Transvenous Atrial Septal Defect Occlusion in Piglets With a “Buttoned” Double-Disk Device

E.B. Sideris, MD, S.E. Sideris, RN, J.P. Fowlkes, RDMS, R.L. Ehly, RT, J.E. Smith, RN, and R.E. Gulde, MD

The feasibility and safety of transvenous closure of atrial septal defects by a new device was tested in 20 piglets, in which atrial septal defects were created by foramen ovale dilatation with angioplasty balloons. The device was small enough to be introduced in a 7F or 8F sheath, and it measured 20–25 mm. It has no hooks and consists of a foam occluder from the left atrium and a counter-occluder from the right atrium, buttoned independently. The animals were observed by angiography and color flow mapping, and they were electively killed at various intervals up to 2 months after occlusion. The device was not thrombogenic and had endothelialized by 2–3 weeks. All atrial defects were found to be completely occluded. Complications occurred only with the first three prototype devices, including counter-occluder detachment, right atrial perforation, and need for double occlusion and pulmonary artery embolization. No such complications occurred in the last 17 experiments because of modifications of the device and operator experience. These observations showed the feasibility of occlusion of moderate-size atrial septal defects in piglets by a new device introduced through a small sheath. The method appears promising for potential human application. (Circulation 1990;81:312–318)

Attrial septal defect occlusion by a transcatheter device was first reported by King and Mills1 and later by Rashkind.2 However, the transcatheter techniques have not been accepted for clinical use because the early results were associated with complications and because of the undisputed success of surgery.3 With the recent strides of interventional cardiology, there appears to be a renewed interest in the transcatheter closure of intracardiac defects.4

In this study, we describe our experience with a newly designed device for the occlusion of artificially created atrial septal defects in piglets. The device was developed with the following objectives in mind. It should be small enough to be inserted transvenously through femoral veins of small children. It should not be thrombogenic. Its application should be simple enough to be performed by cardiologists competent in interventional procedures. It should have advantages over existing devices by relatively easy insertion and fewer associated complications.

Methods

Protocol

Atrial septal defects were created by foramen ovale dilatation with angioplasty balloon catheters in 20 piglets weighing 7–29 kg. The animals were heavily sedated by an initial dose of 10–20 mg/kg i.v. ketamine (100 mg/ml, Vetalar, Fort Dodge Laboratories, Fort Dodge, Iowa). The experiments were performed under sterile conditions. A femoral vein cutdown was performed under local anesthesia with 2% xylocaine, and the animals were heparinized (100 units/kg). A multipurpose marker catheter (Cordis, Hialeah, Florida) was introduced into the right atrium under fluoroscopy and was used to probe the foramen ovale. The marker catheter was used both for wire exchanges and dimension measurements after angiography. An angioplasty catheter (Olbert) with a balloon diameter of 10–12 mm was introduced over a 0.035-in. exchange wire into the left atrium, through the foramen ovale. Three dilatations were performed with dilute contrast material for inflation periods up to 30 seconds. The angioplasty catheter was subsequently replaced by a marker angiographic catheter,
and cineangiograms were obtained by injections of contrast material in the left atrium or the pulmonary artery (Figure 1A). The creation of the septal defect was also confirmed by Doppler echocardiography and color flow mapping with an 880 Phase Array System (Irex) that used a 3.5-MHz transducer. On only two occasions, oximetry was used for shunt estimation. Fifteen of the 20 defects were occluded immediately after their creation. The effectiveness of the occlusion was confirmed by angiography and color flow mapping (Figure 1C). In five instances, the defects were occluded 7–10 days later with prior angiographic and color flow mapping confirmation of their size.

The Device

We used a “buttoned” occluding intracardiac defect device, designed and constructed by us (Figure 2A). Its main components are the occluder, the counter-occluder, and the loading wire. The occluder was made of polyurethane foam with a Teflon-coated 0.018-in. wire skeleton (Cook). The skeleton wires were floppy at the ends (2 mm) and stiffer in their central portion. The wires had an X-shape when unfolded and were nearly parallel in the introducing position (Figure 2B). A 2-mm string loop was attached to the center of the occluder while the loop was closed by a 1-mm knot (button). The counter-occluder was also made of foam in rhomboid shape with a Teflon-coated wire skeleton (Figure 2C). A rubber piece was sutured in its center. The “loading wire” in its final form consisted of a Teflon-coated outside part of a 0.028-in. guide wire (Cook) containing a double 0.005-in. Trilene thread that carried the occluder on one side and was tied on the other side.

