New Device for Closure of Muscular Ventricular Septal Defects in a Canine Model

Zahid Amin, MD; Xiaoping Gu, MD; James M. Berry, RDMS; John L. Bass, MD; Jack L. Titus, MD; Myra Urness, MS; Young-Min Han, MD; Kurt Amplatz, MD

Background—Repair of muscular ventricular septal defects (MVSDs) has always been challenging to the surgeon. Long-term morbidity and mortality are significantly increased if the defects are closed via left ventriculotomy or if they are associated with other complex congenital anomalies. The purpose of this study was to close MVSDs with the Amplatz ventricular septal defect device. This device is constructed from 0.004-in nitinol wire mesh filled with polyester fibers. It is retrievable, repositionable, self-centering, and of low profile.

Methods and Results—MVSDs were created with the help of a sharp punch in 10 dogs. The location of the defects was anterior muscular (n=3), midmuscular (n=3), apical (n=3), and inlet muscular (n=1). The diameter of the defects ranged from 6 to 14 mm. All defects were closed in the catheterization laboratory. The device was placed with the help of transeosophageal echocardiography and fluoroscopy. A 7F sheath was used to deploy the device from the right ventricular side in 8 and the left ventricular side in 2 dogs. Placement was successful in all animals. The complete closure rate was 30% (3/10) immediately after placement and 100% at 1-week follow-up. Pathological examination of the heart revealed complete endothelialization of the device in dogs killed after 3 months.

Conclusions—The Amplatz ventricular septal defect device appears highly efficacious in closing MVSDs. The advantages include a small delivery sheath, complete retrievability before release, and the fact that it is self-centering and self-expanding, thereby making it an attractive option in smaller children. (Circulation. 1999;100:320-328.)

Key Words: catheterization ■ heart defects, congenital ■ heart septal defects ■ surgery

Intraoperative closure of muscular ventricular septal defects (MVSDs) can be very tedious and difficult. After surgery, the incidence of residual defects is high, especially if the defect is located in the apical or anterior muscular septum.1,2 Right ventricular trabeculations make visualization of the defect more difficult. These defects may be approached through the right atrium, right ventricle, or left ventricle.3-4 A left ventriculotomy allows for optimal exposure, but severe left ventricular dysfunction has been associated with this approach, and some of these patients have subsequently been placed on the transplant list.1,5 Muscular and conoventricular septal defects have been closed in the catheterization laboratory with different devices.6-9 Most of these devices were designed for closure of atrial septal defects (ASDs) and patent ductus arteriosus, and the results have been less than optimal. In this report, we describe our experience with a new device that was specifically designed to close the MVSD in a canine model (Figure 1).

Methods

The Amplatz ventricular septal defect (VSD) device was constructed from 0.004-in nitinol wire, modified from the basic design of the ASD device.10 Nitinol is a shape-memory alloy composed of nickel (55%) and titanium (45%). It is biocompatible and has superelastic properties.11-14 The device was woven to form 2 disks with a connecting waist. The diameter of the waist corresponds to the size of the VSD, and the length of the waist matches the thickness of the ventricular septum (Figure 1). The wire is woven in such a way that the outer convex surface of the disk would become slightly concave (rather than bulge outward) after deployment. The flange measures 3 to 7 mm. Unlike the Amplatz atrial septal occluder, both disks have the same diameter (Figure 1). The device was braided with polyester fibers to enhance thrombogenicity. It has a microscrew on one end for attachment to the delivery cable and was designed to collapse before introduction into the delivery catheter. The steps involved in preparing and loading the device before its deployment have been explained elsewhere.10

Creation of MVSD

All animals were cared for in accordance with the guidelines published by the National Institutes of Health “Guide for the Care and Use of Laboratory Animals” (NIH publication No. 80-23, revised 1985). In addition, all aspects of animal care were in accordance with the standards of the Institutional Animal Care and Use Committee of the University of Minnesota. Fourteen adult mongrel dogs weighing 25 to 30 kg each were part of the study. An intravenous line was started, and the dogs received sodium thiopental 25 mg/kg. The dogs were intubated,
Figure 1. Amplatz MVSD device, shown in different sizes.

