—supported by the American Heart Association/American College of Cardiology guidelines on valvular heart disease 2017. It lowers the threshold of recommending mechanical over bioprosthetic valves to 50 years, compared with 60 years in 2014 [Nishimura 2017]. The INSPIRIS RESILIA aortic valve (Edwards Lifesciences, Irvine, California, USA) (INSPIRIS valve), representing the last development in surgical AVR, has been created with a novel RESILIA tissue preservation technology and dry storage method and has been constituted with an extendable stent, offering the best option for later valve-in-valve treatment (Figure 1). As the INSPIRIS valve is a new valve, data regarding outcomes are rare. Therefore, we aimed to evaluate early clinical and hemodynamic outcomes.

## METHODS

This single-center study was conducted to evaluate the in-hospital outcomes after AVR using the latest generation of surgical bioprosthesis INSPIRIS. Between July 2018 and April 2021, 69 patients with severe aortic stenosis and 11 patients with high-grade aortic regurgitation, aged between 50 to 65 years, where a mechanical valve implantation was contraindicated or refused from patients, underwent AVR receiving the INSPIRIS valve at our institution. The study population comprised all 80 consecutive low risk, young patients. Patients with aortic valve endocarditis and concomitant procedures, such as ascending replacement, aortic root replacement, coronary surgery, mitral repair/replacement, Morrow procedure were included in the



Figure 1. Edwards INSPIRIS RESILIA Aortic Valve.

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Table 1. Baseline characteristics

Variable	Study group (N = 80) (%)
Age (years)	60.6 ± 8.3
Male sex	58 (72.5)
Height (cm)	172.9 ± 12.6
Weight (kg)	88.6 ± 22.7
STS-SCORE (%)	2.9 ± 1.7
Euroscore II (%)	3.6 ± 2.4
New York Heart Association class I/II	40 (50)
New York Heart Association class III/IV	40 (50)
Endocarditis	5 (6.2)
Previous cardiac surgery	7 (8.7)
Previous aortic valve replacement	5 (6.2)
Previous coronary artery bypass	2 (2.5)
Syncope	3 (3.7)
Angina pectoris	11 (13.7)
Hypertension	45 (56.2)
Pulmonary hypertension	3 (3.7)
Diabetes	10 (12.5)
Coronary artery disease	27 (33.7)
PTCA/PCI	12 (15)
Left ventricular ejection fraction (%)	54.9 ± 11.1
Peripheral artery disease	2 (2.5)
Previous stroke	12 (15)
Chronic kidney disease	7 (8.7)
Chronic obstructive pulmonary disease	11 (13.7)
Atrial fibrillation	10 (12.5)

STS: Society of Thoracic Surgery-Predicted Risk of Mortality score; PTCA/PCI: percutaneous transluminal coronary angioplasty/intervention

study. Clinical endpoints were defined according to Valve Academic Research Consortium-2 criteria [Kappetein 2013]. An echocardiographic assessment of the valve was performed at discharge. The echocardiography data at discharge were 100% available. All patients gave informed consent for data collection. Approval for the study was obtained from the Ethics Committee of the Medical Faculty of the RUHR University, Bochum, Germany (Reg. No. 19-6804).

Primary outcome was a composite of early mortality, stroke, and myocardial infarction. Secondary outcomes were hemodynamic performances of the valve, paravalvular leakage (PVL), and new pacemaker implantation (PPI) at discharge.

Distributions of quantitative variables are described as means (± standard deviation). Qualitative variables are summarized by count and percentage. Comparisons of the data were assessed using student's t-test. Statistical tests were

