Health Policy Advisory Committee on Technology

Technology Brief

Transcatheter mitral valve replacement for severe mitral regurgitation

December 2015
Summary of findings

Transcatheter mitral valve replacement is a very new technology. Only three studies were identified and described in this brief. Each study used a different valve and the maximum number of patients was five. In each of the studies the patients selected were those deemed not suitable for surgical valve replacement or percutaneous repair with a MitraClip. All three studies demonstrated successful implantation of the device. Across all three studies the longest follow-up of a surviving patient was 90 days. At least one of the authors in each study was a consultant for the company that manufactured the valve. The studies included in this brief were the first human trials describing this technology. Further studies with larger patient numbers and longer follow-up periods are required to determine the true safety and efficacy of these devices beyond implantation.

It is clear that there is strong interest in this technology given the number of devices that are in various stages of development. Several clinical trials were identified that will investigate the safety of these devices in larger series of patients. It has been reported that progress with this technology will be significantly slower than that associated with the development of transcatheter aortic valve replacement, primarily due to the complexity of the mitral valve anatomy and its pathology.19

HealthPACT Advice

HealthPACT noted that this technology is in the early stages of development and is diffusing into the health systems of Australia and New Zealand. None of the iterations of the device are registered on the TGA; however it is currently being used under the TGA’s Special Access Scheme. HealthPACT also noted that although only small numbers of patients have been treated using this minimally invasive approach, the mortality rate in these patients is high. HealthPACT recommends that use of this technology in the public health system should be based on efficacy and cost-effectiveness, and as such larger clinical trials need to be conducted, comparing transcatheter mitral valve replacement to conservative medical management. HealthPACT does not support investment in this technology in clinical practice at this time; however, it is recommended that the evidence be reviewed again in 24 months.
Transcatheter mitral valve replacement for severe mitral regurgitation: December 2015

Technology, Company and Licensing

Register ID WP225

Technology name Transcatheter mitral valve replacement

Patient indication Patients with severe mitral valve regurgitation requiring mitral valve replacement but who are unable to have open surgery or percutaneous repair

Description of the technology

Transcatheter mitral valve replacement is a minimally invasive surgical procedure that replaces a patient’s damaged mitral valve with a bioprosthetic one. The bioprosthetic valve is delivered into the heart using a catheter that has been crimped inside a covering sheath. When the valve is correctly positioned, the sheath is pulled back and the valve is released. The new bioprosthetic valve self-expands, pushing the old valve leaflets out of the way and thereby taking over the job of regulating blood flow through the heart.

Compared with surgical valve replacement, which requires open heart surgery and full or partial splitting of the breastbone (sternotomy or mini-sternotomy), the transcatheter approach can be done through a small opening that leaves the breastbone intact. At present there are several transcatheter mitral valves in various stages of development. They can be delivered either via a transapical or transfemoral approach. With the transfemoral approach, the catheter is passed through the femoral artery in the groin, avoiding the need for a surgical incision in the chest. With the transapical approach, a small incision is made in the chest and the catheter is passed into the heart through a large artery in the chest or through the tip of the left ventricle. Both delivery techniques require the patient to undergo general anaesthesia. The procedure is performed in a hybrid operating suite that has both catheterisation and surgical capabilities. A team consisting of interventional cardiologists, imaging specialists, heart surgeons and cardiac anaesthesiologists work together using fluoroscopy and echocardiography to guide the new valve to the site of the diseased valve. Patients stay in hospital for approximately 3 to 5 days after the procedure.

The bioprosthetic valves are composed of three valve leaflets fashioned from animal heart tissue that are mounted on a self-expanding nitinol frame or stent. The valves have an anchoring mechanism, but they can be repositioned before final deployment. This description is based on three transcatheter mitral valves that have peer-reviewed publications describing their use, and as a result, form the basis of this technical brief: the FORTIS and CardiAQ valves (Edwards Lifesciences Corporation, California, United States of America [USA]) and the Tiara valve (Neovasc Inc., British Columbia, Canada). The Tiara valve is shown in Figure 1.

