OBJECTIVES

We report on the Doppler-assessed regulation of an adjustable pulmonary artery band (PAB) in an animal model and in our first group of patients.

BACKGROUND

Indications for pulmonary artery banding have expanded to include patients requiring a late arterial switch. A telemetry-operated, fully implantable, adjustable PAB system (FloWatch-PAB, EndoArt SA, Lausanne, Switzerland) has been developed to facilitate these operations.

METHODS

The device was implanted in 13 minipigs (age one to five months, weights 3.2 to 12.0 kg). The main study was performed on nine minipigs with adjustments of the PAB at implantation and at 1, 3, 5, 8, and 12 weeks after, assessed by Doppler pressure gradients. Explanation was performed 12 weeks after surgery. A long-term histology study (6 months and 14 months after surgery) was done on the other four minipigs. After approval by the ethics committee, the device was implanted in eight patients with weights between 2.8 and 9 kg to decrease pulmonary blood flow and pressure and to retrain the left ventricle before arterial switch. The device was progressively tightened, with increasing transband Doppler gradients. Follow-up was one to three months.

RESULTS

An excellent correlation between transbanding systolic pressure gradient and degree of PAB constriction was encountered in the minipig study as well as in the human setting. No early or late deaths or reoperations occurred. Malfunction of the device was noted in three of 21 implanted devices. Two were related to surgically inflicted damage at implantation and one to an electronic problem that was fixed by resetting the control device.

CONCLUSIONS

The device offers a Doppler-controllable adjustment of pulmonary blood flow. It permits controlled tightening and release of the band, which improves perioperative and postoperative courses and decreases surgical interventions to adjust tightness of the band. It allows a protracted occlusion protocol, which may provide the best effect on retraining the left ventricle. (J Am Coll Cardiol 2004;44:1087–94) © 2004 by the American College of Cardiology Foundation

The indications for pulmonary artery banding (PAB) traditionally include patients with multiple ventricular septal defects (VSDs) and patients with complex heart disease and increased pulmonary blood flow in which the pulmonary vascular bed needs to be protected while awaiting later surgical repair (1). The indications for PAB have recently expanded, including patients requiring a late switch operation because of late referral or previous atrial palliation (2).

Traditionally, the band is placed around the pulmonary artery (PA) during an operation and tightened progressively to achieve a distal PA pressure that is ideally one-half to one-third of the systemic pressure (3). The intraoperative conditions, however, not infrequently prevent an optimal tightening of the band. The reasons for this are the different hemodynamics under general anesthesia, the perioperative instability of the patients, and the inability of the ventricle to deal immediately with the increased workload. This combination of factors may induce an important risk of complications during the perioperative and postoperative course, which could even lead to surgical interventions to either tighten or open the band sufficiently (4–6).

A telemetry-operated, completely implantable, adjustable PAB was used to facilitate these operations (7). This study reports on the initial experience with the FloWatch implanted in minipigs and compares it to that of our first group of patients.

METHODS

Material used. A new adjustable PAB implant (FloWatch-PAB, EndoArt SA, Lausanne, Switzerland) was used in this study. The banding is adjusted using a passive telemetry system operating at 27 MHz requiring the use of an external control unit (Figs. 1 and 2).

Animal investigation. Animal study was performed after approval by the Animal Ethics Committee of the “Société Vétérinaire du Canton de Vaud” (No. 14131, 24.04.01). The FloWatch was implanted in 13 minipigs age one to five months, divided into two groups, one for the main Doppler study (nine minipigs) and the other for the histology study (four minipigs). The weight of the minipigs in group 1 was...
5.1 ± 1.5 kg at implantation (range 3.4 to 6.9 kg) and 12.7 ± 3.7 kg at explantation (range 19.4 kg). For group 2 the weight was 12 ± 0.4 kg at implantation. The implantation around the main PA was performed through a left thoracotomy with the pigs under general anesthesia.

**ANIMAL DOPPLER STUDY.** The main study was performed on nine minipigs (group 1). The device was implanted and adjustments were performed with Doppler gradient measurements at implantation and at 1, 3, 5, 8, and 12 weeks after implantation. Each time the FloWatch was completely opened, then tightened stepwise in 10% increments until the gradient started to decrease, which was interpreted as a sign of impending right heart failure. The device was then completely reopened and tightened again to the desired position. At each step the transbanding pressure gradients were measured by Doppler. The FloWatch was explanted at 12 weeks by median sternotomy with the subjects under general anesthesia, and the pigs were destroyed. The explanted device underwent testing to ensure its functionality, and histology was performed on the PA and the surrounding capsule.

