Percutaneous implantation of a valve in the descending aorta in lambs

Y. Boudjemline¹ and P. Bonhoeffer²

¹Service de Cardiologie Pédiatrique, Hôpital Necker Enfants Malades, Paris, France; ²Cardiothoracic Unit, Great Ormond Street Hospital, London, U.K.

Aims We assessed the feasibility of percutaneous implantation of a valve in the descending aorta and its function in systemic pressures.

Methods and Results A biological valve harvested from a bovine jugular vein was sutured into a stent. After the creation of aortic insufficiency, the valved stent was percutaneously implanted into eight lambs divided into two groups depending on the severity of the insufficiency created. Haemodynamic and angiographic evaluations were carried out. Anatomical evaluation was finally performed. Aortic insufficiency was created: four lambs had mild insufficiency and four massive insufficiency. A valve was successfully implanted in all and were functioning perfectly in the early follow-up. Despite this competence, animals with massive insufficiency died within 24 h following implantation. None of the animals with mild insufficiency died. The valve was functioning perfectly in the first 2 months following the implantation, but became incompetent after spontaneous healing of the wound of the aortic valve.

Conclusion Percutaneously implanted valves in the descending aorta of lambs with aortic insufficiency function well in the early follow-up. This technique might become an interesting alternative to the standard approach in patients in whom perioperative risk is high.


Introduction

In the early 1950s, before the era of extracorporeal circulation, Hufnagel et al.¹ surgically implanted a mechanical valve in the descending aorta. By relieving about 75% of the total regurgitant flow, this ingenious technique was efficient in patients with severe chronic aortic insufficiency. However, with the development of extracorporeal circulation, native valve replacement became the conventional treatment, making Hufnagel’s technique a forgotten entity. More recently, the development of interventional cardiac catheterization has made percutaneous valve implantation possible²-³. To date, the percutaneous approach is limited to the pulmonary valve. The challenge is now to extend this technique to the other cardiac valves and in particular to the aortic valve. The position of the coronary orifices considerably complicates the percutaneous approach of this valve. Here, we report on the implantation of a newly designed prosthesis in the descending aorta in lambs with controlled aortic valve insufficiency. This is the first step towards left sided percutaneous implants.

Methods

Preparation of the device

A naturally valved venous section harvested from the bovine jugular vein (Medtronic) was selected and prepared. The venous wall was trimmed to remove the unnecessary material and to reduce the overall wall thickness of the device. This segment was then sutured along the commissures with a 7-0 polypropylene thread into a platinum–iridium stent pre-expanded to 18 mm (Numed). The valved segment was then dissected again along the commissures (Fig. 1). However, sufficient material and in particular the supporting structure of the leaflets, was respected to allow safe attachment to the stent and to avoid structural insufficiency. This device was finally cross-linked with a buffered saline solution.
containing glutaraldehyde. Before implantation, the pre-expanded valved stent was immersed for three 5 min cycles and carefully soaked in a physiological saline solution to remove glutaraldehyde. The size of the device when fitted on the delivery system was 16 Fr.

**Preparation of the animals**

Eight lambs weighing 30 kg underwent catheterization for transcatheter valve implantation in the descending aorta. All animals were treated according to European regulations for animal experimentation[4]. Anaesthesia was induced with 10 mg . kg⁻¹ of thiopental and maintained with halothane. The right carotid was then prepared for catheterization. Heparin (100 UI . kg⁻¹) was administered once. First, aortic insufficiency was created in all the lambs, which were then divided into two groups depending on the severity of the aortic insufficiency. We aimed to implant a valved stent into the descending aorta of all the animals. After the procedure, the right carotid was preserved if possible to allow for repeated catheterization. Animals were discharged with low-molecular-weight heparin and low-dose of aspirin once a day.