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* An exception is the FORTIS mitral transcatheter valve which has a sheathless delivery system
Figure 1  The Tiara transcatheter mitral valve (with permission Neovasc Inc., British Columbia, Canada)

Company or developer
Several companies are developing transcatheter mitral valves (Table 1).

Reason for assessment
Transcatheter mitral valve replacement is a novel treatment for patients with severe mitral valve regurgitation (MR) who are unable to undergo surgical replacement or repair.

Stage of development in Australia

☐ Yet to emerge  ☐ Established
☐ Experimental  ☐ Established but changed indication or modification of technique
☒ Investigational  ☐ Should be taken out of use
☐ Nearly established

Licensing, reimbursement and other approval
There are no transcatheter mitral valves listed on the Australian Register of Therapeutic Goods, and none have received United States Food and Drug Administration (FDA) approval or a CE mark. Four transcatheter mitral valves have FDA investigational device exemptions: the transfemoral and transapical transcatheter mitral valve implantation systems by CardiAQ Valve Technologies Inc.; the Tendyne Bioprosthetic Mitral Valve System by Tendyne Holdings, Inc. (Minnesota, USA) and the Tiara valve by Neovasc Inc.

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b CardiAQ Valve Technologies Inc. was acquired by Edwards Lifesciences Corporation in August 2015
<table>
<thead>
<tr>
<th>Device Name</th>
<th>Company</th>
<th>International Status</th>
<th>USA Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atlas™</td>
<td>St. George Medical, Florida, USA</td>
<td>*</td>
<td>Applied for patent</td>
</tr>
<tr>
<td>Caisson TMVR</td>
<td>Caisson International, Minnesota, USA</td>
<td>*</td>
<td>Preclinical assessment underway</td>
</tr>
<tr>
<td>Cephea TMVR</td>
<td>Cephea, California, USA</td>
<td>*</td>
<td>In development</td>
</tr>
<tr>
<td>CardioValve</td>
<td>Valtech, Or Yehuda, Israel</td>
<td>Preclinical assessment planned</td>
<td>*</td>
</tr>
<tr>
<td>Endoovale-transapical</td>
<td>Micro Interventional Devices, Pennsylvania, USA</td>
<td>*</td>
<td>In development</td>
</tr>
<tr>
<td>FORTIS</td>
<td>Edwards Lifesciences, California, USA</td>
<td>Clinical work suspended</td>
<td>USA feasibility study planned</td>
</tr>
<tr>
<td>HighLife Mitral Replacement</td>
<td>HighLife, California, USA</td>
<td>First human study underway</td>
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<tr>
<td>Inovare Mitral</td>
<td>Braile Biomedica, São José do Rio Preto, Brazil</td>
<td>In development</td>
<td>*</td>
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<tr>
<td>Lutter Valve</td>
<td>Lutter†</td>
<td>Preclinical assessment underway</td>
<td>*</td>
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<tr>
<td>MAESTRO</td>
<td>Mitraxil, Jerusalem, Israel</td>
<td>In development</td>
<td>*</td>
</tr>
<tr>
<td>Medtronic TMVR</td>
<td>Medtronic Inc., Minneapolis, USA</td>
<td>Preclinical assessment underway</td>
<td>Preclinical assessment underway</td>
</tr>
<tr>
<td>Mehr TMVR</td>
<td>Mehr Medical, Massachusetts, USA</td>
<td>*</td>
<td>Applied for patent</td>
</tr>
<tr>
<td>MitrCare</td>
<td>Emory University, Georgia, USA</td>
<td>*</td>
<td>In development</td>
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<tr>
<td>MitralHeal</td>
<td>MitrHeal, Tel Aviv, Israel</td>
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<td>*</td>
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<td>Mitriltech TMVR</td>
<td>Mitriltech, Or Yehuda, Israel</td>
<td>Applied for patent</td>
<td>*</td>
</tr>
<tr>
<td>MitrAssist Valve</td>
<td>MitrAssist Medical Ltd, Tel Aviv, Israel</td>
<td>Preclinical assessment underway</td>
<td>*</td>
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<tr>
<td>MITRICARES Device</td>
<td>MITRICARES, Paris, France</td>
<td>Applied for patent</td>
<td>*</td>
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<td>Nakostech TMVR</td>
<td>Nakostech, Paris, France</td>
<td>*</td>
<td>Applied for patent</td>
</tr>
<tr>
<td>Navigate TMVR</td>
<td>Navigate Cardiac Structures Inc., Ohio, USA</td>
<td>Preclinical assessment underway</td>
<td>Preclinical assessment underway</td>
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<tr>
<td>Saturn</td>
<td>HT Consultant†</td>
<td>Preclinical assessment underway</td>
<td>*</td>
</tr>
<tr>
<td>SINOMED TMVR</td>
<td>SINOMED, Tianjin, China</td>
<td>Preclinical assessment underway</td>
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<tr>
<td>Tiara</td>
<td>Neovasc Inc., British Columbia, Canada</td>
<td>International feasibility study underway</td>
<td>USA feasibility study underway</td>
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<tr>
<td>Tendyne TMVR</td>
<td>Tendyne Medical Inc., Maryland, USA</td>
<td>First human study underway</td>
<td>USA feasibility study underway</td>
</tr>
<tr>
<td>TMVI-TA</td>
<td>CardIQ Valve Technologies Inc., Massachusetts, USA</td>
<td>CE mark trial planned</td>
<td>IDE accepted for feasibility study</td>
</tr>
</tbody>
</table>

