

Case Report

The First Implantation of the Novel Biological Heart Valve, the Inspiris Resilia Aortic Tissue Valve in Africa

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Abstract: The durability of artificial bioprosthetic or tissue heart valves is limited by structural valve deterioration (SVD) due to long-term calcification especially in young patients and in Africa. A novel bioprosthetic valve, the Resilia Inspiris Aortic Tissue Valve has been developed which, in preclinical studies, has shown reduced calcification thus improving durability. The *Inspiris Resilia Aortic Valve* is a stented tri-leaflet valve made from bovine pericardial tissue. The tissue is created by treating bovine pericardial tissue with Edwards Integrity Preservation. It incorporates a stable capping anticalcification process, which blocks residual aldehyde groups known to bind with calcium. Tissue preservation with glycerol allows the valve to be stored without a traditional liquid-based solution, such as glutaraldehyde. Therefore, the valve is stored under dry packaging conditions and consequently does not require rinsing prior to implantation. The novel tissue preservation technology significantly improves hemodynamic and anticalcification properties compared with the standard artificial bioprosthetic aortic valve, the Perimount tissue valve. The experience of the implantation of this valve in Africa is limited for there seems to be no published experience of the behaviour of the implantation of this special long lasting bioprosthetic valve in Africa and therefore the purpose of this paper is to share our initial experience of the first successful implantation of this *Inspiris Resilia Aortic Valve*TM in Ghana, Africa. The implantation was done in a 57-year-old patient who presented with symptomatic moderate to severe aortic valve regurgitation with adequate left ventricular systolic function. He has been followed-up for a year now with well-healed wounds and a transthoracic echocardiography revealing a well-seated valve with no regurgitant flow or paravalvular leak. This is the first report describing the use of the new Inspiris Resilia Aortic valve which has increased durability and does not require anticoagulation in Africa as far as we know.

Keywords: Aortic Valve, Inspiris Resilia Aortic Valve, Open Heart Surgery, Bioprosthetic Valve

1. Introduction

The durability of artificial bioprosthetic heart valves is limited by structural valve deterioration (SVD) due to

long-term calcification especially in young patients and in Africa. A novel bioprosthetic or tissue valve called RESILIATM has been developed which, in preclinical studies, has shown reduced calcification thus improving durability. The *Inspiris Resilia Aortic Valve*TM is a stented tri-leaflet

valve comprising of bovine pericardial tissue. The tissue is created by treating bovine pericardial tissue with Edwards Integrity Preservation. It incorporates a stable capping anticalcification process, which blocks residual aldehyde groups known to bind with calcium. Tissue preservation with glycerol allows the valve to be stored without a traditional liquid-based solution, such as glutaraldehyde. Therefore, the valve is stored under dry packaging conditions and consequently does not require rinsing prior to implantation. The novel tissue preservation technology significantly improves hemodynamic and anticalcification properties compared with the standard artificial bioprosthetic aortic valve, the Perimount tissue valve. The Inspiris Resilia Aortic valve received FDA approval in 2017 and since then it has been subjected to a number of short-term trials producing generally excellent results. However the experience of the implantation of this valve in Africa is limited for there seems to be no published experience of the behaviour of the implantation of this special long lasting bioprosthetic valve in Africa and therefore the purpose of this paper is to share our initial experience of the first successful implantation of this *Inspiris Resilia Aortic Valve* in Ghana, Africa.

2. Case Report

Patient was a 57-year-old known hypertensive for 2 years who was diagnosed and managed for biventricular failure secondary to valvular heart disease 8 months prior to presentation at a peripheral hospital and subsequently referred to the Komfo Anokye Teaching Hospital for further management. He had been having recurrent episodes of exertional dyspnea, orthopnoea, nocturnal cough and bipedal swelling. This was not associated with chest pains or palpitations.

He had been stable with a BP of 160/66 mmHg, Heart Rate of 57 bpm which was regular, of good volume. Respiratory rate was 22 cycles/min with saturation of 96% in room air. Apex beat was present at the left 6th intercostal space 1cm lateral to the mid-clavicular line. There was a Grade 3/5 diastolic murmur loudest at the right parasternal border. Air entry was adequate bilaterally with few bilateral basilar crepitations. Abdomen was full, soft and non-tender with no palpable abdominal masses.

Electrocardiogram showed sinus bradycardia with Echocardiography showing dilated left atrium and left ventricle with eccentric left ventricular hypertrophy. The trileaflet aortic valve leaflets were thickened mostly at the tips with non-coaptation resulting in moderate-to-severe aortic regurgitation. The mitral valve leaflets were mildly thickened. Left ventricular ejection fraction was 52% with normal left ventricular diastolic function.

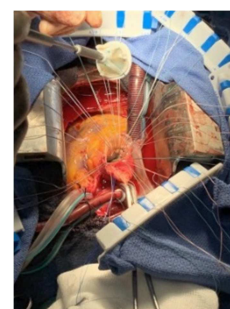
All hematological and biochemical investigations were within normal ranges.