Figure 2. Epicardial echocardiogram still frame obtained from right ventricular free wall. Transducer is aimed anteriorly to show MVSD (A) close to inferior wall of right ventricle.
and anesthesia was maintained with a mixture of oxygen and 1% to 2% isoflurane. The dogs were prepared for surgery and draped in the usual sterile fashion. A median sternotomy was performed to enter the chest. After the pericardium was opened, 2 stay sutures were applied for gentle traction on the right ventricular free wall. The dogs received heparin 50 U/kg. A purse-string suture was placed on the left atrial appendage with 5-0 prolene. A left atriotomy was performed, and the index finger of the surgeon’s left hand was inserted through the atriotomy into the left ventricle. A small right ventriculotomy was performed between the traction sutures. A sharp punch instrument with a lock mechanism was inserted through the ventriculotomy, aiming toward the right ventricular apex. The punch diameter was 10 mm for the first 5 dogs and 12 mm for the remaining dogs. The punch was locked and withdrawn. In 4 animals, the procedure was repeated to increase the size of the VSD and to create an oval defect. The left atrial purse string was tied, and the right ventriculotomy was closed with running 5-0 prolene sutures. During the procedure, the dogs received packed red blood cells. An epicardial echocardiogram was obtained to assess the size and location of the defect (Figure 2). Hemostasis was achieved, and 2 chest tubes were placed. The sternum was closed with sternal wires. The subcutaneous tissue and skin were closed with Tyron and Dexon, respectively. The animals were extubated in the operating room. Chest tubes were removed on postoperative day 1 or 2. The animals received analgesics and antibiotics for 3 days after the operation.

Closure of MVSD

After the dogs had been allowed to recover from surgery for 3 to 6 weeks, they were brought to the catheterization laboratory. Under general endotracheal anesthesia, the right and left groins were prepared and draped in sterile fashion. A transesophageal probe was placed to measure the size of the VSD in diastole and the thickness of the septum. A cutoff was performed on the right and left groins to access the femoral vessels. Right and left heart catheterization was performed, and saturations were obtained to calculate left-to-right shunt. A pigtail catheter (Cook Cardiology) was passed retrogradely across the aortic valve, and a left ventricular angiogram was obtained to delineate the location of the defect (Figure 3). The pigtail catheter was removed, and a Cobra catheter (Medi-tech) was passed into the left ventricle with the help of a wire. The VSD was crossed, and a floppy wire (Cook Cardiology) was introduced through the catheter to the main pulmonary artery. A snare (Microvena Corporation) was introduced through the femoral vein and advanced into the main pulmonary artery. The floppy wire was snared and gently pulled out through the femoral vein. Thus, one end of the wire remained outside the body at the femoral artery side and the other at the femoral vein side.

A 7F delivery sheath was introduced over the wire across the defect. The wire was removed. The device was screwed to the delivery cable and drawn in the loader. The device was loaded in the delivery sheath and slowly advanced under fluoroscopic guidance. Once it was across the defect, fluoroscopy and transesophageal echocardiography were used to deploy the left disk by pushing on the cable. The sheath and the cable were then pulled toward the VSD until mild tension was felt and the echocardiogram revealed the disk approximating the left side of the muscular ventricular septum. While gentle traction was kept on the device, the sheath was withdrawn to release the right disk. The steps involved in deployment of the device are outlined in Figure 4. Fluoroscopy and transesophageal echocardiography verified optimal placement of the device. To check retrievability before release, the device was pulled back in the delivery sheath in 4 dogs after successful deployment.
No difficulty was encountered during this maneuver. The device was detached by rotating the delivery cable counterclockwise with a vise. The wire and the delivery catheter were removed. A pigtail catheter (Cook) was passed through the femoral artery and advanced to the left ventricle. A left ventriculogram was performed to assess closure of the defect after 30 minutes. A Berman angiographic catheter was introduced through the right femoral vein to obtain right heart saturations. The defect in 1 dog (dog 6) resembled the number 8. This dog required 2 devices for complete closure (Figure 5).

Two dogs underwent closure of the defect from the left ventricular side. After the septum was crossed with the Cobra catheter, an Amplatz stiff 0.035-in wire (Cook) was introduced into the main pulmonary artery. The Cobra catheter was removed and the delivery sheath introduced over the wire into the right ventricle. The wire was removed and the device introduced through the sheath into the right ventricle. The right ventricular disk was deployed first, and the rest of the device was deployed as outlined above.

