Background—Our purpose was to describe a 13-year experience with patients undergoing transcatheter device closure of unrepaired congenital or postoperative residual ventricular septal defects (VSDs).

Methods and Results—Since 1989, 170 patients (median age, 3.9 years) have undergone catheterization for closure of 1 or more congenital (n = 92) or postoperative (n = 78) residual VSDs using successive generations of STARFlex-type devices. Outcomes included echocardiographic assessment of residual flow and device position, assessment of VSD shunt/severity, and adverse events. Among 168 patients in whom device implantation was performed, between 1 and 7 devices were placed per patient (median, 1), with multiple devices placed in 40%. There was a significant decrease in left-to-right shunting after device implantation (P < 0.001) and significant improvement in VSD size/severity, and device position proved stable. Of 332 adverse events, 39 were related to the device and 261 were related to the catheterization; all but 5 occurred in the periprocedural period. At a median follow-up of 24 months (0 to 154 months), 14 patients had died and 18 had device(s) explanted.

Conclusions—Congenital and postoperative VSD closure using STARFlex-type devices resulted in stable improvement in clinical status and decreased interventricular shunting. Although periprocedural events occurred frequently, late events caused by the device were rare. Transcatheter device closure is an effective management option for patients with complex muscular VSDs that are difficult to approach surgically and for postoperative residual VSDs. (Circulation. 2004;110:501-507.)

Key Words: catheterization ▪ heart septal defects ▪ ventricles

Although surgical closure remains the mainstay of treatment for most ventricular septal defects (VSDs), some defects cannot be adequately approached without a ventricular incision. Device closure is an attractive alternative for treatment of muscular defects within the apical or anterior ventricular septum. This is especially true in patients with associated complex congenital heart disease and/or multiple VSDs. Similarly challenging are postoperative residual VSDs, which are often clinically significant yet difficult to close surgically.1-6 Transcatheter device closure is an alternative strategy for management of both complex muscular and postoperative residual VSDs.

Since first reporting transcatheter closure of muscular VSDs in 1988,7 we have performed device closure as primary treatment for simple defects, as an adjunct to surgery in patients with more complex disease, and as a means to reduce shunting from postoperative VSDs without further exposure to cardiopulmonary bypass.8-10 To date, published reports of this approach are limited to small series with relatively limited follow-up.11-19 Since 1989, 168 patients with unrepaired congenital VSDs and postoperative residual VSDs have undergone transcatheter closure with successive generations of STARFlex-type devices as a part of approved regulatory trials. A subset of this experience was used to obtain FDA approval of the second-generation CardioSEAL device for closure of specific VSDs (NMT Medical Inc).

Methods

Patients

The study population consists of all patients who underwent transcatheter closure of unrepaired congenital VSDs or postoperative residual VSDs as part of studies conducted at Children’s Hospital, Boston, Mass, between February 1989 and September 2002. There were 2 cohorts of patients. The initial group of 74 patients (cohort 1, February 1989 to June 1995) was enrolled prospectively in regulatory studies conducted by C.R. Bard, Inc, to evaluate the performance of the Clamshell septal occluder (C.R. Bard, Inc), whereas the
database was created retrospectively in 1996. The more recent group of 96 patients (cohort 2, May 1996 to August 2002) is part of an ongoing regulatory study evaluating the CardioSEAL and STARFlex septal occluders (NMT Medical, Inc) in high-risk patients. Cohort 1 consisted of successful implantations only; cohort 2 included all implantation attempts. Data are included from 4 centers (Children’s Hospital, Boston, Mass; The Children’s Hospital of Philadelphia, Philadelphia, Pa; Rush Presbyterian–St Luke’s Medical Center, Chicago, Ill; and Columbia-Presbyterian Hospital, New York, NY) that have used these devices to close VSDs. Permission to perform the implantation procedures and to collect follow-up information was obtained from the appropriate institutional review boards.

Patients were referred by a primary cardiologist for consideration of device closure of the VSD. For patients enrolled in cohort 2, data were reviewed by an interventional cardiologist to certify the technical feasibility of device placement and by an independent cardiologist and cardiovascular surgeon to determine whether the patient met admission criteria. Patients were selected for device closure if they had (1) 1 or more VSDs that were ascertained to result in sufficient hemodynamic derangement to warrant intervention and (2) either a type of VSD that was technically difficult to close surgically or an overall medical condition with associated surgical risks sufficient to justify the known and potential unknown risks of the device. Written informed consent for device placement and follow-up evaluation was obtained from the patient or parent/legal guardian.