Table 1  Development status of transcatheter mitral valves as described by Levin and Thompson (2015)†
Transcatheter mitral valve replacement for severe mitral regurgitation: December 2015

<table>
<thead>
<tr>
<th>Technology</th>
<th>Company</th>
<th>Location</th>
<th>Status</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMVI-TA</td>
<td>CardiAQ Valve Technologies Inc., Massachusetts, USA</td>
<td>First human study underway</td>
<td>IDE accepted for feasibility study</td>
<td></td>
</tr>
<tr>
<td>TMVI-TF</td>
<td>CardiAQ Valve Technologies Inc., Massachusetts, USA, acquired by Edwards Lifesciences Corporation in August 2015</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMVR</td>
<td>Twelve, California, USA</td>
<td>First human study underway</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Tresillo</td>
<td>Transcatheter Technologies, Regensburg, Germany</td>
<td>Preclinical assessment planned</td>
<td>*</td>
<td></td>
</tr>
</tbody>
</table>

*no current activity
†location of company unable to be identified
‡CardiAQ Valve Technologies Inc. was acquired by Edwards Lifesciences Corporation in August 2015
IDE: investigational device exemption; TMVI-TA: transcatheter mitral valve implantation - transapical; TMVI-TF: transcatheter mitral valve implantation - transfemoral; TMVR: transcatheter mitral valve replacement; USA: United States of America

Australian Therapeutic Goods Administration approval

- [ ] Yes
- [x] No
- [ ] Not applicable

Technology type: Device
Technology use: Therapeutic

Patient Indication and Setting

Disease description and associated mortality and morbidity

The mitral valve, which is composed of two flaps of tissues called leaflets, lies between the left ventricle and left atrium in the heart. It opens when blood flows from the left atrium into the left ventricle and then closes to prevent the oxygenated blood that has just passed into the left ventricle from flowing backwards. MR, also called mitral incompetence, occurs when the heart’s mitral valve doesn’t close properly and blood leaks from the left ventricle back into the left atrium. It is one of the most common forms of heart valve disorder in Western countries.², 8, 9

MR is classified as primary or secondary. Primary MR occurs when there is a problem with the leaflets of the mitral valve. The most common causes of primary MR are:

- mitral valve prolapse
- rheumatic valve disease
- endocarditis (inflammation of the heart tissue)
- valve calcification
- chord rupture (when the strings holding the valve in place snap)
- ischaemic heart disease.¹⁰

Secondary MR, also known as functional MR, occurs when there is a problem with the structures that hold the valve in place. The most common causes of secondary MR are heart

Transcatheter mitral valve replacement for severe mitral regurgitation: December 2015
failure, coronary artery disease, complications due to a heart attack and hypertrophic cardiomyopathy (a type of heart muscle disease).\textsuperscript{11}