All dogs underwent cardiac catheterization at 2 weeks, 1 month, and 3 months after placement of the device. Again, each animal was placed under general anesthesia, and vascular access was obtained through the femoral vessels. Right and left heart saturations were obtained, and a left ventriculogram was performed to check the position of the device and quantify any residual shunt. A transthoracic echocardiogram was performed before the dog was extubated (Figure 6).

Pathology
The animals were killed after 1 month (n=2) and 3 months (n=6) after device implantation. One dog (dog 6) was killed after 18 months. This dog had 2 devices placed. The heart, lungs, and great vessels were removed and fixed in a buffered physiological solution containing formaldehyde (10%) and glutaraldehyde (2%) and sent out for gross and microscopic examination. The devices from dog 6 were explanted, cleaned, and subjected to gross inspection, light microscopy, and scanning electron microscopy with ×3000 magnification.

Results
Fourteen dogs underwent creation of MVSDs. Two dogs died during the operation because of ventricular fibrillation. One dog died 4 days after creation of the defect before any intervention was performed. One VSD closed spontaneously 3 weeks after the surgery. Ten dogs had successful placement of the Amplatz device. The defects were located in the apical muscular (n=3), anterior muscular (n=3), midmuscular (n=3), and inlet muscular (n=1) region. The shape of the defects was round in 6 and oval in 4 dogs. The size of the defects at the time of creation and at the time of closure is outlined in the Table. One dog died of ventricular fibrillation 3 hours after placement of the device. The device was placed from the right ventricular side. The dog was
apparently healthy before the procedure. Thoracotomy revealed the right chest cavity to be filled with dark, unclotted blood. Presumably this was old blood from creation of the MVSD. A detailed pathological examination of the heart and lungs was performed by one of us (J.L.T.). There was no evidence of cardiac perforation or damage to the valves or pulmonary arteries. The device was in the optimal location, with the disks astride the defect. The left disk was fully expanded, but the right

Figure 5. Left, Left ventricular angiogram in dog 6; 1 device is in place. Shunt from large MVSD (white arrow) is evident. Asterisk indicates left ventricle. Right, Left ventricular angiogram in same dog after placement of second device. Defect is completely closed. Black arrows point toward 2 devices. Asterisk indicates left ventricle.

Figure 6. Transthoracic echocardiogram after placement of device in MVSD. Transducer was placed in left axilla. White arrow points toward device.
The disk was only partially expanded. This was the first dog in whom closure of VSD was attempted. Cardiac catheterization time was considerably longer (≈4.5 hours) in this dog than in the remaining dogs (<2 hours). This caused an increase in anesthesia time, blood loss, and cardiac manipulation. Cardiac manipulation also increased the chances of dysrhythmias. The dog developed ventricular fibrillation. The dog was resuscitated with cardioversion, epinephrine, and lidocaine but never reverted to sinus rhythm.

The technical success rate was 100% (10/10). The complete VSD closure rate was 30% (3/10) immediately after placement, 77% (7/9) after 1 week, and 100% (9/9) at the last catheterization. The dog with a figure 8–type VSD had complete closure after placement of the second device.

Hemodynamic data before closure of the VSD revealed a ratio of pulmonary to systemic blood flow (Qp/Qs) from 1.5:1 to 4.8:1 (mean, 2.8:1). Pulmonary artery systolic pressures ranged from 25% to 75% of systemic pressure. Qp/Qs after closure of the VSD was 1. The immediate residual shunt was minimal when the device waist was slightly shorter than the thickness of the septum and the diameter of the device slightly bigger than the VSD.

Pathology
Gross pathological examination of the dogs that were killed after 1 month revealed no evidence of dislodgement (partial or complete) of the device. The device was partially covered with a glistening, smooth, thin layer of endocardium (Figure 7). The endocardial layer over the device was not continuous with the surrounding septal endocardium. A small area over the device was devoid of endocardium in 1 specimen. In dogs that were killed after 3 months, there was complete coverage of the device with glistening endocardium (Figure 8); although wires were visible in 2 dogs, there was continuity between the endocardium over the device and the surrounding septal wall. No openings in or around the device were seen. A piece of the tissue covering the device was removed and examined under light microscopy. A thin layer of collagen covered with flat endocardial cells was seen. The endocardial cells were continuous with the surrounding endocardium. Gross microscopic examination of the lungs did not show any evidence of embolization or any other abnormality.

