Minimally invasive off-pump valve-in-a-ring implantation: the atrial transcatheter approach for re-operative mitral valve replacement after failed repair

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Abstract

Objective: Based upon recent developments in transcatheter technology, this study was designed to evaluate the feasibility and haemodynamic performance of transcatheter valve-in-a-ring (VinR) implantation for potentially failed mitral repair using a minimally invasive, transatrial, off-pump approach. Methods: Adult sheep (54.3 ± 3.0 kg) underwent mitral valve repair with a 26 mm complete annuloplasty ring (PhysioTM) using standard conventional techniques. To simulate the redo operation, a transcatheter 23 mm pericardial prosthesis (Edwards SapienTM) mounted on a balloon-inflatable steel stent was deployed within the annuloplasty ring. VinR implantation was performed off-pump under rapid pacing in four and on-pump in three animals using an antegrade transatrial approach under fluoroscopic guidance. Results: Transcatheter VinR implantation was successful in all seven sheep. Mean transvalvular gradient was 4.9 ± 0.3 mmHg. VinR function was excellent with no leak in one, good with mild leak in five (trans-stent: four, paravalvular: one) and sufficient with moderate central leak in one animal, respectively. Valve deployment required 10.0 ± 0.7 min and all transcatheter prostheses were confirmed in good position on postmortem analysis, without any signs of valve dislocation or embolisation. In an in-vitro model, the minimum force required to dislodge the valve was 32.9 ± 5.2 N, which was well above the normal estimated forces generated by the left ventricle. One animal was kept alive to assess mid-term outcome and is still well 12 months after the VinR implantation. Conclusions: Transatrial, transcatheter mitral VinR implantation is feasible using a minimally invasive off-pump approach. VinR implantation is a promising concept for re-operative surgery for selected patients after failed mitral valve repair.

Keywords: Mitral valve; Minimally invasive; Transcatheter valves; Redo surgery

1. Introduction

Mitral valve repair is the optimal therapy for patients with acquired mitral regurgitation and is associated with a significantly better long-term outcome compared to mitral valve replacement. Superiority of mitral valve repair has also been demonstrated for high-risk patients suffering from chronic ischaemic mitral regurgitation (IMR). The most common surgical approach to repair IMR is a downsizing mitral annuloplasty usually combined with coronary revascularisation. Despite acceptable early mitral valve repair results long-term outcome in this particular high-risk subgroup is poor with frequent progression of left ventricular failure and high rates of recurrent mitral regurgitation [1]. Several groups have shown that up to 30% of patients experience late recurrence of severe recurrent mitral regurgitation [2,3]. On the other hand it has been clearly demonstrated that re-operative mitral valve replacement in these high-risk patients is associated with a substantial risk for mortality, reaching as high as 30% [2].

Based upon recent developments in transcatheter technology, the valve-in-a-valve (VinV) concept is now a promising option for high-risk patients requiring re-operative procedures due to degenerated bioprosthesis [4,5]. We have recently demonstrated feasibility of the VinV technique in humans [6]. The idea of implanting a transcatheter bioprosthesis off-pump within the annuloplasty ring could turn out to be an elegant option in patients suffering from failed mitral repair.

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(VinR) implantation for potentially failed mitral repair using a minimally invasive, transatrial, off-pump approach.

2. Material and methods

2.1. Study design

After obtaining approval from the local research ethics board, seven adult sheep (54.3 ± 3.0 kg) were included in this trial. All animals were treated according to the institutional guidelines for the care of laboratory animals. All procedures were performed with general anaesthesia under the care of a veterinarian and standard haemodynamic monitoring was applied. All values are reported as mean values ± SEM.

2.2. Implantation of the conventional annuloplasty ring

A 26 mm complete rigid annuloplasty ring (Physio™, Edwards Lifesciences, Irvine, California) was surgically implanted via a left lateral thoracotomy in all sheep using standard techniques.

2.3. Transcatheter off-pump VinR implantation

A 23 mm Edwards Sapien™ transcatheter pericardial xenograft 9000 (Edwards Lifesciences, Irvine, California) was used in all animals. The size of the transcatheter prostheses was selected after in-vitro laboratory testing (Fig. 1, Edwards Lifesciences laboratories, Irvine, California). The transcatheter implantation proceeded in the following manner (Fig. 2): (1) the left atrium was punctured and using fluoroscopic guidance, a 0.035 in. Amplatz superstiff guidewire (Boston Scientific, Natick, Massachusetts) was introduced from the left atrium into the left ventricle; (2) a 33 Fr introducer sheath was then placed over the guidewire into the left atrium. The Sapien™ valve was then positioned within the annuloplasty ring under fluoroscopic guidance; (3) anchoring of the valved stent was then performed by active balloon dilatation under rapid ventricular pacing (170 beats/min).

2.4. Haemodynamical and morphological assessment

Epicardial echocardiography (5 MHz transducer, Vivid i, GE Healthcare, Munich Germany) was performed to assess flow velocity, transvalvular gradients and to detect potential para- or transvalvular prosthetic insufficiency (Fig. 3). In addition, left ventriculography was performed for confirmation of VinR function (Axiom Sensis, Siemens, Munich Germany). Postmortem, the hearts were excised and the position of the transcatheter delivered prosthesis was examined macroscopically. To test the stability of its anchoring within the annuloplasty ring, the forces needed to dislodge the VinR from the left ventricle to the left atrium were measured using a Newton meter.