MR can be acute or chronic. Chronic MR comprises mild MR that progresses slowly over many years. Patients may have no symptoms for decades and may be unaware that they have the condition. When present, symptoms can include:

- blood flowing turbulently through the heart (heart murmur)
- shortness of breath (dyspnoea), especially with exertion
- fatigue, especially during times of increased activity
- heart palpitations
- swollen feet or ankles.\textsuperscript{9}

Acute MR, which is rarer, occurs suddenly and is a medical emergency. Patients with acute severe MR can have the following symptoms: low blood pressure, shortness of breath, dizziness and fainting.\textsuperscript{11}

MR is also classified according to its severity (mild, moderate or severe). Mild MR may not cause problems. Severe MR, in which approximately 50 per cent of the blood in the heart is leaking backwards, can lead to heart failure, atrial fibrillation and pulmonary hypertension if not treated.\textsuperscript{9, 11}

Common diagnostic tests to diagnose MR include:

- echocardiograms
- electrocardiogram
- chest x-rays
- cardiac MRI
- cardiac catheterisation
- computed tomography angiogram
- exercise tests or stress tests.\textsuperscript{9}

**Number of patients**

MR is one of the most prevalent heart valve diseases in Western countries. It becomes more common with age and affects almost 10 per cent of individuals over 75 years of age.\textsuperscript{8, 12} In 2012 to 2013 there were 2,975 hospitalisations in Australian public hospitals for MR.\textsuperscript{13} The data did not report on the number of patients with severe MR or the number of patients who were unable to undergo valve replacement using conventional surgical techniques.

No information was identified on the number of people with MR in New Zealand.
Speciality: Cardiology
Technology setting: Tertiary Setting

Impact

Alternative and/or complementary technology
Transcatheter mitral valve replacement using bioprosthetic mitral valves is a novel technology for patients with severe MR who are in need of a new valve but are unable to undergo open surgery or percutaneous repair.

Current technology
Fixing the valve through open heart surgery is the gold standard treatment for patients with severe MR. However, around 49 per cent of patients with severe, symptomatic MR are not referred for surgery because they are too ill or weak to withstand the stress of the procedure. Patient characteristics associated with the decision not to operate include older age, congestive heart failure and diabetes. Patients with a left ventricular ejection fraction of less than 60 per cent and an MR grade of 3 out of 4 are also more frequently denied surgery. Percutaneous mitral repair treatments are available, but these procedures are only suitable for very specific forms of mitral valve disease and anatomic subsets. As a result, there is a subset of patients with severe MR for whom there is no treatment currently available.

International utilisation

<table>
<thead>
<tr>
<th>Country</th>
<th>Level of Use</th>
<th>Trials underway or completed</th>
<th>Limited use</th>
<th>Widely diffused</th>
</tr>
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<tbody>
<tr>
<td>Australia</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
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<td>Belgium</td>
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<td>✓</td>
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<td></td>
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<tr>
<td>Canada</td>
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<td>✓</td>
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</tr>
<tr>
<td>Denmark</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>France</td>
<td></td>
<td>✓</td>
<td></td>
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<tr>
<td>Poland</td>
<td></td>
<td>✓</td>
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<tr>
<td>The Netherlands</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>United Kingdom</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States of America</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Diffusion of technology in Australia

The St Vincent’s Hospital in Sydney is participating in a clinical trial (NCT02321514) on the Tendyne Bioprosthetic Mitral Valve System (Table 4). In addition, the Flinders Medical Centre is in the process of obtaining ethics approval for a clinical trial on this mitral valve system.

Cost infrastructure and economic consequences

The main cost of the procedure is the cost of the device. In a recent article on mitral valves it was reported that an executive from Tendyne Holdings, Inc. stated the price of their mitral valve will be equivalent to or greater than the current price for a prosthetic aortic valve, which is approximately USD $30,000. The infrastructure requirements for this procedure would be the same as those needed for a transcatheter aortic valve implantation (TAVI). While TAVI procedures are performed in Australia, there is no diagnosis-related group (DRG) listed for them.