He was on Tab. Lasix 40mg BD, Tab. Lisinopril 5mg OD, Tab. Bisoprolol 2.5mg OD and Tab. Aldactone 50mg OD. He was advised and subsequently consented for surgery and he was booked for aortic valve replacement with the novel

bioprosthetic valve considering his age. Preoperative labs included an Hb of 12.4g/dl, Platelets: 108×10^3 /UI, WBC: 4.80×10^3 /UI, Urea: 5.51mmol, Creatinine – 89 umol/L, BUN/Cr: 29.0, Na^+ - 136mmol/L, K^+ : 3.9mmol/L and Cl⁻: of 103mmol/l. The chest x-ray showed clear lung fields with cardiothoracic ratio (CTR) of 0.8.

Patient underwent a standard open-heart surgery with Aortic Valve Replacement using a size 23mm Inspiris Resilia Aortic Valve with Serial No. 6542812 by Edwards Lifesciences®. Intraoperative findings included a moderately enlarged heart in sinus rhythm with thickened and fibrotic right, left and non-coronary aortic valve leaflets.

The approach was a standard median sternotomy with single stage veno-aortic cannulation using size 34Fr single stage venous cannula, 22Fr aortic cannula and a size 16Fr antegrade cardioplegia cannula. We used crystalloid cardioplegia for ischemic cardiac arrest and temperature was cooled to 32°C. Total cross-clamp or Ischemic time was 99 minutes with total cardiopulmonary bypass time being 119 minutes. The total surgical time, was 5 hours and 32 minutes. Intraoperatively, he was transfused 4 Units of FFP and 4 Units of platelets. He was extubated after 8 hours in the intensive care unit where he spent two days. Mediastinal tubes were removed on postoperative day 2 and he was then transferred to the ward. He was transfused extra 10 units of platelets and 6 units of fresh frozen plasma on account of thrombocytopenia (Platelet: 55×10^3 /uL) and slightly increased chest drain on post-operative day 1. He made a gradual recovery and was subsequently discharged home on post-operative day 5 on Tab. Amlodipine 10mg OD, Tab. Bisoprolol 5mg OD, Tab. Lasix 40mg OD and Tab. Aspirin 75mg OD. The Soluble Aspirin was continued for three months. He has subsequently been reviewed on out-patient basis at 1-week, 2-weeks, 1-month and 3-months. He has been followed-up for a year now with well-healed wounds, doing well and going on with his normal activity. A post-operative transthoracic echocardiography revealed a well-seated valve with no regurgitant flow or paravalvular leak.



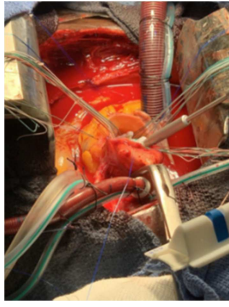


Figure 1. Showing the Inspiris Resilia Aortic Valve, the intraoperative photos of the exposed and arrested Heart and the Valve during implantation.

3. Discussion

3.1. History of Artificial Heart Valves

Though the need for surgical repair or replacement of diseased heart valves been recognized right from the 1920s, all efforts geared toward it were deemed insufficient. Several attempts, including surgical attachment of polymeric leaflets were tried but were unsuccessful due to calcification, rupture and stiffening of the leaflets [1]. The search continued unabated until in 1952 when Dr Charles Hufnagel invented and subsequently implanted a methacrylate chamber containing an acrylic ball. This device was not implanted into the heart but rather in the descending thoracic aorta [2, 3]. The first patient to receive this valve was a 30-year-old woman with aortic valve regurgitation in 1952 and since then over 200 patients were documented to have had the Hufnagel valve implanted which remained functional for over 30 years with no accompanying use of anticoagulation. The acrylic ball subsequently was modified to a silicone-coated hollow nylon ball due to the reported valve noise associated with the methacrylic ball [2]. The Hufnagel valve was only useful in alleviating symptoms and not replacement of the diseased valves due to its extra-cardiac implantation site [2, 3]. This was followed up by Dr Dwight Harken in 1960 with the double-caged ball valve known as the Harken-Soroff valve. This was an intra-cardiac valve implanted at the aortic annulus in 17 patients, two of which were successful. This was closely followed up by the Starr-Edwards ball valve by Dr Albert Starr and Mr Lowell Edwards in 1960 which was a single-caged ball valve [2–4].

The surge in invention of artificial heart valves continued with various modifications of the ball valve by several cardiac surgeons [2]. In 1965, the first non-tilting disc valve known as the Kay-Shiley disc valve was invented by Dr Jerome Kay and Mr Donald Shiley [4]. In 1975, the first tilting disc valve known as the Bjork-Shiley tilting disc valve was implanted. The Hall-Medtronic tilting disc valve, invented by Karl-Viktor Hall, Arne Woien and Robert Kaster was approved in 1977. That, along with the Starr-Edwards and the St Jude bileaflet valve approved in 1977 are reported to have the longest duration of implantation and the largest number of reported implants [5]. Currently, the bileaflet valve is the most common design of mechanical artificial heart valve being utilized [6].