The measurements at implantation were performed with the pigs under general anesthesia with isoflurane. For all the other adjustments the piglets were sedated with Ketaminol 10% (25 mg/kg im). The animals were placed under a heating lamp to maintain body temperature and kept on room air. Continuous wave Doppler echocardiography was performed with the pigs in the supine position from the parasternal short axis view using a commercially available echocardiography system and a 3.5 MHz mechanical transducer. The cursor was placed across the center of the device to obtain the maximum and mean velocities. Each measurement was repeated three times and averaged (8).

**LONG-TERM HISTOLOGY STUDY.** This was performed in three minipigs six months after implantation (group 2) and in one minipig 14 months after implantation. After explantation the PA was observed macroscopically, then sliced, stained, and assessed in a microscopically qualitative and semi-quantitative manner to characterize local tolerance parameters.

**Human investigation.** After approval by the Research Ethics Committee of the Medical Faculty of the University of Lausanne (No. 44/02, 08.04.02) for implantation in humans, the FloWatch was implanted in eight patients. The characteristics of the patients are listed in Table 1. Additional procedures performed at the same time as FloWatch implantation included patent ductus arteriosus ligation in Patients 1, 3, and 4 and division of the anterior arch in Patient 2. The device was implanted by left lateral
thoracotomy in Patients 1 and 2 and by median sternotomy in the others. The FloWatch was tightened stepwise over a period of several weeks with increasing transband Doppler gradients. The measurements were performed with continuous wave Doppler in the parasternal short axis view using a 7.5-MHz or 5-MHz phased-array transducer with the cursor aligned parallel to the PA in the center of the device to get the maximum velocity. The Doppler measurements were made by the same cardiologist for all the patients. Three measurements were obtained at each adjustment and averaged. Follow-up was from one to three months. Adjustments were performed on average six times per patient (range 1 to 12) with 65% of the adjustments performed in the first week, 20% in the second week, and 15% within three months after implantation. Ninety-two percent of the adjustments were made to tighten the band; in 8% to release it. No early or late mortality occurred and no reoperations were required because of the device, but device dysfunction occurred in two patients.

Statistical analysis. All data were expressed as mean ± SD. Comparisons were made with student t test. Differences were considered to be significant for p < 0.05.

RESULTS

Animal investigation. Animal doppler study. One of the nine piglets included in the Doppler study died suddenly of unknown cause three weeks after implantation. The last measurements had been performed one week before death and had shown a maximum gradient of 31 mmHg. The device was tightened at 35% at time of death. Autopsy showed no etiology and the device was functioning normally. One other device did not react to the programmed regulations at any time after implantation. A perforation of the membrane covering the piston of the device, occurring most likely at implantation, was found at explantation. An important corrosion of all the electromechanical parts inside the device, which was caused by contact with body fluid, explains this absence of reaction. These two minipigs were therefore not included in this study.

Figure 3 shows recordings of the systolic transbanding pressure gradient measured on a given pig. This figure illustrates that over time the pressure gradient increases and that the rate of this increase could be modulated by the chosen degree of FloWatch regulation: between weeks 3 and 5, the cardiovascular adaptation was greater than between weeks 1 and 3 because of the important degree of tightening during this period (35%, as opposed to 20% between weeks 1 and 3). However, if we compare the evolution of all seven minipigs (Fig. 4), a remarkable difference exists between the regulation range of the FloWatch and the resulting Doppler pressure gradients at implantation (week 0) and after 1, 3, 5, 8, and 12 weeks. In week 0 only a limited response to tightening is registered, whereas at 5, 8, and 12 weeks, the achieved gradient with the same regulation range of the device is significantly increased. An excellent correlation between the systolic pressure gradient and the percentage stroke of the device could be established.

Another way to measure the efficacy of the device is to plot the evolution of the gradient regulation range (Fig. 5). This graph shows that the regulation range (range between white squares and white dots) increases significantly with time. In all seven minipigs, the PA re-expanded completely after removal of the FloWatch. This suggests that a surgical reconstruction of the PA may be avoided. The explanted devices were all functioning and the PA and device-surrounding capsule were analyzed. The results were identical to those in the animal histology study.

Animal histology study. The weight of the three minipigs in the six months group (group 2) at explantation was 25.1 ± 3.2 kg (mean ± SD) and 40.5 kg for the one minipig evaluated after 14 months. At explantation it was shown that the adjustability of the FloWatch was still effective in all four minipigs (strong response of the transbanding gradient) and thus that the fibrotic tissues do not alter the possibility to activate and adjust the device. Each FloWatch was found to be encapsulated in a fibrotic