Training would be required in order to perform transcatheter mitral valve replacement, even for those who have performed TAVI procedures, due to the greater technical challenges associated with the complex anatomy of the mitral compared with the aortic valve.

Ethical, cultural, access or religious considerations

No ethical, cultural, access or religious considerations for transcatheter mitral valve replacement were identified.

Evidence and Policy

Safety and effectiveness

Three prospective case series studies (level IV interventional evidence) were identified for inclusion in this technology brief. The studies represent the first clinical evaluations of three different transcatheter mitral valves. An overview of the studies is provided in Table 2.
Table 2  Included study characteristics

<table>
<thead>
<tr>
<th>Study/location</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Length of follow-up, number of patients and losses to follow-up</th>
<th>Conflicts of interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bapat et al 2014</td>
<td>Patients with high surgical risk and severe MR and NYHA Class II symptoms or greater who were considered poor candidates for MitraClip (Abbott Laboratories, Illinois, USA) based on anatomical findings. In addition, patients were required to have a native annular diameter distance measuring between 30 and 44 mm, a posterior leaflet length of &gt;0.5 cm and an anterior leaflet length &lt;2.3 cm as assessed by echocardiography</td>
<td>Able to have mitral valve surgery or percutaneous mitral valve repair with MitraClip. Other exclusions included patients with leaflet prolapse in the P2 segment, mitral regurgitation that is predominantly commissural and a small left ventricle</td>
<td>Length: maximum of 76 days n=5 Losses: 0</td>
<td>Five of the 16 authors are consultants for Edwards Lifesciences, the valve manufacturer</td>
</tr>
<tr>
<td>Sondergaard et al 2015</td>
<td>Symptomatic severe MR and class IV heart failure</td>
<td>Able to have mitral valve surgery or percutaneous mitral valve repair with MitraClip</td>
<td>Length: maximum of 90 days n=3 Losses: 0</td>
<td>One of the authors is a consultant for the valve manufacturer, CardiAQ Valve Technologies Inc.</td>
</tr>
<tr>
<td>Chueng et al 2014</td>
<td>End-stage ischaemic cardiomyopathy and severe functional MR</td>
<td>Able to have mitral valve surgery or percutaneous mitral valve repair with MitraClip</td>
<td>Length: maximum of 69 days n=2 Losses: 0</td>
<td>One of the 8 authors is a consultant for Neovasc Inc. and another is the medical director of Neovasc Inc., the valve manufacturer</td>
</tr>
</tbody>
</table>

MR: mitral regurgitation; NR: not reported; NYHA: New York Heart Association; NR: not reported; USA: United States of America

Bapat et al 2014

This study describes the first five patients treated with the FORTIS transcatheter mitral valve. At least two of the patients were male and one was female. The sex of the other patients was not reported, nor was the age of any of the patients. The device was inserted via a transapical approach in high surgical risk patients with severe MR and New York Heart Association (NYHA) class II symptoms or greater. Patients were assessed by a heart team consisting of cardiothoracic surgeons and cardiologists who deemed that the risk with conventional mitral valve surgery was too high. The longest reported follow-up time was 76 days post-implantation.

Effectiveness and safety

The device was successfully implanted in all five patients. In two patients there was no evidence of residual MR and in another two there was minimal or trace MR after the procedure. MR after implantation was not reported in the fifth patient, although it was
stated that the implantation was smooth and an excellent result was obtained. Three patients survived beyond 30 days and two patients were alive at the time of reporting, although the length of time between implementation and reporting was not provided. Three of the five patients died. The first patient, who was discharged on day 15, was readmitted on day 37 with signs of heart failure and died on day 76 post-implantation. The 30-day follow-up assessment of this patient revealed marginal improvement despite having only minimal MR after the procedure. The second patient had a technically difficult procedure because of an apical aneurysm that made it difficult to place the purse-string access in a suitable position. The patient developed acute renal failure on day one and required re-intubation for pulmonary oedema on day two. Despite aggressive treatment the patient died on day four. Trans-oesophageal echocardiography revealed increasing MR and some valve displacement. The third patient was discharged on day nine, but was readmitted on day 15 with cardiac decompensation, abdominal pain and systemic inflammatory response syndrome. Echocardiography demonstrated reduced leaflet mobility in two of the three leaflets. Antibiotics and heparin were commenced but the patient died on day 15 post-implantation.