Biological or tissue valves originated from the work of Donald Ross in 1962, when he first implanted a cadaveric

aortic valve. However, the scarcity of homografts led to the use of xenografts [1, 3]. A group of colleagues led by Jean-Paul Binet in 1965 reported a 100% survival rate in 5 patients who had received xenograft with no anticoagulation therapy [1]. Xenografts were initially retrieved from pigs (porcine) heart valves, and later on valves were developed from the pericardium of cows. The first of such valves was the Ionescu-Shiley valve which was developed in 1971 [3].

3.2. Artificial Bioprosthetic (Tissue) Heart Valves

Artificial heart valves are broadly classified into mechanical and bioprosthetic (Tissue) heart valves. Mechanical heart valves are made of synthetic components such as polymers and metals or carbon. They have high durability profile and usually outlive their patients but very thrombogenic and as such require long-term anticoagulation therapy [6, 7]. They are less preferred among young individuals, pregnant or women in reproductive age, in developing world where anti-coagulation monitoring might be a challenge [8] and moreover the side effects of embryopathy or teratogenicity associated with the long-term anticoagulation that these patients had to be on, especially the oral anticoagulant, warfarin.

On the other hand, the bioprosthetic heart valves are composed of biologically-derived tissues mounted on stents covered with fabric. They may be of human or animal origin, hence they are either homograft or xenograft artificial heart valves respectively. Homografts may be of cadaveric origin or a valve from another site of the patient's own heart which is termed as an autograft. Xenograft valves are commonly derived from porcine (pig) aortic valves or manufactured from bovine (cow) pericardium [7].

First generation xenograft valves developed in the 1960s were porcine origin and since then, several modifications have been made to improve their durability [7]. In a bid to render them immunologically inactive, they were fixed with formalin. However, it resulted in early calcification and fibrosis. Glutaraldehyde-impregnated porcine valves provide better durability while remaining immunologically inactive [3]. Bovine pericardial valves were first invented in the 1970s and comprised of leaflets made from bovine pericardium mounted onto a stent with a surrounding suturing ring [7]. Treatment with anti-mineralization agents such as alpha-oleic acid and surfactants help reduce cusp calcification, thereby improving durability and longevity [7].

Since their inauguration, there has been a gradual shift in preference from the use of mechanical heart valve to biological heart valves due to their lack of thrombogenic complications and the elimination of lifelong anticoagulation requirement. However, its major drawback is its durability as compared to mechanical valves. As such, it is deemed a less safe option for implantation in younger patients who are less than 50 years as compared to mechanical valves since the patient may outlive the valve. And this more common in areas of the world with high life expectancy as in high income countries due to the risk of structural valve deterioration [8, 9]. Therefore, the search of a longer lasting bioprosthetic (tissue)

heart valve has continued.

3.3. Inspiris Resilia Aortic Valve

The need for improved bioprosthetic heart valve durability and reduced risk of structural valve deterioration has led to the invention of the RESILIA™ tissue by Edward Lifesciences. It is a trileaflet bovine pericardial tissue valve mounted on a frame similar to the two famous tissue valves, the Carpentier-Edwards Perimount™ and the Magna Ease™ valves with an advanced preservation technology rendering it resilient [10]. The treatment involves stable capping which causes permanent binding of all residual aldehyde groups with potential to bind calcium which increases risk of structural valve deterioration. The tissue also undergoes glycerolization, a procedure where the valve is preserved in glycerol instead of the traditional liquid-based solutions like glutaraldehyde thereby allowing dry storage prior to implantation. The valve is also sterilized in ethylene oxide, thereby obviating the need for washing before implantation [10–12]. It also has an expandable frame that has the potential to allow valve-in-valve implantation or procedures in future [8].

The Inspiris Resilia Aortic valve received FDA approval in 2017 and since then it has been subjected to a number of short-term trials producing generally excellent results. A multicentre study conducted in 2018 on 133 patients followed up over one year to assess the hemodynamic performance of the RESILIA™ tissue valve showed excellent hemodynamic performance as evidenced by increased effective orifice area and low rates of paravalvular leak as excellently demonstrated by our first implantation in Ghana monitored over a year. There was also documented all-cause mortality rate of about 2% indicating good safety outcomes. However, the duration of the study did not allow for adequate time to ascertain long-term durability of the valve [12]. Similarly, we continue to follow our patient carefully to really understand the outcome. The COMMENCE trial also demonstrated commendable early safety profile and effectiveness of the Resilia™ tissue valve as well. Noted in this study was the absence of any case of structural valve deterioration yet, after one year of follow-up though the study is to run for a minimum of 5 years [10].

4. Conclusion

The Novel permanent bioprosthetic or tissue Aortic Valve, the Inspiris Resilia Aortic Valve implantation in Ghana, Africa demonstrates excellent hemodynamic performance and safety outcomes in the first year of implantation. However longer follow-up and more implantation will be important to confirm the durability and behaviour of this novel bioprosthetic valve in Africa.

Conflicts of Interest

The authors declare that they have no competing interests.

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