Device Implantation

The Clamshell and CardioSEAL are low-profile double-umbrella devices, with hinged arms attached to Dacron fabric. The major enhancement of the STARFlex version of the CardioSEAL consists of a flexible, self-centering mechanism and a smaller delivery profile.20,21 Implantation procedures were performed as previously described.22,23

Follow-Up and Outcome Assessment

Preclosure and follow-up (immediately after, 6 months after, and most recent) assessments were performed and evaluated for all patients. Follow-up assessments were performed until at least 12 months (cohort 1) or 24 months (cohort 2), after which follow-up was collected in a registry format. Patient demographics and comorbid conditions were collected. Outcomes included survival, echocardiographic assessment of residual flow and device position, VSD assessment score, and adverse events.

Echocardiographic Assessment

Echocardiographic assessment included device arm position and integrity, contact with valve structures, residual flow through the defect, and ratio of VSD diameter to aortic annulus diameter. Flow through the VSD was characterized as none, trivial (single-color flow jet with proximal jet width <1 mm), small (single-color flow jet with a proximal jet width of 1 to 2 mm in all views in children weighing <20 kg or 1 to 3 mm in larger children and adults), or greater than small (single-color flow jet with proximal jet width >2 mm in children <20 kg or >3 mm in older children and adults; alternatively, multiple defects with small or greater than small shunting). Device position was categorized as correct, incorrect, or uncertain. Devices that were ultimately explanted were graded according to the last position documented by echocardiography. For cohort 2, a core laboratory at an unaffiliated institution was responsible for the final interpretation of the echocardiograms.

VSD Size/Severity Assessment

A VSD size/severity assessment scale was designed to assess clinical significance of the VSD in cohort 2 patients. Assessment was performed using 1 of 2 parallel yet equivalent scales: patients with native or surgically induced right ventricular outflow tract obstruction were evaluated according to the size of the VSD normalized to the aortic valve annulus diameter, and patients in whom the VSD resulted in a left-to-right shunt were evaluated according to the hemodynamic size of the shunt (Table 1). This scale allowed for unified analysis of outcomes in patients with and without obstruction to pulmonary blood flow.

Adverse Events

Adverse events were ascertained at each assessment point on the basis of clinical evaluation. Events were graded as not serious (minimal transient impairment), moderately serious (moderate transient impairment or requiring intervention), or serious (life-threatening). For this report, adverse events were categorized as device-related or catheterization-related. Device arm fractures, device explantations, and deaths were also recorded. For cohort 2, a Safety and Data Monitoring Committee composed of unaffiliated professionals independently reviewed all adverse events and was responsible for final attributability and severity classification.

Data Analysis

Continuous data are presented as mean±SD or median (range). Continuous and categorical variables were compared between groups using the 2-sample t test or Fisher exact test, respectively. Paired ordinal data (eg, VSD size/severity assessment) were compared by use of the Wilcoxon signed-rank test. Differences in VSD size/severity assessment from before implantation to most recent follow-up were compared between groups with the Mann-Whitney test. Freedom from device explantation or death was assessed by the Kaplan-Meier product-limit method, with comparisons between diagnostic subgroups performed by use of the log-rank test. Relationships between outcomes and patient characteristics were explored by logistic regression analysis.

Results

Patients

A total of 170 patients were enrolled, as follows: 74 patients in cohort 1 and 96 patients in cohort 2. Enrollment was consistent across the study period, and all but 5 patients were enrolled at a single institution. Median follow-up was 24 months (0 to 154 months). Nine patients (5%) were lost to follow-up (ie, no data after hospital discharge in those surviving to discharge). Demographic and diagnostic data are summarized in Table 2. Patients with un repaired congenital VSDs were significantly younger (median, 2.3 years [0.3 to
TABLE 2. Demographic and Diagnostic Data