In the first three experiments, the loading wire system contained a 0.007-in. floppy steel wire instead of the Trilene thread.

In 11 experiments, the diameter of the occluder was 20 mm, and in nine experiments, it varied from 22 to 25 mm (Table 1).

Procedure

A 7F or an 8F long sheath (Cordis) was introduced into the left atrium under fluoroscopy over a 0.035-in. exchange wire. The occluder was dipped into heparin solution, folded, and introduced into the long sheath. A 7F NIH catheter cut at the end was advanced over the loading wire until it pushed the occluder through the long sheath into the left atrium. The occluder resumed its original shape and was pulled gently against the atrial septum. The loading wire was threaded through the rubber piece of the counter-occluder that was introduced into the long sheath (Figure 2C). The counter-occluder was then...

FIGURE 1. Angiograms of experimental atrial septal defect creation and repair by the “buttoned” device. Panel A: Left atrial angiogram, showing an atrial septal defect created by a 10-mm diameter angioplasty balloon. Panel B: Buttoning of the device. It requires pulling the occluder against the left atrial septum and simultaneously pushing the counter-occluder against the right atrial septum with the long sheath. Panel C: Pulmonary angiogram after detachment of the device. The released device can be seen occluding the defect. COC, counter-occluder; D, device; LA, left atrium; LSH, long sheath; OC, occluder.
advanced by the pusher catheter, and the long sheath was withdrawn in the midright atrium. The counter-occluder was delivered into the midright atrium while still on the loading-wire axis in a fashion parallel to the atrial septum.

Buttoning involved the introduction of the 1-mm knot of the occluder (button) through the rubber piece of the counter-occluder (buttonhole). This is accomplished by pulling the occluder against the septum and pushing the counter-occluder with the end of the long sheath simultaneously (Figure 1B). If the attachment of the device was considered satisfactory, the loading wire was detached. The detachment involved cutting the end of the wire that was outside

FIGURE 2. The device. Panel A: Photograph of the actual device with the occluder, counter-occluder, and loading wire. Panel B: Diagram of the occluder, folded and expanded. Panel C: Diagram of the counter-occluder at rest and on the loading wire through the sheath. Panel D: Diagram of buttoning. The knot of the occluder (button) is through the rubber piece of the counter-occluder (buttonhole). The device is still attached to the loading wire by the double Trilene thread. Panel E: Diagram of detachment. The loading wire is cut outside the femoral vein and is pulled over the double Trilene thread. The thread is pulled as a single strand, releasing the device. as, atrial septum; bt, button; coc, counter-occluder; fl, double thread; la, left atrium; Ish, long sheath; lw, loading wire; oc, occluder; PC, pushing catheter; ra, right atrium; rp, rubber piece.
the femoral vein just above the external knot of the double Trilene thread. Subsequently, the hollow wire was pulled out over the double Trilene thread, and the thread was pulled out as a single strand (Figure 2E). After the detachment of the device, pulmonary angiography and color flow mapping were performed (Figure 1C). The animals were returned to the “farm” after recovery.

Follow-up evaluation was performed by two-dimensional Doppler echocardiography and color flow mapping within 24 hours before the elective sacrifice. The animals were killed electively at 5 (three piglets), 10 (two), 15 (two), 20 (eight), 30 (four), and 60 days (one) after the occlusion of the defect with Euthanasia T-61 solution (Hoechst, Somerville, New Jersey). The heart and lungs were removed together and carefully examined. Subsequently, the right and the left atria were opened, and the occluded atrial septal defect and the remaining parts of the heart were examined.

The tissues were examined for degree of endothelialization, presence or absence of thrombi, endocardial trauma, perforations, and embolizations. The atrial portion of each heart was preserved in formaline solution for further study or photography (Figure 3).

### Results

#### Size of the Created Defects

All created defects approximated in size the diameter of the angioplasty balloon as assessed by angiography. In the five animals in which the occlusion was performed 7–10 days later, angiography or color flow mapping showed that the defect was still present. The crest of the defect could not always be delineated by echocardiography, but a variable shunt could be shown by color flow mapping in all instances.