Both of the surviving patients were discharged on day six. It was reported that they continued to slowly improve. The study did not state the length of the follow-up period for the surviving patients.

Sondergaard et al 2015

A consecutive series of three patients with a Society of Thoracic Surgeons mortality score greater than 22 per cent were selected for transcatheter mitral valve implantation with the CardiAQ device. The patients ranged from 78 to 89 years in age; two were female and one was male. The device was inserted via a transapical approach using fluoroscopy and trans-oesophageal guidance.

All patients had symptomatic severe MR and were deemed unsuitable for mitral valve surgery or percutaneous mitral valve repair. Trans-oesophageal echocardiography and cardiac multi-slice computed tomography were used to determine patient suitability. Anatomical features taken into consideration were: mitral annulus diameter (<40 mm was preferred to minimise the risk of paravalvular leak after implantation); the presence of a very acute aorto-mitral angle, which would potentially increase the risk of left ventricle outflow tract obstruction; and the presence of sub-valvular calcification.

Patient comorbidities included previous coronary artery bypass surgery (n=2), severe pulmonary hypertension (n=1) and moderate to severe chronic renal failure (n=3). The follow-up period varied between patients, with the longest being 90 days.
Effectiveness and safety

Accurate positioning and deployment of the CardiAQ transcatheter mitral valve was achieved in all three patients. Two of the patients spent 14 days in hospital. The third patient died in hospital on day nine post-procedure due to severe hospital-acquired pneumonia. An autopsy revealed no prosthesis-related complications. Longer term follow-up results are described in Table 3.

Table 3  Follow-up of patients after transcatheter mitral valve replacement surgery

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patient 1 (day 90)</th>
<th>Patient 2 (day 60)</th>
<th>Patient 3 (day 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residual MR</td>
<td>Trace</td>
<td>Trace</td>
<td>Trace</td>
</tr>
<tr>
<td>Valve function</td>
<td>Stable position, normal function</td>
<td>Stable position, normal function</td>
<td>Stable position, normal function</td>
</tr>
<tr>
<td>Leaflet motion</td>
<td>Some restriction</td>
<td>Unrestricted</td>
<td>Unrestricted</td>
</tr>
<tr>
<td>Valve gradient</td>
<td>2 mm Hg</td>
<td>2 mm Hg</td>
<td>3 mm Hg</td>
</tr>
<tr>
<td>LVOT gradient</td>
<td>PG 8 mm Hg, MG 4 mm Hg</td>
<td>PG 10 mm Hg, MG 5 mm Hg</td>
<td>PG 10 mm Hg</td>
</tr>
<tr>
<td>LV function</td>
<td>Normal</td>
<td>40%</td>
<td>&lt;20%</td>
</tr>
<tr>
<td>LV apical pseudoaneurysm</td>
<td>Not present</td>
<td>Not present</td>
<td>Not present</td>
</tr>
</tbody>
</table>

LV: left ventricle; LVOT: left ventricular outflow tract; MG: mean gradient; MR: mitral regurgitation; PG: peak gradient

Cheung et al 2014

This study described the first two cases of transcatheter mitral valve implantation for MR using the Tiara device. The valve was implanted transapically in a woman aged 61 years and a man aged 73 years. Both patients had severe functional MR, NYHA class IV heart failure with depressed left ventricular ejection fraction (15% to 25%), pulmonary hypertension and additional comorbidities. Both patients were assessed by a multidisciplinary heart team who deemed that the risk with conventional mitral valve surgery was too high. Percutaneous repair with a MitraClip was also ruled out for anatomical reasons. The maximum follow-up period was two months following the implantation of the device.

Effectiveness and safety

Postoperatively, a left ventricular angiogram showed no significant MR and an invasive pressure measurement confirmed an unobstructed left ventricular outflow tract in both patients. Repeat transthoracic echocardiograms in both patients on day four, and at one and two months post-implantation demonstrated normal valve function, with no evidence of thrombus formation, paravalvular leakage or left ventricular outflow tract obstruction.