<table>
<thead>
<tr>
<th></th>
<th>Total patients 170</th>
<th>Unrepaired congenital VSD (n=92)</th>
<th>Postoperative residual VSD (n=78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>170</td>
<td>92 (54%)</td>
<td>78 (46%)</td>
</tr>
<tr>
<td>Male</td>
<td>80 (48%)</td>
<td>45 (48%)</td>
<td>35 (45%)</td>
</tr>
<tr>
<td>Age at implantation, y</td>
<td>3.9 (0.3–73)</td>
<td>3.9 (0.3–73)</td>
<td>3.9 (0.3–73)</td>
</tr>
<tr>
<td>Unrepaired congenital VSD</td>
<td>92 (54%)</td>
<td>45 (48%)</td>
<td>35 (45%)</td>
</tr>
<tr>
<td>Single muscular defect</td>
<td>34 (20%)</td>
<td>17 (19%)</td>
<td>17 (22%)</td>
</tr>
<tr>
<td>Multiple muscular defects</td>
<td>58 (34%)</td>
<td>25 (27%)</td>
<td>33 (43%)</td>
</tr>
<tr>
<td>Postoperative residual VSD</td>
<td>78 (46%)</td>
<td>35 (38%)</td>
<td>43 (55%)</td>
</tr>
<tr>
<td>Multiple muscular defects</td>
<td>26 (15%)</td>
<td>11 (12%)</td>
<td>15 (19%)</td>
</tr>
<tr>
<td>Intentionally fenestrated VSD patch</td>
<td>10 (6%)</td>
<td>5 (6%)</td>
<td>5 (6%)</td>
</tr>
<tr>
<td>Residual patch-margin VSD</td>
<td>42 (25%)</td>
<td>18 (20%)</td>
<td>24 (31%)</td>
</tr>
<tr>
<td>Associated cardiovascular anomalies</td>
<td>99 (58%)</td>
<td>32 (35%)</td>
<td>67 (86%)</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>32 (19%)</td>
<td>20 (22%)</td>
<td>12 (16%)</td>
</tr>
<tr>
<td>Transposition of the great arteries</td>
<td>21 (12%)</td>
<td>10 (11%)</td>
<td>11 (14%)</td>
</tr>
<tr>
<td>Double-outlet right ventricle</td>
<td>18 (11%)</td>
<td>10 (11%)</td>
<td>8 (11%)</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>11 (6%)</td>
<td>6 (7%)</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>Other</td>
<td>17 (10%)</td>
<td>8 (9%)</td>
<td>9 (12%)</td>
</tr>
<tr>
<td>Previous pulmonary artery band</td>
<td>30 (18%)</td>
<td>16 (18%)</td>
<td>14 (18%)</td>
</tr>
</tbody>
</table>

Values are n (%) except as noted. All percentages calculated as percent of total patients.

TABLE 3. Procedural Details

<table>
<thead>
<tr>
<th></th>
<th>Total (n=170)</th>
<th>Unrepaired Congenital VSD (n=92)</th>
<th>Postoperative Residual VSD (n=78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant successful</td>
<td>168 (99%)*</td>
<td>91 (99%)*</td>
<td>77 (99%)*</td>
</tr>
<tr>
<td>More than one device implanted</td>
<td>68 (40%)†</td>
<td>45 (50%)†</td>
<td>23 (30%)†</td>
</tr>
<tr>
<td>No. of devices placed per patient§</td>
<td>1 (1–7)</td>
<td>1 (1–5)</td>
<td>1 (1–7)</td>
</tr>
<tr>
<td>&gt;1 catheterization procedure with intent to implant device</td>
<td>31 (18%)*</td>
<td>20 (22%)*</td>
<td>11 (14%)*</td>
</tr>
</tbody>
</table>

*Percentage of patients in whom device implant was attempted, known for cohort 2 only.
†Expressed as percentage of patients in whom implant was successful.
‡P<0.01 vs patients with postoperative residual VSD.
§Data are presented as median (range).

TABLE 4. Devices Used

<table>
<thead>
<tr>
<th>Device type</th>
<th>No. of Devices (%)</th>
<th>No. of Device Arm Fractures (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clamshell (4/89–1/97)</td>
<td>159 (54%)</td>
<td>28 (18%)</td>
</tr>
<tr>
<td>CardioSEAL (1/97–7/02)</td>
<td>84 (28%)</td>
<td>8 (10%)</td>
</tr>
<tr>
<td>STARFlex (2/99–8/02)</td>
<td>53 (18%)</td>
<td>7 (13%)</td>
</tr>
</tbody>
</table>

Device size, mm
17 74 (25%) 2 (3%)
23 147 (50%) 21 (14%)
28 48 (16%) 10 (21%)
33 23 (8%) 9 (39%)
38 1 (0.3%) 0 (0%)
40 3 (1%) 1 (33%)
Total 296 43 (15%)*

Values are n (%) except as noted.
*Percentage of total devices.
†Percentage of specific device type.