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Diagnosis</th>
<th>Age at Implantation [weeks]</th>
<th>Weight at Implantation [kg]</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>CAVSD</td>
<td>4.5</td>
<td>3.5</td>
</tr>
<tr>
<td>2</td>
<td>Multiple VSDs/double aortic arch</td>
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<td>6.44</td>
</tr>
<tr>
<td>3</td>
<td>Multiple VSDs</td>
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<td>4.2</td>
</tr>
<tr>
<td>4</td>
<td>Univentricular heart</td>
<td>10.2</td>
<td>3.7</td>
</tr>
<tr>
<td>5</td>
<td>d-TGA</td>
<td>4.6</td>
<td>3.24</td>
</tr>
<tr>
<td>6</td>
<td>VSD/arch hypoplasia</td>
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<td>DORV/straddling TV</td>
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<td>8</td>
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<td>6</td>
</tr>
<tr>
<td>Median</td>
<td></td>
<td>10</td>
<td>3.95</td>
</tr>
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</table>

CAVSD = complete atrioventricular septal defect; DORV = double-outlet right ventricle; d-TGA = d-transposition of the great arteries; TV = tricuspid valve; VSD = ventricular septal defect.
capsule. No device was found to have migrated or rotated around the artery. In addition, the fibrotic capsule was as thin and smooth as those found around pacemakers (Fig. 6). In the minipig at 14 months, the device was removed as would be done during a standard surgical repair. This removal was very easy and caused no damage to the PA. The PA re-expanded completely after removal of the device and the explanted devices were all functioning normally. The macroscopic analysis of the PA and of the device-surrounding capsule showed no major abnormal signs. The pacemaker-like capsule was 2- to 4-mm thick. The PA

Figure 3. Example of systolic transbanding pressure gradient as a function of FloWatch regulation range as obtained in one minipig. At implantation (week 0) the FloWatch was adjusted to get the curve. Afterward, the degree of adjustment was set to 20% (= starting working point, in white). After one week, natural growth and cardiovascular adaptation lead to the second curve (= arrival working point, in black). After full-range regulation to get the curve, the degree of regulation was again set to 20% (= working point). Two weeks later, a slower cardiovascular adaptation leads to the third curve. Then the degree of adjustment was increased to 35% (= starting working point, in white). This augmented load induces an important cardiovascular adaptation, which leads to the curve at week 5 (solid line). At week 5, the degree of regulation was diminished to 20%, which induces no more cardiovascular adaptation for the following 7 weeks.

Figure 4. Systolic transbanding pressure gradient in function ofFloWatch regulation range for the minipig Doppler study. Only points with at least five measurements for the same adjustment range are represented in the graph. Error bars indicate SD (5 ≤ n ≤ 7). Solid lines are a mathematical fit based on a hemodynamic model of stenosis.

Figure 5. Evolution of the systolic transbanding pressure gradient range of the minipig Doppler study. White squares = situation with the FloWatch fully open (degree of regulation set to 0%, corresponding to the left end of each curve in the example on Fig. 3); white circles = maximum values tolerated by the minipig (corresponding to the right end of each curve in the example on Fig. 3); black diamonds = working points (corresponding to the gray working points of each curve in the example on Fig. 3). Error bars indicate SD (6 ≤ n ≤ 7).
showed no thrombus, but generally exhibited a limited folding and thickness narrowing in the area compressed by the FloWatch. The microscopic analysis showed a device-surrounding capsule infiltrated with some macrophages and few lymphocytes or giant cells. Lymphocytes were usually located at the material interface. The microscopic analysis of the PA showed some alterations of the media including limited degenerative signs. In two cases the reduction of PA wall thickness was 50%. The neointima was always interrupted: in several segments of the PA endothelial cells were not visible.

**Human investigation.** There are clearly two different patterns of results, depending on the indication for PAB. The first is to retrain the left ventricle in transposition of the great arteries when the left ventricle has involuted. As is pictured in Figure 7, these curves most closely match the pig study. This figure shows the slowly increasing gradients with increasing percentage stroke over time and the consequently increasing left ventricular wall thickening, with simultaneous stabilization of the gradient occurring around four weeks after implantation.

The second pattern is summarized in Figure 8, which groups all patients in whom the FloWatch was placed to decrease pulmonary blood flow and pulmonary pressures. In these patients the subpulmonary ventricle had already been subjected to a significant volume overload and the possibility to use the right-to-left shunt as an escape mechanism. In these patients the adaptation was much quicker with the possibility to tighten the device more rapidly without risking ventricular failure. In two cases malfunction of the device was noted. In Patient #3 (at 55% occlusion and a gradient of 135 mm Hg), reopening had to be done with the patient under general anesthesia (to ensure a better coupling). After this complete reopening, a 70 mm Hg residual gradient remained which allowed the patient to continue his growth course. Surgical correction was performed three months later, at which time the device was explanted. Post-explantation evaluation of the device showed a perforated...
membrane, which probably occurred at implantation and caused the problem. In Patient #6 the occlusion of the device was gradually increased to 55% with a gradient of 70 mm Hg, at which point it was noticed that the device could be tightened but released only with difficulty. This was due to a communication problem between the device and the control unit and could be modified by resetting the parameters of the microchip card of the control unit without having to explant the device.

