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Evolution of Bioprosthetic Valves, Where We Are Heading

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Abstract: Bioprosthetic heart valves are made from animal tissue and used to replace damaged or diseased heart valves. The first bioprosthetic valve was implanted in 1960, and since then, there have been significant advances in their design and development. Early valves were made from glutaraldehyde-preserved porcine valves and had a high risk of calcification. In the 1980s, cryopreserved porcine valves were introduced, which are less likely to calcify. Tissue-engineered heart valves, made from cells and tissues grown in the lab, are still in development but have the potential to offer longer lifespans and lower risk of rejection. Continuous research and development are happening to improve design, swing ring, cuff size, ring material, storage solution, rinsing time, anticalcification treatment, ease of implant for surgeons, and making these valves future ready for interventional procedures. Currently we are having fourth generation of these valves (Company classification). The evolution of bioprosthetic heart valves has led to improved outcomes for patients with heart valve disease. These valves are now a standard treatment option and offer a good quality of life and long-term survival. Initial results of both bovine fourth generation bioprosthetic valves Medtronic Avalus (PERIGON trial) and Edwards Inspiris resilia (COMMENCE trial) are good. The evolution of bioprosthetic heart valves is an ongoing process. As new technologies are developed, these valves are likely to become even more durable and effective.

Keywords Bioprosthetic Valves, Evolution, Bovine, Porcine, COMMENCE Trial, PERIGON Trial

1. Introduction

Bioprosthetic heart valves are used to replace or repair diseased or damaged heart valves. They are made from animal tissue, such as bovine pericardium or porcine valves, and are designed to mimic the function of a natural heart valve. Bioprosthetic valves remained a valve of choice among elderly patients above 60yrs since long time. Though there are different valves of different generations (According to Manufacturer’s Companies) available for implant in patient’s needing valve replacement. These valves are divided into different generation (1-4th) depending upon durability and development in tissue, their parts over the years [1]. Now days rapid deployment, polymeric and tissue engineered heart valves are also evolving. Further development is happening to decrease chance of prosthesis-patient mismatch (PPM) [2] more durability [3, 4] and lower valve gradient even at long term.

2. Methods

2.1. Early Development

The first bioprosthetic heart valves were implanted in the 1960s [1]. These early valves were made from porcine valves and were sewn into place during open-heart surgery. However, they were prone to calcification and other complications, and their lifespan was limited.

2.2. The Introduction of Bovine Pericardium

In the 1970s, bovine pericardium was introduced as a material for bioprosthetic valves [1]. This material is less likely to calcify than porcine valves, and it has a longer lifespan. Bovine pericardial valves are now the most common type of bioprosthetic heart valve. Tissue treatment changed over time latest tissue treatment include Resilia [4] by Edwards and AOA (alpha amino oleic acid) tissue treatment by Medtronic.

2.3. Types of Bioprosthetic Valves

1) Stented porcine bioprostheses: These valves are made from porcine aortic valves that have been treated with glutaraldehyde to preserve them. They are the most common type of bioprosthesis and are available in both aortic and mitral positions. Initial generations of valves were mainly porcine.
2) Stented pericardial bioprostheses: These valves are made from bovine pericardium, which is the lining of the heart. They are less commonly used than stented porcine bioprostheses, but they may be a better option for patients who have had an allergic reaction to porcine valves. Now future development is happening mainly on bovine tissue. Recent generations of biological valves are made up of bovine tissue.
3) Stentless bioprostheses: These valves do not have a metal stent. They are made from porcine or bovine tissue that is sewn directly to the heart. Stentless bioprostheses have a lower risk of blood clots than stented bioprostheses, but they may also have a higher risk of valve failure.
4) Homograft's: These valves are made from the tissue of a human donor. They are the most durable type of bioprosthesis, but they are also the most difficult to obtain.

2.4. Other Key Developments

1) Better anti-calcification treatment
2) Future ready for valve in valve and MIS
3) Better sewing ring/stent material/dual stent/Improved design to avoid distortion/stress
4) More chances of upsize in TAVI (Transcatheter aortic valve replacement) [5, 6]
5) Ease of implant/surgeon friendly/One cut release
6) High profile to low profile design
7) Intra-annular to supra-annular design
8) Hart stent to soft stent
9) Larger cuff size to smaller cuff size
10) Wet storage to dry storage
11) Decrease in rinsing time or no rinsing
12) Better anticalcification treatment
13) Future readiness for valve in valve transcatheter procedures
14) Single stent to dual alloy stent
15) Improved design (externally mounted leaflet design to internally mounted leaflet design) to avoid distortion, stress and early leaflet damage [7]
16) Better effective orifice area and more chances of upsizing during transcatheter valve replacement procedure (TAVI/TMVR/TPVR/TTVR)
17) Better swing ring and stent material [8] to avoid distortion [9]

2.5. The Development of Transcatheter Bioprosthetic Valves

In recent years, there has been a trend towards the development of transcatheter bioprosthetic heart valves. These valves are delivered to the heart through a catheter, which is a minimally invasive procedure. Transcatheter bioprosthetic valves are still under development, but they have the potential to offer a number of advantages over traditional surgical valves, including shorter recovery times and lower risks of complications.

2.6. Current Challenges and Opportunities

Despite the progress that has been made, there are still some challenges and opportunities facing the future of bioprosthetic heart valves.