Follow-Up Evaluation

Echocardiographic Assessment of Residual Flow and Device Position

Among patients in whom precatheterization VSD shunting could be assessed (ie, patients with a prospective assessment and without native or surgically induced obstruction to right ventricular outflow), 91% had “greater than small” shunting before device closure, versus 14% at most recent follow-up (P<0.001 for all postimplantation time points versus preimplantation; Figure 1, top). Of the 111 patients in whom precatheterization VSD shunting was not assessed prospectively (ie, patients in cohort 1) or could not be assessed secondary to native or surgically induced obstruction to right ventricular outflow, assessment of VSD flow at most recent follow-up was possible in 86, 87% of whom had “less than small” (n=39) or small (n=36) shunting, with “greater than small” in the remaining 13% (n=11). Figure 1, bottom shows device position at follow-up.

VSD Size/Severity Assessment

VSD size/severity assessment data for cohort 2 are presented in Figure 2. Baseline VSD size/severity did not differ according to demographic or diagnostic features. Patients who...
ultimately required multiple devices or multiple procedures for device placement had lower preimplantation VSD size/severity scores, indicating larger defects ($P=0.002$ and $P=0.01$, respectively). There were significant improvements in VSD size/severity after device implantation, which were noted at all postimplantation time points (Figure 2) and in both diagnostic subgroups. Among the entire cohort, VSD size/severity improved by $\geq 1$ in 71 patients (91%) and $\geq 2$ in 51 (65%). Compared with before implantation, VSD size/severity was significantly improved at most recent follow-up in both unrepaired congenital (median, 3 to 4) and postoperative residual (median, 2 to 4) subgroups ($P<0.001$). The improvement in VSD size/severity was more pronounced in patients with unrepaired congenital than those with postoperative residual VSDs ($P=0.04$). There was a trend toward greater improvement in VSD size/severity among patients who had multiple devices or multiple procedures ($P=0.08$), reflecting the lower preimplantation VSD size/severity in these patients. VSD size/severity at most recent follow-up did not differ according to other demographic or diagnostic features.

**Adverse Events**

A total of 332 adverse events were reported in 153 of 170 patients (90%) who underwent attempted VSD closure (Table
Nearly half (160 of 332) of the adverse events were graded as moderately serious or serious. There were 39 adverse events related to the device, 26 of which were moderately serious or serious, including 6 that were ongoing at the time of most recent follow-up. Only 1 device-related event was detected after hospital discharge. There were 261 events related to the catheterization procedure, of which 134 were graded as moderately serious or serious. Only 17 of these were ongoing at most recent follow-up, and 4 were detected after hospital discharge. The frequency of complications did not differ over time.

Device Arm Fracture, Device Explantation, and Death
Device arm fractures were observed on follow-up evaluation in 10% to 18% of devices, with a higher incidence with the Clamshell devices and larger devices (Table 4).

During the follow-up period, 18 patients had 1 or more devices explanted a median of 3.6 months (1 day to 24 months) after placement, representing 6% of the total devices placed and 11% of patients in whom device placement was attempted. The reason for device explantation was clearly related to the device in 13 of 18 patients (Table 6).

During the follow-up period, there were 14 deaths, for an all-cause mortality of 8.2%. The median duration from catheterization to death was 8 months (2 days to 10 years). Causes of death were cardiovascular in 7 patients: 3 had preexisting progressive multiorgan dysfunction that did not improve after VSD closure; 1 was a 3.5-month-old infant with a nearly absent ventricular septum and severe congestive heart failure who developed hypotension during the catheterization procedure and suffered progressive hemodynamic demise (at autopsy, a single ventricle was observed); 1 suffered postoperative complications after surgical closure of persistent multiple VSDs and removal of the VSD device; 1 had a presumed arrhythmia; and 1 succumbed to progressive congestive heart failure. The other 7 deaths were a result of aspiration asphyxia (n=1), respiratory syncytial virus infection (n=1), progressive pulmonary fibrosis (n=1), sepsis (n=1), and unknown (n=3).

As depicted in Figure 3, patients with a postoperative residual VSD had a significantly lower Kaplan-Meier probability of freedom from device explantation or death (P=0.01). On multivariate analysis, there were no significant
differences in outcomes (survival, improvement in VSD size/severity) on the basis of patient characteristics.