In two animals, oximetry revealed a pulmonary to systemic flow ratio of 1.4:1 and 1.5:1, suggesting relatively small defects or decreased right ventricular compliance. Autopsy findings in two additional animals, one killed immediately after creation of the defect and another a week later, showed total destruction of the foramen ovale structure with a clean round opening equal in diameter to the angioplasty balloon used.

#### Follow-up and Efficacy of Occlusion

All defects appeared to be fully occluded according to angiography and color flow mapping performed immediately after occlusion. All animals except one

### Table 1. Summary of Experimental Information

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recovered from the procedure in good condition, eating well and thriving. In all animals, color flow mapping within 24 hours of their sacrifice showed complete occlusion and good cardiac function.

**Endothelialization and Thrombogenicity**

The device was found to be fully endothelialized in 13 of 15 animals that were killed 2 weeks or more after occlusion (Table 1). Endothelialization appeared to originate in the areas of direct pressure contact of the device to the atrial wall. The counter-occluder appeared to be endothelialized before the occluder. The portion of the device endothelialized last was the midleft atrial aspect of the occluder (nontouching surface).

Exposed areas of the wire were not endothelialized well. In those cases in which more than one occluder or counter-occluder was inserted, the endothelialization process was slower. The most distant parts from the atrial wall were the least covered by endothelium. An occluding device that was embolized in the lower lobe of the left lung was found to be fully endothelialized. A counter-occluder that was detached in the right atrium was partially endothelialized and was well attached to the right atrial wall. The device was not thrombogenic, even in areas of exposed skeleton wires or detached parts.

**Complications**

Complications occurred in the first three experiments and were mostly related in design imperfections or the inexperience of the operator.

*Detachment of the counter-occluder.* Detachment occurred in two cases. In one, the detached counter-occluder fell in the right atrium, and repeated attempts to remove it were unsuccessful and ended in atrial perforation and hemopericardium. In the other case, the detached counter-occluder was left in the right atrium and was partially endothelialized without other ill effects.

This problem did not reoccur with improvement of the releasing mechanism. The latter change consisted of replacing the central 0.007-in. floppy wire used in the first three prototypes with double Trilene thread. 

*Perforation of the atrial chamber.* One animal suffered atrial perforation and hemopericardium after the procedure and was killed after 5 days. 

*Double occlusion.* In the above cases with detachments, the atrial defect was probed by a wire, and the long sheath was positioned distally to the first occluder. A new occluder was released and pulled against the first one, and a counter-occluder was buttoned as usual. The defects were closed completely, and the animals did well. However, the triple device was bulky and poorly endothelialized.

*Pulmonary artery embolization.* In one case, a 7F long sheath was used with a device made with thicker skeleton wire. There was poor expansion of the occluder in the left atrium. The occluder was withdrawn into the right atrium, advanced into the right ventricle, and deliberately released. It embolized into the lower lobe of the left lung. The left lung remained fully expanded, and as mentioned before, the part was fully endothelialized. Subsequently, the atrial septal defect was occluded with a new device.

**Discussion**

The device described and applied in this study can be classified in the same category as the Rashkind occluders. It is made of polyurethane foam with a metal skeleton like the Rashkind occluders. However, unlike the Rashkind umbrella device, there are no hooks in our device. The previously known King and Mills device required a 23F introducer. A modified Rashkind double-disk device for closure of atrial septal defects is currently under investigation.
It requires an 11F sheath to be introduced, and all the components of the system are contained in the loading catheter. Our device is made of two independent disks, the occluder and the counter-occluder, which are introduced separately and are eventually buttoned together. The occluder has a folding skeleton, so it can be introduced directly into a 7F or 8F sheath. The size difference between occluder and defect ranged from 8 to 15 mm. However, a difference of over 12 mm is considered optimal to compensate for defect irregularity or excessive operator force. A small left atrial size poses an obvious limitation to the use of larger occluders and should be taken into consideration before an attempt is made. Sizing of the defect is of great importance. Also, the device should be applied in defects with adequate tissue around them like the typical secundum atrial septal defect. Otherwise, the procedure will result in partial occlusion of the defect. Even though we used 20–25-mm devices for 10–12-mm defects in animals ranging in weight from 7 to 29 kg and did not encounter problems, we cannot speculate on the cutoff defect size over which the method should not be applied. Clearly though, each case should be treated individually, and factors like accurate size of the defect, choice of the right size occluder, and left atrial size should be taken into consideration.