The 61-year-old patient was discharged five days after treatment and had significant improvements after two months in brain natriuretic peptide levels, 6-minute walk test results and NYHA functional class.
The 73-year-old patient experienced an episode of post-haemodialysis hypotension on postoperative day 21, which required cardiopulmonary resuscitation and re-intubation. The patient recovered and was discharged five weeks post-implantation. At 2 months the patient had recurrent heart failure. A repeat transthoracic echocardiogram revealed poor left ventricular function, although the valve prosthesis was functioning well and had eliminated the MR. Despite this, the patient experienced cardiac failure and died on day 69 post-procedure.

**Economic evaluation**
No economic evaluation studies on transcatheter mitral valve implantation were identified.

**Ongoing research**
A total of five clinical trials on transcatheter mitral valves were identified from a search of ClinicalTrials.gov and the Australian and New Zealand Clinical Trials Registry (Table 4). Four of the trials were recruiting and one had not started recruiting; all were case series studies.

**Other issues**
At the time of writing this technical brief, Edwards Lifesciences had temporarily halted its clinical trial of the FORTIS valve because of evidence of valve thrombosis. This valve was used in one of the studies discussed in this brief.

All three studies had one or more authors who were consultants to the company who produced the valve used in the study.

It should be noted that there is interest in using transcatheter mitral valve replacement for the treatment of other mitral valve disorders, such as mitral stenosis (clinical trial NCT02370511).

**Number of studies included**
All evidence included for assessment in this technology brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT web site.

Total number of studies: 3
Total number of Level IV studies: 3

**Search criteria to be used (MeSH terms)**
(mitral regurgitation) AND ((transcatheter mitral valve implantation) OR transcatheter mitral valve replacement)

**Literature search date**
27th July 2015
<table>
<thead>
<tr>
<th>Study Location</th>
<th>Design</th>
<th>Number of patients</th>
<th>Intervention</th>
<th>Primary outcomes</th>
<th>Trial status (Estimated completion date)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT02276547 United States of America, Belgium, Canada</td>
<td>Single or multicentre</td>
<td>30</td>
<td>Transcatheter mitral valve replacement (TMVR) with the Tiara valve</td>
<td>Freedom from all-cause mortality and major adverse events defined as disabling stroke, myocardial infarction, renal failure requiring dialysis, life-threatening bleeding and cardiac surgical or transcatheter reintervention</td>
<td>Recruiting (December 2015)</td>
</tr>
<tr>
<td>NCT02428010 Poland</td>
<td>Single centre</td>
<td>10</td>
<td>TMVR with the Twelve valve</td>
<td>Adverse events</td>
<td>Recruiting (September 2016)</td>
</tr>
<tr>
<td>NCT02478008 Denmark, France, the Netherlands, United Kingdom</td>
<td>Single or multicentre</td>
<td>60</td>
<td>TMVR with the CardiAQ valve (transapical approach)</td>
<td>Composite major adverse event rate</td>
<td>Recruiting (December 2016)</td>
</tr>
<tr>
<td>NCT02515539 United States of America</td>
<td>Single or multicentre</td>
<td>20</td>
<td>TMVR with the CardiAQ valve (transfemoral and transapical delivery systems)</td>
<td>Composite major adverse event rate</td>
<td>Not yet recruiting (July 2021)</td>
</tr>
<tr>
<td>NCT02321514 United States of America, Australia</td>
<td>Single or multicentre</td>
<td>30</td>
<td>TMVR with the Tendyne Bioprosthetic Mitral Valve System</td>
<td>Safety assessed by freedom from device or procedure related adverse events Performance assessed by freedom from device malfunction</td>
<td>Recruiting (July 2016)</td>
</tr>
</tbody>
</table>
References


Transcatheter mitral valve replacement for severe mitral regurgitation: December 2015 13


14. Mirabel, M., Lung, B. et al (2007). 'What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery?'. European heart journal, 28 (11), 1358-65.