Table 2. Procedural characteristics

Variables	Study group (N = 80) (%)
Baseline $\Delta$ P max (mm Hg)	78.6 ± 22.8
Baseline $\Delta$ P mean (mm Hg)	46.7 ± 14.8
Aortic valve replacement	80 (100)
Contraindications of mechanical valve	
Well-informed patient's desire, refusing lifelong anticoagulation	72 (90)
Women contemplating pregnancy	3 (3.7)
Redo due to mechanical valve thrombosis	2 (2.5)
Low patient compliance due to heroin-abuse	1 (1.2)
Low patient compliance due to mental retardation	1 (1.2)
Patient with cerebral cavernoma	1 (1.2)
Partial J-sternotomy/right anterior thoracotomy	49 (61.2)
Concomitant	35 (43.7)
Coronary artery bypass	12 (15)
Mitral valve replacement (Medtronic Hancock II porcine heart valve)	1 (1.2)
Mitral valve repair	4 (5)
Replacement of ascending aorta/aortic root	14 (17.5)
Aortic root enlargement	1 (1.2)
Closure of ventricular septal defect	1 (1.2)
Morrow procedure	2 (2.5)
CPB time (min)	89.2 ± 18.9
Cross-clamp time (min)	64.2 ± 16.8
Prosthesis diameter (mm)	24 ± 2
21 mm	15 (18.7)
23 mm	26 (32.5)
25 mm	23 (28.7)
27 mm	16 (20)

CPB, cardiopulmonary bypass

two-sided, and *P*-values of .05 or less were considered statistically significant.

## RESULTS

### Baseline characteristics

Table 1 shows the preoperative data of our patient population. The mean age was 60.6 ± 8.3 years. The mean Society of Thoracic Surgery-Predicted Risk of Mortality score was 2.9 ± 1.7%. Of the patients, 72.5% were male. New York Heart Association class III/IV was registered in 50% of the patients. There were five patients (6.2%) who underwent AVR due to endocarditis. Previous aortic valve replacement was registered

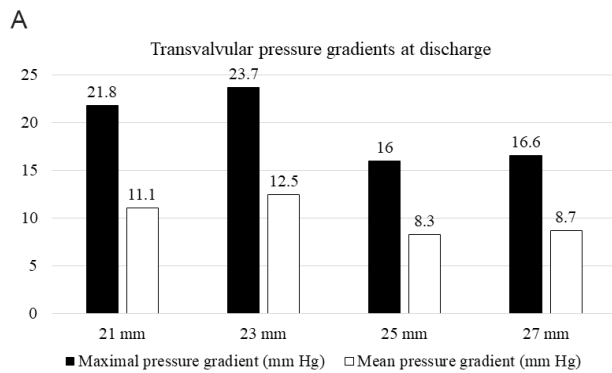


Figure 2A. Maximal and mean transvalvular pressure gradients at discharge.

in five patients (6.2%). Previous coronary artery bypass grafting was registered in two patients (2.5%).

#### Procedural characteristics

All valves successfully were implanted. There was no intra-procedural death. Vascular injury was not registered. No redo or valve-in-valve procedure were necessary. We performed concomitant procedures in 35 patients (43.7%). Four patients (5%) underwent mitral valve repair with ring, due to mitral annulus dilatation, and one patient (1.2%) underwent mitral valve replacement, due to mitral valve stenosis using the Medtronic Hancock II porcine heart valve. High grade aortic regurgitation was registered in 11 patients (13.7%). A high-grade aortic regurgitation was registered mainly due to endocarditis. Table 2 shows detailed procedural data.

#### Postoperative anticoagulation

Basically, our anticoagulation preference for biological valves still is the oral anticoagulation with vitamin K antagonist during the first three postoperative months. In this study group, all patients underwent vitamin K antagonist therapy postoperatively. In patients with concomitant coronary artery disease, 100 mg of Aspirin was given. In patients with chronic atrial fibrillation, monotherapy with vitamin K antagonist was the therapy regime. After the third postoperative month, a monotherapy with new oral anticoagulants was recommended.

#### In-hospital clinical outcomes

The in-hospital all-cause mortality and all-stroke were 2.5% and 1.2%, respectively. We registered one myocardial infarction. The acute kidney injury network 2/3 (AKIN 2/3) was very low. We saw two patients with gastrointestinal complications, requiring endoscopic and surgical interventions. The new permanent pacemaker implantation rate (PPI) was 0%, and the new onset left bundle branch block (LBBB) was observed only in four patients (5%) (Table 3).