Gross examination of the explanted devices from animal 6 revealed no wire breakage or fracture of the device. Light microscopic (×40 magnification) examination of the wires revealed a smooth, shiny surface identical to a new device. Examination by scanning electron microscopy with ×3000 magnification revealed a relatively smooth wire surface with a granular texture, typical of the oxidized nitinol surface. There was no difference in surface texture between the control wire and the explanted wire (Figure 9). There was no evidence of corrosion.

<table>
<thead>
<tr>
<th>Dog</th>
<th>VSD Size at Creation, mm</th>
<th>VSD Size at Closure, mm</th>
<th>Results at Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>4</td>
<td>Died 3 hours later</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>6</td>
<td>Complete closure</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>6</td>
<td>Complete closure</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>6</td>
<td>Complete closure</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>7</td>
<td>Complete closure</td>
</tr>
<tr>
<td>6</td>
<td>10 (×2)</td>
<td>10 and 14</td>
<td>Complete closure</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>4</td>
<td>Complete closure</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td>4</td>
<td>Complete closure</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
<td>6</td>
<td>Complete closure</td>
</tr>
<tr>
<td>10</td>
<td>8</td>
<td>7</td>
<td>Complete closure</td>
</tr>
</tbody>
</table>

In dog 6, ×2 indicates 2 defects.

Figure 7. Device in situ 1 month after closure of defect. Wire frame is covered with glistening, gray endocardium. A small portion of the device is devoid of endocardium. Endocardium over the device is not continuous with endocardium over the ventricular septum.
Discussion

MVSDs are a challenging surgical problem. Trabeculations in the right ventricle can make closure difficult, and even with good intraoperative exposure, the risk of residual VSD is high. These defects, when associated with other complex anomalies, significantly increase morbidity and mortality. In a recent study, multiple VSDs were the only risk factors related to early mortality in patients who had double-outlet right ventricle. Kitagawa et al recently published the operative results of MVSD closure in 33 patients. Despite impressive results, 10 patients had residual VSDs, and 5 required reoperation. In addition, right or left ventriculotomy was used in 12 patients. Right ventricular apical incision may lead to right ventricular dysfunction and arrhythmias, and left ventriculotomy may lead to left ventricle dysfunction and failure.

Pediatric cardiologists have been interested in closing VSDs for several years. Multiple attempts to close MVSDs in the cardiac catheterization laboratory have led to moderate success. Most of the devices that have been used in the past required a large (>8F) delivery system. Additionally, these devices were originally designed for closure of ASDs. The ventricular septum is thicker than the atrial septum; therefore, a device that conforms to the size, shape, and contours of the VSD is more desirable. An ideal device would be one that has a simple delivery mechanism, can be delivered through a small delivery system, is self-centering and self-expanding, has a low profile, and is easily retrievable. The device used in the present animal model can be delivered through a 7F delivery sheath, has a very simple delivery mechanism, is self-centering and self-expanding, and is completely retrievable. Nitinol tends to conform to the shape of the defect because of its malleability. This is the first study in which an MVSD was closed with a device specifically constructed for closure of MVSDs. It has a slimmer profile than the Amplatzer (AGA Medical Corporation) ASD occluder. Its wider waist prevents deformity and hence decreases any chance of dislodgement of the device. The flange size can be as small as 5 mm, which keeps the outer rim of the device away from valves and the chordae tendineae.

In the present study, 2 defects were closed from the left ventricular side. Our recommendations, however, are that these defects be closed from the right ventricular side. Currently available catheters are stiff and may increase the chance of arrhythmias and damage to the aortic valve. In addition, introduction of a stiff wire to the pulmonary artery may increase risk of cardiac perforation. Once malleable delivery sheaths and catheters are available, closure from the left ventricular side will become an attractive option.

The size of the MVSD closed with the device in the present study changed during the cardiac cycle (smaller in systole and bigger in diastole). To minimize leakage, the deployed device corresponded to the diastolic measurement of the defect. This made the waist of the device squeeze during systole. Visual inspection of devices explanted after 18 months did not show any evidence of damage to the waist or any other part of the device. Light and electron microscopic examination did not reveal any corrosion. In addition, recent experiments have effectively proved that nitinol can dissipate more strain than steel alloy, and therefore, we do not anticipate an increased risk of fracture. Our current recommendation is to select the device that corresponds to the diastolic VSD diameter. If the defect is oval, the larger diameter should be used to select the device. This will prevent leakage and enhance endothelialization. We believe that once endothelialization has occurred, there is no danger of device embolization.