![Fig. 1. (A) Angiography of the left ventricle with the Physio™ annuloplasty ring in the mitral position. (B) Exact positioning of the transcatheter prosthesis. (C, D) Deployment by balloon-inflation. (E, F) Final result after VinR implantation.](image1)

![Fig. 2. Valve-in-a-ring: Edwards Sapien™ transcatheter valve within Edwards Physio™ annuloplasty ring.](image2)

![Fig. 3. Two-dimensional epicardial echocardiography demonstrating the transvalvar gradients across the implanted valve-in-a-ring.](image3)
Table 1
Mitrval VinR function according to angiographic and echocardiographic measurements. Severity of mitral regurgitation (grade) was assessed by left ventriculography and location was assessed by epicardial echocardiography.

<table>
<thead>
<tr>
<th>Animal number</th>
<th>VinR deployment</th>
<th>MR grade</th>
<th>MR location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Successful</td>
<td>1</td>
<td>Trans-stent</td>
</tr>
<tr>
<td>2</td>
<td>Successful</td>
<td>1</td>
<td>Paravalvular</td>
</tr>
<tr>
<td>3</td>
<td>Successful</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>Successful</td>
<td>2</td>
<td>Trans-stent/central</td>
</tr>
<tr>
<td>5</td>
<td>Successful</td>
<td>1</td>
<td>Trans-stent</td>
</tr>
<tr>
<td>6</td>
<td>Successful</td>
<td>1</td>
<td>Trans-stent</td>
</tr>
<tr>
<td>7</td>
<td>Successful</td>
<td>1</td>
<td>Trans-stent</td>
</tr>
</tbody>
</table>


3. Results

3.1. Implantation of the conventional annuloplasty ring

Conventional mitral annuloplasty with a 26 mm Carpentier-Edwards Physio™ ring (complete, rigid) was successfully performed without complication in all animals. Mean duration of cardiopulmonary bypass was 34.9 ± 4.8 min. After weaning from bypass, left ventriculography and epicardial echocardiography revealed excellent function of the implanted annuloplasty ring with only trace transvalvular leak in one animal. Transvalvular pressure gradients (P\text{max} = 6.2 ± 2.4 mmHg; P\text{mean} = 3.3 ± 1.1 mmHg) and transvalvular flow velocities (V\text{max} = 1.2 ± 0.2 m/s; V\text{mean} = 0.8 ± 0.1 m/s) were low.

3.2. Valve-in-a-ring implantation off-pump

All transcatheter valves were successfully implanted within the radiopaque rigid annuloplasty ring in a good position without distal or proximal dislocation. In one animal, the valve was deployed too far to the atrium, resulting in a moderate trans-stent leakage (Table 1). After termination of rapid pacing, all animals were haemodynamically stable. At the time of haemodynamic assessment (echocardiography and angiography), all animals were stable off-pump. Mean arterial pressure was stable after VinR implantation with 61 ± 2.8 mmHg (baseline 72.7 ± 2.2 mmHg) and a central venous pressure of 12.3 ± 0.8 mmHg (baseline 11.1 ± 0.7 mmHg). Epicardial echocardiography and aortic root angiography revealed no detrimental effect on the aortic valve after deployment of the transcatheter mitral valve. Compared to the conventional prosthesis, the transvalvular pressure gradients (P\text{max} = 10.5 ± 1.0 mmHg; P\text{mean} = 4.9 ± 0.3 mmHg) and flow velocities (V\text{max} = 1.5 ± 0.1 m/s; V\text{mean} = 0.9 ± 0.1 m/s) of the VinR were marginally higher compared to baseline after annuloplasty. In all sheep, the delivery sheath was removed and the atrial access site safely closed without complication. Mean procedure time from puncture of the left atrium, deployment of the VinR to sheath removal was 10.0 ± 0.7 min.

Postmortem examination confirmed secure positioning of the transcatheter prosthesis within the conventional annuloplasty ring in all animals. Using a Newton meter the forces needed to dislodge the valve-in-a-ring were measured at a mean of 32.9 ± 5.2 N, with a range of 19.1–48.3 N.

4. Discussion

Over the last two decades, mitral valve repair rather than replacement has become the standard approach in patients with mitral regurgitation. Several studies have clearly demonstrated the superiority of mitral valve repair over replacement [7,8] including elderly patients [9]. Despite the poor long-term prognosis of some higher risk subgroups including IMR, improved survival after repair rather than replacement in high-risk subgroups of patients with chronic mitral regurgitation has been demonstrated [10].