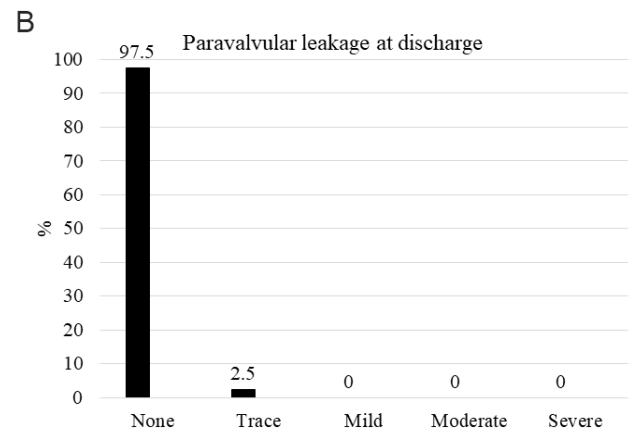


Figure 2B. Paravalvular leakage at discharge.

#### Hemodynamics

The baseline echocardiographic data in this study population confirmed severe aortic stenosis (Table 2). Preoperative and at discharge, the peak/mean gradients were  $78.6 \pm 22.8/46.7 \pm 14.8$  mmHg and  $19 \pm 7.2/10.2 \pm 4.1$  mmHg, respectively,  $P < .001$ . We found no severe, moderate, or mild PVL at discharge. We observed only two patients (2.5%) with trace PVL. Of note, trace PVLs were registered in patients with bicuspid valves and after redo with INSPIRIS in previously bicuspid valve. Figures 2A and 2B show hemodynamic details.

## DISCUSSION

A mechanical valve is the first choice at our center for patients aged between 50–65 years. However, we are witnesses of a grown patient's interest toward minimally invasive procedures and better life quality in contemporary times, associated with increased request to avoid lifetime oral anticoagulation. The advancements of TAVR procedures, patient's information possibilities, and the initial education through physicians have played a crucial role in this development. As the TAVR treatment is not recommended by recent guidelines for this young population, we offer a surgical treatment with the INSPIRIS bioprosthesis, which is the most recent development in AVR technology. It represents diverse novelties in the bioprosthesis valves: The bovine pericardial tissue undergoes RESILIA tissue technology, incorporating a stable capping anticalcification process, which permanently blocks residual aldehyde groups that are known to bind with calcium. Further, tissue preservation with glycerol replaces the traditional storage in liquid-based solutions, such as glutaraldehyde. The dry storage method eliminates tissue exposure to the residual unbound aldehyde groups commonly found in glutaraldehyde storage solutions and maintains long-term protection of collagen. In contrast to the Carpentier-Edwards PERIMOUNT Magna Ease aortic bioprosthesis, in the INSPIRIS valve, the ends of the cobalt-chromium alloy band are secured by a polyester shrink sleeve on the sizes 19–25

Table 3. In-hospital clinical outcomes

Variables	Study group (N = 80) (%)
Hospital stay	7 ± 2
All-cause mortality	2 (2.5)
All stroke	1 (1.2)
Myocardial infarction	1 (1.2)
Acute kidney injury network	
Stage 1	3 (3.7)
Stage 2	0 (0)
Stage 3	3 (3.7)
Delirium	9 (11.2)

mm to allow the internal orifice of the valve to expand. The polyester support band allows expansion at each commissure when subjected to radial forces. These features are promising long durability and facility in TAVR therapies as a valve-in-valve procedure in the future.

This valve has been newly introduced, and the information is minor. The key findings of the study are: 1) The use of the novel aortic bioprosthetic is safe without valve related complications. 2) The INSPIRIS valve shows very promising hemodynamics at discharge. 3) We registered no rhythm disorders requiring PPI. No mild/moderate/severe PVL were observed.

The finding of necessity of concomitant procedures in our study, representing a young and low-risk population, appears interesting. The use of the INSPIRIS valve in isolated AVR was safe and successful. The safety was reached when concomitant procedures were performed, such as mitral or ascending aorta procedures. We also used this valve in patients with endocarditis. We registered no endocarditis, valve thrombosis, or valve functional disorder. Thrombocytopenia was observed in only one patient. One patient experienced stroke, and one patient suffered myocardial infarction. Currently, very few data are reported on INSPIRIS safety. Our clinical findings are in the line with recently published safety studies [Puskas 2017; Bartuś 2018; Bartuś 2021].