DISCUSSION

Pulmonary artery banding is a palliative operation and is used in a variety of heart lesions (1,9–12). Two categories of patients benefit from this operation: those with an excess of pulmonary blood flow and a subsequent increased PA pressure, who cannot undergo a complete repair in infancy (univentricular hearts, multiple VSDs of the Swiss Cheese type) and those with left ventricles requiring retraining to be able to sustain high pressures (late arterial switches) (2,13–15). The difficulty with the traditional band lies in achieving a tight enough band during surgery (6,16,17). This issue is complicated by the altered hemodynamics during anesthesia, the intraoperative instability or cyanosis of the patients, and the inability of the ventricle to cope with the suddenly increased workload. A number of these patients will therefore require a second operation either to tighten or loosen the band.

In the wake of the trend to perform late switches on patients with either a previous atrial palliation or in patients presenting late for an initial arterial switch, preparative PAB has been advised to retrain the left ventricle (2,13–15). Various techniques to do this have been described (18–26). Mee (2) described a partly exteriorized banding, which allowed gradual tightening in the intensive care during the
first days after the operation. This gradual tightening of the band allowed an optimal preparation of the left ventricle for its new role after the subsequent switch operation. This observation parallels the results in the animal study, where a rapid closure of the banding resulted in a lower gradient caused by relative pump failure of the untrained ventricle, whereas gradual tightening over weeks resulted in a better ventricular performance and thus a larger gradient. The study in minipigs demonstrates very well the relationship between the adjustments of the band, the Doppler gradients, and the gradual tightening of the FloWatch. The transposition patient seems to parallel this observation. A second advantage of the gradual narrowing of the band might be located in the type of hypertrophic response of the ventricle. Bauer et al. suggest that a gradual, protracted, and stepwise increase of ventricular pressure loading will in contrary to an acute one, allow the maintenance of the cascade of messenger ribonucleic acid for a longer time, which would allow more useful trophic alterations, such as neoangiogenesis and myosin increase, to occur (27). The left ventricular retraining, as suggested by Mee (2) for ventricles without off-load capabilities such as VSDs finds an optimal and sterile substitute in the telemetrically operated banding device described in this study.

Banding of the pulmonary artery in the presence of a VSD or in single-ventricle anatomy, as off-load capability for the right ventricle, occurs in a totally different hemodynamic situation, which allows the tightening of the banding to be performed faster. The major advantage of the FloWatch here is in its reopening capability. As was shown in the animal study and in several patients, the device can be reopened gradually in adaptation to the natural growth. This allows a tight banding early on to prevent congestive heart failure and a gradual reopening accompanying growth, pending the ideal moment for surgical correction. The closure and reopening capacity of the FloWatch, as shown in Figure 5, proves to function well and to cover the range required for patients in need of PAB. Moreover, the pacemaker-like fibrous capsule surrounding the FloWatch never prevented the device from being adjusted, even after a 14-month follow-up. Finally, no dangerous injury to the PA or surrounding structure has been observed in any animal experiment. Thus, the long-term safety and reopening capability of the device should allow for reopening the banding gradually in adaptation to the natural growth, as has already been shown in some patients.

This differentiated use of the device will eventually result in various implanting and adjustment protocols for the selected indications. The indications for the use of the FloWatch might also be extended once the experience grows. One of these indications might include patients with aortic arch hypoplasia and VSD to allow spontaneous growth of the arch while congestive heart failure is being prevented and the pulmonary vascular bed is protected (28).

Limitations of this study include the relatively small number of minipigs included in the animal investigation, which allowed only the implementation of one protocol and prevented extensive comparison of various time schedules used in the tightening of the PA. In addition, only a limited number of invasive flow and pressure measurements were performed in order to improve survival of the experimental animals. This leaves Doppler studies as the predominant “gold standard.” The human study group is small and consists of a varied group of diagnoses and indications, preventing meaningful statistical analysis; however, the initial results of the European trial are encouraging (29). Finally, it is important to realize that device failure has been a problem which should be solved; the membrane especially seems to be prone to puncturing, and surgeons should pay specific attention to this at implantation.

**CONCLUSIONS**

The described technology of progressive, noninvasively controllable adjustment of pulmonary blood flow in the animal model and in a variety of forms of congenital heart disease permits not only accurate tightening, but also release of the pulmonary banding if required. This will allow improvement of the perioperative and post-operative course of these patients and may prevent multiple surgical interventions to adjust the tightness of the PAB. The animal study suggests that in patients without a ventricular decompression option (i.e., a VSD), a protracted occlusion protocol may be the safest and provide the best effect on retraining of the ventricle.

**REFERENCES**

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