**Creation of controlled aortic insufficiency**

A guide wire was positioned in the aortic root through the right carotid. A Mullins sheath was then advanced into the area of the native aortic valve and precisely placed, using timely contrast injections, in front of one leaflet. A trans-septal needle was inserted into the Mullins sheath and advanced with the sheath into the left ventricle through the leaflet. A guide wire was inserted in the sheath after the retrieval of the trans-septal needle. A balloon catheter was finally loaded on the guide wire, advanced and inflated in the perforated leaflet. An 18 or 10 mm balloon catheter was used to create a hole and severe or a mild aortic insufficiency.

**Deployment strategy**

The implantation strategy was the same in the two groups. A guide wire was introduced and positioned in the descending aorta through the right carotid. After rinsing (see below), the valved stent was then crimped down on the outer balloon of the delivery system and covered before its skin insertion (Fig. 2). The delivery system was loaded onto the guide wire and advanced into the descending aorta. The valved stent was then uncovered and deployed by subsequently inflating the inner and the outer balloons. The expansion of the balloons fixed the device to the wall of the aorta. The balloons were finally deflated and retrieved with the delivery system leaving the valved stent in the deployed position.

**Competence evaluation**

The left ventricular and aortic pressures were measured before and after the onset of the insufficiency and after implantation. Angiographies were performed before the procedure to define the anatomy of the aortic root, after the onset of the insufficiency to evaluate its severity and after implantation to verify the position and the function of the implanted valve. Haemodynamic and angiographic studies were repeated each month if animals were still alive.

**Graft retrieval and anatomic study**

All grafts were explanted at the death of the animals. When the explantation was programmed, heparin (300 . UI . kg⁻¹) was administered before harvesting. The valved stent was then harvested with a section of the descending aorta, and rinsed to remove excess intraluminal blood. All grafts were inspected and the competence of the valve was grossly tested by passing a fluid in the graft. All hearts were dissected and inspected macroscopically.

**Results**

Creation of aortic insufficiency was successful in all lambs. Four had the creation of a massive aortic
insufficiency and four a mild insufficiency haemodynamically and angiographically. All lambs received a valved stent in the descending aorta just after the departure of the brachio-cephalic trunk. The valved stents were expanded at a mean diameter of 20 mm (± 2 mm). All implanted valves were perfectly competent in the early evaluation.

Animals with severe aortic insufficiency

The mean transvalvular gradient at the closure of the valve was 50 mmHg (± 5 mmHg). All animals had tachycardia after the implantation. Lambs with massive insufficiency died within 24 h (12 ± 3 h) following implantation. At autopsy, macroscopic examination of the explanted valves confirmed the good function of all implanted valves and showed normal left ventricular volume. Examination of the aortic valve revealed a complete tear of one leaflet, explaining the severity of the insufficiency (Fig. 3).

Figure 3 Anatomical view showing a complete tear of one leaflet in a lamb with massive aortic insufficiency.

Figure 4 Anatomical view showing the scar healing the wound in a lamb with mild aortic insufficiency.

Animals with mild aortic insufficiency

The mean transvalvular gradient at the closure of the valve during diastole was 10 mmHg (± 3 mmHg). No elevation of the diastolic left ventricular pressure was noted in this group. None of the lambs with mild insufficiency died. All animals were strictly asymptomatic during all the follow-up. Cardiac catheterization at 1 and 2 months confirmed the good function of the implanted valves and the persistence of aortic insufficiency in all animals. At 3 months aortic insufficiency had disappeared but none of the implanted valves were competent. At autopsy, examination of the native valve showed a fibrous scar on one leaflet, rendering the native valve perfectly competent (Fig. 4). This scar was found in all lambs. Macroscopic examination of the valved stents also confirmed the incompetence of all implanted valves (Fig. 5). At histology, these valves were totally or subtotally covered by an intimal proliferation that impinged their function.
Discussion

The history of aortic valve replacement began in the early 1950s when Hufnagel et al. first reported the successful implantation of a valve[5]. They surgically implanted a mechanical valve in the descending aorta. Its insertion did not require cardiac arrest or extracorporeal circulation, methods which were not available at this time. This pioneering surgery was performed in patients with severe chronic aortic insufficiency. In these patients, valve insertion into the descending aorta was estimated to relieve 75% of the total regurgitant flow, leading to considerable improvement of the clinical status[5]. The long-term results were also good with this palliative technique. However, with the development of extracorporeal circulation, orthotopic valvar replacement became the technique of choice and this ingenious technique became a forgotten entity.