It's relevant to emphasize the excellent outcomes, regarding rhythm disturbances after implantation of INSPIRIS. We registered no PPI, whereas the LBBB rate was very low. On the other side, we registered no mild, moderate, or severe PVL, and the procedures were conducted without vascular injury. It has been proven that all of these features affect the outcomes after TAVR and still represent a rigorous barrier to use TAVR in a young population.

The INSPIRIS valve was developed to enhance the durability of the bioprostheses. One of the main mechanisms to achieve the intended goal is that the RESILIA pericardial tissue undergoes an aldehyde capping process that permanently reduces calcium binding [Shang 2017]. Data up to five-years durability of INSPIRIS are promising [Bartuś 2021]. However, long-term data (over 15 years) are necessary to confirm the desired durability. Beyond the preservation methods and manufacturing details of the RESILIA pericardial tissue,

Table 4. Periprocedural complications

Variables	Study group (N = 80) (%)
Re-thoracotomy for bleeding	3 (3.7)
Major/minor vascular complications	0 (0)
New permanent pacemaker implantation	0 (0)
Paravalvular leakage ≥ 2	0 (0)
P mean > 20 mm Hg	2 (2.5)
Atrial fibrillation	19 (23.7)
LBBB	4 (5)
Thrombocytopenia	1 (1.2)
Valve leaflet thrombosis	0 (0)
Valve dysfunction/deterioration	0 (0)
Re-SAVR	0 (0)
Endocarditis	0 (0)
Gastrointestinal complications	2 (2.5)
Mediastinitis	0 (0)
Wound healing disorder	0 (0)

SAVR, surgical aortic valve replacement; LBBB, left bundle branch block

relevant early outcomes, such as low transvalvular pressure gradients, absence of PVL and valve leaflet thrombosis, are paramount for long-term durability. In our study, we saw that INSPIRIS exhibited very good transvalvular pressure gradients even in the small valves. We registered only two trace PVL and no valve leaflet thrombosis. These might be early signs of a promising concept. However, long-term durability data are missing. It is well known that biological valves degenerate earlier in young patients. Renal failure is also a well-documented predictor of earlier degeneration of biovalves. Young age, in combination with renal failure, will be the most challenging population with regard to long-term durability of the INSPIRIS valve. Whether the stable capping anticalcification process of RESILIA tissue technology will overcome an early valve degeneration process in patients with renal failure with defective calcium metabolism will be a very interesting topic in the future. Actually, there are no data highlighting this important issue. Additionally, the fact that renal failure and preoperative chronic kidney disease rates are relatively low in this patient population are positive insights of our study. We registered only 3.7% stage 1 and 3.7% stage 3 acute kidney injury postoperatively, whereas the rate of the preoperative chronic kidney disease was relatively low (8.7%).

The treatment of the aortic valve disease has reached nowadays high levels of improvement. Characterization of each available aortic valve prosthesis is of high relevance in contemporary circumstances, not only because of different methods available (TAVR, surgical AVR) with multi-approach modality (trans-femoral, trans-subclavian, trans-carotid, transapical transcatheter approaches, or minimal invasive surgical approaches, such as upper partial sternotomy or right anterior

thoracotomy) but because of numerous different surgical and transcatheter bioprostheses, as well. The need to know which bioprosthetic valve expresses the best hemodynamic characteristics is becoming more relevant. A recent trial recently compared hemodynamic performances of a transcatheter valve with a group of surgical bioprostheses [Pibarot 2020]. However, better information will be achieved comparing each valve separately. Comparative studies with INSPIRIS valves are lacking. In a recent publication, Shala and Niclauss reported INSPIRIS to exhibit significantly better early hemodynamic characteristics than PERIMOUNT Magna Ease [Shala 2020].

The fact that INSPIRIS valve is safe with very good hemodynamic characteristics without valve-related complications, such as PPI and PVL, in accordance with the possibility to facilitate transcatheter redo interventions in the future encourages us to implant this valve in young patients who refuse to receive mechanical valves. One limitation of this study is that it is a non-randomized, single-center study with a limited number of patients.

## CONCLUSION

The INSPIRIS valve can be safely implanted with very good hemodynamic performance, without early valve-related complications in young, low-risk patients.

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