Current results indicate that the durability of mitral valve repair for leaflet prolapse are comparable to the durability of mechanical valves, leading to a low number of patients requiring redo surgery [8]. In contrast, due to the progression of left ventricular failure, durability of mitral repair in patients suffering from chronic ischaemic mitral regurgitation is limited [1]. Recurrence of significant mitral regurgitation has been reported in up to 30% of patients at 6 months [2,3,11]. On the other hand it has been clearly demonstrated that re-operative mitral valve replacement in high-risk patients is associated with a substantial risk for mortality, reaching rates up to 30% [2]. Therefore a less invasive approach for re-operative mitral valve surgery might be beneficial in this high-risk population.

Re-operative mitral valve surgery can be performed by using a lateral minithoracotomy thus avoiding repeat sternotomy [12]. However, most of these approaches are being performed on-pump. In contradiction transcatheter approaches for heart valve therapy aim at a further reduction in the invasiveness by avoiding cardiopulmonary bypass. Current concepts of percutaneous edge-to-edge repair or percutaneous annuloplasty are at an early stage of clinical development. It is questionable whether they will be an option in the setting of a failed surgical repair in high-risk patients with chronic ischaemic mitral regurgitation.

Off-pump transcatheter aortic valve implantation has gained increasing acceptance in high-risk patients using the retrograde transfemoral [13] or the antegrade transapical [14] approach. Furthermore after experimental testing transapical valve-in-a-valve implantation has been successfully introduced into clinical practice in patients with degenerated xenografts [4,6].

Transcatheter replacement of the native atrio-ventricular valves is not a clinical reality yet due to several technical problems arising from the large size and irregular shape of the annulus, potentially resulting in complications with prosthesis fixation and perivalvular leak. Nonetheless, two acute animal studies have been published pioneering feasibility of transcatheter valve implantation in the native mitral [15] and tricuspid [16] position using a custom-made nitinol stent. In cases where a degenerated bioprosthesis or a complete rigid annuloplasty ring was already implanted in the mitral position, anchoring of a transcatheter delivered valve seems to be technically feasible. Thus, mitral valve-in-a-valve implantation has been performed using the retrograde transapical [4] or the antegrade transatrial approach [5]. Despite proven feasibility and safety of the transapical access itself, when addressing the mitral position, the transatrial approach offers some specific advantages: (1) the ease of antegrade crossing, (2) atrial access site is less prone
to bleeding complications and (3) more linear and co-axial angle to the mitral valve.

In summary, a transatrial, antegrade, transcatheter VinR implantation is feasible in an experimental model using an off-pump technique. The valve-in-a-ring concept is the first truly minimally invasive technique for the surgical treatment of recurrent mitral regurgitation after failed ischaemic mitral repair. By avoiding repeat sternotomy, cardiopulmonary arrest and cardiopulmonary bypass, the VinR technique may lower the potentially higher mortality rate of re-operative mitral replacement in selected high-risk patients after failed surgical repair. Based on our experience reported here, we believe the VinR technique is ready for human application in selected high-risk patients.

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References


Appendix A. Conference discussion

Dr D. de Canniere (Brussels, Belgium): The geometry of the ring and the valve, they are, of course, different. And could you correlate the amount of trace MR or higher grade MR to the situation of the valve in the ring so that the distortion of maybe 2 leaflets of the valve is more common if it is in a certain position, or was there no correlation?

Dr Kempfert: You’re absolutely right. The shape of a mitral annuloplasty ring is oval. Now, if you implant a Sapien valve as a valve-in-a-ring in it, the annuloplasty ring and the new valve will result in an almost completely circular shape. But having said that, almost completely circular means that the shape of the new valve is not 100% circular. Now it depends on the rotation of the valve inside the ring. If the rotation is not optimal, then you might end up with a cusp prolapse causing central transvalvular leak. Unfortunately, as you all know, with the Sapien valve at present it is impossible to control the rotation of the valve.

Dr J. Gummert (Jena, Germany): I have a question about the indication. It’s a very nice and inventive application and niche market for the percutaneous valve therapy. And as you pointed out in the introduction of your presentation, of course, ischaemic mitral regurgitation is a different disease. It’s a ventricular disease. And maybe this is the reason why the results of surgical valvuloplasty are not so good, 25% at 2 years, 45% at 5 years.

So my question would be, do you think there are real indications? Because if you have a failure 5 years after a mitral repair in coronary patients, do you still hope to treat your reverse remodelling of those ventricles? I mean, do we need to do something to these patients? Or are we going to affect the prognosis, and therefore is there a real, except in very large centres with high volumes like yours, are there many indications out there, do you think?

Dr Kempfert: You’re right, we will probably not see a great number of these patients, but given the high mortality rate, if a re-operation has to be performed, and it is performed in many centres on a routine basis, there seems to be at least an indication in selected patients. Therefore I believe that this technique might really improve the outcome, especially because it avoids cross-clamping, which in my opinion is critical in these patients with left ventricular failure prone to low cardiac output syndrome after cross-clamping. Probably the most frequent indication for the transcatheter technique will be a valve-in-a-valve procedure in patients with a degenerated bioprosthesis.

Dr Gummert: One comment, though, I think it’s very nice that you can preserve the apparatus of the mitral valve completely in this case actually. So you don’t have to bother to do certain things if you do, for instance, conventional valve replacement. So here you have the compete apparatus and you have a competent valve, that’s maybe even an interesting concept for other cases as well.