Recently, we reported successful closure of MVSD in an 8-month-old baby with this device. The defect was...
successfully closed in the operating room and measured 15×3 mm.

It is difficult to compare the Amplatz VSD device with other devices in a meaningful fashion. All other devices were designed for ASDs, whereas our device was specifically designed for MVSDs. Our device can be custom-built, if necessary, to close any size defect.

Angiographic and echocardiographic follow-up can be reliably used in patients who undergo device closure of VSDs. In one study,9 VSD location and size were determined by echocardiography and angiography and later confirmed intraoperatively. With these modalities, the thickness of the septum, size of the defect, and distance of the VSD rim from AV and semilunar valves can be measured. However, there is a possibility of

Figure 9. Scanning electron microscopy (×3000 magnification) micrographs of nitinol wire. A, Control. B, Wire removed from dog after 18 months. The relatively smooth wire surface with granular texture is typical of an oxidized nitinol surface. Surfaces appear identical.
underestimating the diameter of the defect by 2-dimensional echocardiogram and possibly overestimating the diameter by color flow echocardiography.

Anticoagulation was not used in this animal model. There was no incidence of any thromboembolic phenomenon. Oral anticoagulation, however, is recommended to prevent systemic embolization. Evidence of clot formation was seen in another study (Z. Amin, MD, et al, unpublished data, 1998) when a modified form of this device was used to close conoventricular septal defects.

In conclusion, we believe that the Amplatz VSD device will serve as a valuable tool in the future to close congenital MVSDs. It may also be useful in infarction-related VSDs, which carry a high mortality when closed in the operating room.26

Study Limitations

This study has several limitations. The defects were created iatrogenically and may not resemble congenital MVSD. Congenital MVSDs can have a serpiginous course and are frequently oval rather than round. In addition, there are multiple openings on the right ventricular side compared with 1 or 2 openings on the left ventricular side. Trabeculations on the right ventricular side may not allow the disk to expand fully and hence may render it unstable. Although we were able to create an oval defect in 4 dogs, they were not as complex as congenital defects can be.

We relied on the echocardiographic diameter of the VSD instead of angiographic diameter. We did not measure the diameter in the catheterization laboratory by balloon occlusion. Additionally, the punch used to create the VSD traversed the muscular septum obliquely, not perpendicularly, hence making the measurement difficult. Overall, this deficiency did not appear to affect the outcome of this study.

Because there was no incidence of device embolization in this study, it is not possible for us to speculate on the problems that may arise should this device embolize. In a few clinical studies,25 embolization of other devices after placement in the ventricular septum resulted in migration to the pulmonary artery. Future studies are needed to examine the effect of embolization and to assess retrievability after release of this device.

The dogs were followed up for only 3 months (excluding dog 6) in this study. We believe that studies with longer follow-up will serve as a valuable tool in the future to close congenital MVSDs. Additionally, the punch used to create the VSD traversal the muscular septum obliquely, not perpendicularly, hence making the measurement difficult. Overall, this deficiency did not appear to affect the outcome of this study.

Because there was no incidence of device embolization in this study, it is not possible for us to speculate on the problems that may arise should this device embolize. In a few clinical studies,25 embolization of other devices after placement in the ventricular septum resulted in migration to the pulmonary artery. Future studies are needed to examine the effect of embolization and to assess retrievability after release of this device.

The Acknowledgments

The authors are grateful to Dr Albert P. Rocchini for his valuable suggestions and support during the study. The authors are also grateful to Dr Julian I.E. Hoffman and Dr Phillip Moore for constructive criticism during preparation of the manuscript.

References


New Device for Closure of Muscular Ventricular Septal Defects in a Canine Model
Zahid Amin, Xiaoping Gu, James M. Berry, John L. Bass, Jack L. Titus, Myra Urness, Young-Min Han and Kurt Amplatz

Circulation. 1999;100:320-328
doi: 10.1161/01.CIR.100.3.320

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/100/3/320

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/