Discussion
Effectiveness of Transcatheter Device Closure of VSDs
We have presented data from 170 patients who underwent attempted transcatheter device closure of VSDs over a 13-year period. Devices were implanted successfully in 94 of 96 patients in cohort 2, representing a 99% success rate. VSD closure was effective in the majority of cases, as evidenced by stable device position and significantly decreased interventricular flow by echocardiography at all postimplantation time points. Patients with both unrepaired congenital and postoperative residual VSDs had significant improvement in VSD size/severity after device closure, with more than 90% of patients in both groups improving by at least 1 category. Patients with unrepaired congenital VSDs tended to have lower VSD size/severity (ie, larger VSDs and shunts) before device implantation. This group also demonstrated greater improvement in VSD size/severity, with follow-up VSD size/severity not significantly different from the postoperative residual VSD group. These findings suggest that small and large VSDs are equally well closed with a transcatheter approach.

The majority of patients in this study (69%) had defects in the muscular interventricular septum, which are frequently difficult to close surgically or entail potentially deleterious approaches such as ventriculotomy.1–6 Accordingly, in many of these challenging patients, transcatheter device closure of unrepaired VSDs was undertaken as 1 element of a combined (surgical and interventional catheterization) management strategy. The remainder of our cohort had either intentionally fenestrated VSD patches, which we have discussed in a separate report,24 or postoperative residual defects along the margin of patches used to close VSDs in the membranous or outflow portions of the septum. Such defects are generally small, discrete, and amenable to device closure because of their size and location.

Technical and Device Considerations
Depending on the location of the VSD(s) and other cardiovascular anatomic features, several technical approaches were used. There was no discernible relationship between the location of the VSD and outcome. Frequently, multiple devices were necessary to close multiple defects, and multiple procedures were required in 18% of patients. Neither of these factors appeared to affect outcome adversely.

Device arm fractures were reported more frequently among the earlier cohort but occurred consistently in 15% of devices. The higher frequency of arm fractures observed in Clamshell devices is probably related to design issues rather than follow-up, because late fracture detection is unusual. In addition, there was a higher incidence of arm fracture in larger devices. Of note, the fractures were noted incidentally and did not appear to be clinically significant according to our measured outcomes.

Adverse Events
Adverse events were common, occurring in 90% of patients, and nearly half (48%) were categorized as moderately serious or serious. Most events occurred as a part of the hemodynamic instability associated with device positioning in these lengthy, complex procedures, which require vigilant anes-
thetic management.9 Events specifically related to device positioning were less common than hemodynamic instability, but important events such as embolization and valve impingement did occur and were often serious. Thirteen patients (7.7% of 168 patients who received implants) ultimately had 1 or more devices explanted because of malposition, embolization, or ineffective closure. These events highlight the importance of appropriate VSD selection and the technical expertise required to accomplish these procedures.

Fourteen patients died during the follow-up period. In 1 patient, the cause of death was directly attributable to the device or the cathetherization procedure when the device was placed. Four patients were severely ill before VSD closure and never recovered, ultimately dying of multiorgan failure. Otherwise, where information was available, deaths appeared to be secondary to progression of underlying illness or unrelated events. We have previously determined that intracardiac implants are unlikely to cause sudden cardiac death.25

**Limitations**

There are several limitations of this study, especially for cohort 1. VSD size/severity assessment was not performed in patients in cohort 1 because this database was reconstructed in a retrospective manner. Thus, efficacy could not be assessed for patients in cohort 1 with right ventricular outflow tract obstruction. Also, we have no record of patients in cohort 1 who underwent catheterization with intended VSD closure but did not have a device implantation attempted. We chose to include cohort 1 patients to evaluate the long-term efficacy of a device closure strategy.

**Conclusions**

Transcatheter device closure is an effective management option in patients with unrepaired congenital muscular VSDs in locations that require ventriculotomy for surgical closure and postoperative residual VSDs. Despite the complexity of the population, only 1 patient died as a result of the procedure, and 8% required surgical device removal. The majority of patients had successful and sustained defect closure, with a significant reduction in shunting. Although adverse events were common, they were generally manageable and did not outweigh the benefits. Further analysis is necessary to determine whether devices in the ventricular septum have long-term effects on septal mechanics or ventricular function.

**References**


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**Note:** The references at the end of the text are cited in the context of discussing the efficacy, complications, and outcomes of transcatheter device closure of ventricular septal defects (VSDs). The study by Kauth et al. focuses on the outcomes of transcatheter device closure in a specific cohort, highlighting the importance of appropriate VSD selection and technical expertise. The text integrates findings from various studies to support the conclusions made, emphasizing the benefits of transcatheter closure, but also acknowledging its limitations.
Transcatheter Device Closure of Congenital and Postoperative Residual Ventricular Septal Defects

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