We recently reported the successful implantation of a biological valve in the pulmonary position using a percutaneous approach in animals[2] and in humans[3]. Our biological valve is harvested from the bovine jugular vein. Preliminary in vitro testing simulating pulmonary hypertension showed that this valve was competent at high pressures (data not shown). This encouraged us to use this valve as a substitute for aortic valve replacement. The anatomical configuration of the aortic root considerably complicates implantation in a native position through a percutaneous technique, making aortic valve replacement easier in the ectopic position.

Like Hufnagel et al., we hypothesized that the implantation of a valve in the ascending aorta between the coronary arteries and the truncus brachio-cephalicus would lead to rapid myocardial ischaemia by the impairment of the coronary flow. Indeed, in diastole, at the closure of the valve, the blood volume between the prosthetic and natural valves would be too low to allow for satisfactory coronary perfusion. Further, the insufficiency of the native valve would worsen the situation due to preferential regurgitant flow into the left ventricle. We therefore decided to reproduce, through a percutaneous approach, Hufnagel’s experimentations and to implant a valve in the descending aorta in a model of modulated aortic insufficiency.

Despite the excellent feasibility and the perfect function of implanted valves, we were unable to reproduce Hufnagel’s results in the group of animals with massive aortic insufficiency. Indeed, all these animals died rapidly after the implantation. Because we relieved most of the regurgitant flow, we attributed the death mainly to the functional impairment of the coronary flow usually seen in acute aortic insufficiency[6-11]. We did not measure the regurgitant volume or the coronary flow, which would have confirmed this hypothesis.

Interestingly, in the group of animals with mild insufficiency, the valve, as expected, was functioning during the first 2 months following the implantation. After that, the aortic insufficiency disappeared secondary to the healing of the wound we created on the valve leading to the failure of the implanted valve. We obtained the same findings in our previous report[2] when the devices were implanted in the pulmonary trunk, not impinging on the function of the native valve. In those cases, acute testing showed the perfect function of the implanted valves. Two months later, however, these valves were entirely covered by an intimal proliferation. Interestingly, the removal of this tissue showed non-altered and perfectly functioning valves underneath the layer of tissue, excluding the hypothesis of incompetence secondary to rejection. This problem does not occur in the animal and human experience where a valve is implanted in the absence of a functioning native valve.

This confirmed our hypothesis that minimal back flow is necessary for any implanted valve to work durably and that unused valves are rapidly covered by tissue that impinges the function of the valve.

The device we developed here could be easily implanted in humans through the femoral artery in patients in need of surgery but where surgery is not an option because of associated pathologies and high co-morbidity[12]. According to Hufnagel et al., the implantation of such a valve in the descending aorta just beyond the origin of the left subclavian would lead to improvement of left ventricular function and thus of the clinical status. However, no data are yet available on the long-term function of the venous valve under systemic pressures. These studies are obviously needed before considering human application. This type of technique has, however, the advantage of permitting successive implantations in case of degeneration by simply implanting a new valve inside the first one. This would allow stabilization, or improve left ventricular function and the clinical status of severely ill patients and/or lead to conventional valve replacement with lower mortality.

In conclusion, the opportunity to implant a valve in the descending aorta through a percutaneous approach would be helpful in patients in whom surgical aortic valve replacement is risky. Further improvements are obviously needed before considering the implantation of such a device in a native position.
The authors thank Allen Tower, Mike Martin, and Douglas Villanave for their technical expertise, supports and encouragements. The study would not have been possible without the grants of the ‘Fondation de l’Avenir’ and the ‘Fédération française de Cardiologie’, Paris, France. The research was carried out in the Centre d’Expérimentation et de Recherches Appliquées, Paris, France.

References