We believe that the absence of hooks may prevent endocardial injury or potential problems with the conduction system. The latter is more critical in the event that a similar device is used for the transcatheter occlusion of ventricular septal defects. One desirable feature of the device is the independent insertion of its components, which makes manipulation and application easier and safer. Moreover, reversal of the procedure is possible at all stages before the release of the device because it is made of flexible skeleton wires with floppy ends. Thus, if there is need for removal of the device after full expansion, this can be accomplished as follows. The device is first pulled to the end of the long sheath. Subsequently, the loading wire and the long sheath are pulled simultaneously. This results in flexion and collapse of the device while it is passing through the venous system. This maneuver has been performed several times with a femoral vein cut-down. However, the collapsed device could possibly be extracted through a larger sheath, percutaneously.

Endothelialization begins at the “touching” edges and the inside surface of the occluder and extends progressively to the entire device. These observations are in agreement with those of other investigators with the Rashkind occluder. According to their histologic studies, the occluder rapidly acquires a fibrin-platelet infiltrate and undergoes fibrous investment and incorporation that makes it impermeable, whereas within 10 days of placement, the polyurethane mesh stimulates a granulomatous inflammatory reaction. Similarly, in our series, the device was fully endothelialized in 13 of 15 animals with follow-up beyond 2 weeks. Indeed, the device was so well incorporated in the left atrial wall that it could not be removed without considerable force. Although our long-term observations are limited because only one animal was observed for 2 months, we believe on the basis of the available anatomic observations that the position of the buttoned device remains stable.

An argument can be made that acutely created defects may close by themselves. This study was not designed to quantify the long-term shunt size of the defects created by dilatation of the foramen ovale by angioplasty catheters. However, the anatomic observations made acutely and for a week later support the view that most of these defects remain open. Occlusion of larger defects is also technically feasible through the 8F sheath, since the sheath can accommodate larger folding occluders.

In a hypothetical clinical setting, no bed confinement would be necessary for the 2–3 weeks required for full endothelialization, and there would be no need for long-term anticoagulation. We believe that the initial complications observed in this study were due to imperfections of the prototype device or to inexperience of the operators, since initial complications were avoided in the last 17 experiments. However, based on the present animal work regarding the safety of the method, there are several precautions that should be considered before it is recommended for use in humans. Attention to sterility and aggressive heparinization are of great importance. The procedure should be interrupted and restarted if clotting or kinking of the sheath is suspected or if excessive resistance is found in advancing the occluder or counter-occluder. Excessive resistance in advancing the occluder or release into a pulmonary vein rather than the left atrium could prevent full expansion. Expansion is automatic, and it is caused by the resilience of the foam material or the elastic properties of the skeleton wires. If the defect is undersized and if a small occluder is selected, the occluder should be pulled out through a femoral vein cut-down and replaced by a larger occluder. If the whole device is pushed into the left atrium after vigorous buttoning, it also should be pulled out. However, introducing a second counter-occluder in the right atrium and buttoning it to the first occluder-counter-occluder complex should be an acceptable practice, since in the two cases observed, the only problem was a somewhat delayed endothelialization. In the highly unlikely situation where unbuttoning occurs after release (a complication that did not occur in the last 17 experiments) double occlusion should not be attempted because it creates a bulky and poorly endothelialized device. Instead, surgery should be performed. The method seems to have a wide safety margin, and we postulate that complications needing immediate surgical intervention will be extremely rare. Therefore, we believe that with proper instruction individual pediatric cardiologists can learn to perform the technique safely.
In comparison to surgical repair, transcatheter occlusion of atrial defects with the described device offers several obvious theoretical advantages: 1) No general anesthesia, thoracotomy, open heart surgery, chest tubes, or prolonged hospitalization is required. 2) No complications related to surgery, such as postoperative bleeding, arrhythmias, or pericardiotomy syndrome, are likely.

We should acknowledge, however, that the surgical repair of the atrial septal defect results in less than 1% mortality in experienced hands. Furthermore, pediatric cardiologists in many places do not catheterize simple atrial septal defects because the surgeon is able to recognize and correct possible associated partial anomalous pulmonary veins. A plan for transcatheter atrial septal defect occlusion requires the performance of a diagnostic cardiac catheterization to rule out the presence of anomalous pulmonary veins and to measure the size of the defect and the left atrium.

Clinical trials will prove whether this technique can stand the challenge of the effective and relatively safe alternative to surgery.

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References


KEY WORDS • septal defects • implants, artificial • angioplasty
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