Challenges

1) Calcification: Calcification is a major problem for bioprosthetic heart valves. It can cause the valve to stiffen and narrow, which can lead to redevelopment of disease.
2) Thrombosis: Thrombosis, or the formation of blood clots, is another challenge for bioprosthetic heart valves. Blood clots can block blood flow and cause serious complications (stroke, organ ischemia etc.).
3) Durability: Bioprosthetic heart valves have a limited lifespan (8-15years). The valves can degenerate over time, which can lead to valve failure.

Opportunities

1) Tissue engineering: Tissue engineering is a promising field that could lead to the development of new and improved bioprosthetic heart valves. Tissue-engineered valves would be made from the patient's own cells, which would reduce the risk of rejection.
2) Polymeric heart valves: Development is happening in polymeric tissue for biological valves. Still more development and in development of ideal tissue is lacking. Singh et al [8] had given a review of current technologies and future direction in their review article.
3) Transcatheter valves: Transcatheter valves [10] are less invasive than traditional surgical valves. This could make them a more attractive option for patients, especially those who are at high risk of complications from surgery.
4) Personalized medicine: Personalized medicine is a field that is developing rapidly. This could lead to the development of bioprosthetic heart valves that are specifically designed for each patient. This would improve the chances of a successful outcome.

2.7. The Future of Bioprosthetic Heart Valves

The evolution of bioprosthetic heart valves has led to a number of improvements in the treatment of heart valve disease. These valves are now more durable and less likely to cause complications, and they can be implanted using less invasive procedures. As a result, bioprosthetic heart valves have become a valuable option for patients with heart valve disease. Though ongoing research and development is occurring in polymeric, tissue engineered heart valves.

3. Results

The results of currently available bioprosthetic valves [11] are generally good. The valves are effective at improving blood flow and relieving symptoms of heart valve disease. However, all bioprosthetic valves eventually need to be replaced, as they can degenerate over time. The rate of valve degeneration depends on the type of valve and the patient's individual factors (Gender, age of implantation, atrial fibrillation, location in heart etc.).

In general, stented porcine bioprostheses have a lifespan of 10-15 years, while stentless bioprostheses can last up to 20 years. Homograft's can last for 20-30 years or more.

The risks of bioprosthetic valves include:

1) Blood clots: Blood clots can form on the valve, which can lead to stroke, organ damage or heart attack.
2) Valve failure: The valve can degenerate or become calcified over time, which can lead to valve failure.
3) Infection: The valve can become infected (Infective endocarditis), which can be a serious complication.

The risks of bioprosthetic valves are generally lower than the risks of mechanical valves. However, it is important to discuss the risks and benefits of all valve options with your doctor before making a decision.

4. Discussion

Ongoing Trials

The Avalus PERIGON trial [12] and the Inspiris resilia COMMENCE trial [13] were two large, randomized controlled trials that evaluated the safety and effectiveness of two new bioprosthetic heart valves, the Avalus valve (Medtronic) and the Inspiris resilia valve, respectively. Both trials enrolled patients who were undergoing aortic valve replacement (AVR) due to severe aortic stenosis or regurgitation.

The Avalus PERIGON trial enrolled 1118 patients and had a mean follow-up time of 3 years. The trial found that the Avalus valve was safe and effective, with a 1.8% rate of mortality, a 1.4% rate of stroke, and a 2.4% rate of valve-related complications. The Inspiris resilia COMMENCE trial enrolled 694 patients and had a mean follow-up time of 4.3 years. The trial found that the inspiris resilia valve was also safe and effective, with a 1.2% rate of mortality, a 1.6% rate of stroke, and a 0.1% rate of valve-related complications.

Both trials also found that the two valves had similar hemodynamic performance and clinical outcomes. However, the INSPIRIS RESILIA valve was found to have a lower rate of paravalvular regurgitation.

The results of these trials suggest that both the valves are safe and effective options for AVR. The choice of valve will depend on the individual patient's factors, such as their age, health, and activity level.

The Avalus valve is a stented bioprosthesis made from bovine pericardium. It is available in aortic position.

1) The Inspiris Resilia valve is also a stented bioprosthesis made from bovine pericardium. It is available in both aortic and mitral position.
2) The inspiris resilia valve has a unique design that allows it to be opened wider if it starts to degenerate over time. This feature could potentially extend the lifespan of the valve. Valve is future ready and allow valve in valve transcatheter valve replacement with higher size valve in future [14].

5. Conclusion

The future of bioprosthetic heart valves is bright. As research continues, new and improved bioprosthetic valves are being developed. These valves are likely to be more durable, less likely to cause complications, and easier to implant. As a result, bioprosthetic heart valves will continue to be a valuable option for patients with heart valve disease. In future valve in valve [11] procedure after few years of implantation of tissue valve can be done safely. Recently there is development in the use of end-to-end smart deep learning framework for real time assessment and best design for TAVI [15]. More development is needed in search of ideal material, valve design and higher durability. Though initial results of newer generation Edwards and Medtronic tissue valves are promising [11]. PERIGON trial [12] (Medtronic) done on Avalus bioprosthesis for aortic position and COMMENCE trial [13] (Edwards) done on 'inspiris resilia' aortic valve showed comparable results, though Edwards inspiris resilia claiming higher durabilty (20-25years) with its newer Resilia anticalcification treatment. Till now five years results of both valves are available and follow up results at 10years are awaited.

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