AMPLATZER™

# Muscular VSD Occluder

## Instructions for Use

### Device Description

The AMPLATZER™ Muscular VSD Occluder is a self-expanding, double-disc device made from a nitinol wire mesh. The 2 discs are linked together by a short waist corresponding to the size of the ventricular septal defect (VSD). The device has radiopaque markers at each end. In order to increase its closing ability, the discs and waist are filled with polyester fabric. The polyester fabric is securely sewn to the device by polyester thread. The device is available in multiple sizes. See Table 9 on page 11.

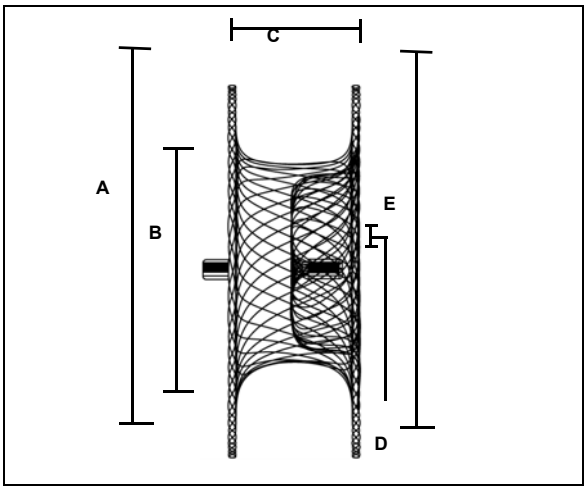


**Figure 1. AMPLATZER™ Muscular VSD Occluder.**

A. Distal disc
B. Device size (at waist)
C. Waist length
D. Delivery cable connector
E. Proximal disc

The AMPLATZER™ TorqVue™ Delivery System is intended to facilitate the attachment, loading, delivery, and deployment of the AMPLATZER™ Occluder devices. The AMPLATZER™ TorqVue™ Exchange System is intended for removal of an AMPLATZER™ Delivery Sheath and subsequent exchange for an AMPLATZER™ Delivery Sheath of equal or larger diameter. Refer to the AMPLATZER™ TorqVue™ Delivery and Exchange Systems Instructions for Use for complete information on these systems.

STERILE EO

℞ ONLY

LATEX Does not contain natural rubber latex components

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**Indications and Usage**

The AMPLATZER™ Muscular VSD Occluder is indicated for use in patients with a complex ventricular septal defect (VSD) of significant size to warrant closure (large volume left-to-right shunt, pulmonary hypertension, and/or clinical symptoms of congestive heart failure) who are considered to be at high risk for standard transatrial or transarterial surgical closure based on anatomical conditions and/or based on overall medical condition.

High-risk anatomical factors for transatrial or transarterial surgical closure include patients:

- Requiring left ventriculotomy or an extensive right ventriculotomy.
- With a failed previous VSD closure.
- With multiple apical and/or anterior muscular VSDs (“Swiss cheese septum”).
- With posterior apical VSDs covered by trabeculae.

**Contraindications**

The AMPLATZER™ Muscular VSD Occluder is contraindicated for the following:

- Patients with defects less than 4 mm distance from the semilunar (aortic and pulmonary) and atrioventricular valves (mitral and tricuspid)
- Patients with severely increased pulmonary vascular resistance above 7 Wood units and a right-to-left shunt and documented irreversible pulmonary vascular disease
- Patients with perimembranous (close to the aortic valve) VSD
- Patients with post-infarction VSD
- Patients who weigh less than 5.2 kg. (Patients smaller than 5.2 kg were studied in the clinical trial, but due to poor outcome, these patients have been contraindicated for device placement. Data from these patients has not been included in the overall analysis.)
- Patients with sepsis (local/generalized)
- Patients with active bacterial infections
- Patients with contraindications to antiplatelet therapy or agents

**Warnings**

- Patients who are allergic to nickel may have an allergic reaction to this device.
- The AMPLATZER™ Muscular VSD Occluder and delivery system should only be used by those physicians trained in transcatheter defect closure techniques.
- Physicians must be prepared to deal with urgent situations, such as device embolization, which require removal of the device. This includes the availability of an on-site surgeon.
- Embolized devices must be removed. Embolized devices should not be withdrawn through intracardiac structures unless they have been adequately collapsed within a sheath.
- Use on or before the last day of the expiration month noted on the product packaging.
- The device is sterilized using ethylene oxide and is for single use only. Do not reuse or resterilize. Attempts to resterilize the device may result in device malfunction, inadequate sterilization, or patient harm.
- Do not use the device if the packaging sterile barrier is open or damaged.
- Do not release the AMPLATZER™ Muscular VSD Occluder from the delivery cable if the device does not conform to its original configuration or if the device position is unstable. Recapture the device and redeploy. If still unsatisfactory, recapture the device and replace with a new device.
- Device closure in patients who have suffered a previous thromboembolic stroke should be discussed with the patient or family. In addition, consultation with a neurologist and hematologist is suggested to determine if the benefit of device closure outweighs the risk.

**Precautions**

Handling

Store in a dry place.

Sizing

Accurate defect sizing is crucial and mandatory for AMPLATZER™ Muscular VSD Occluder device selection. The VSD should be assessed and sized at end diastole by transesophogeal echocardiography (TEE) or angiography to determine the appropriate device size. Device selection should be 2 mm larger than the defect size.

Procedural

- The physician should exercise clinical judgment in situations that involve the use of anticoagulants or antiplatelet drugs before, during, and/or after the use of this device.
- This device should only be used by physicians who have been trained in transcatheter techniques and who should determine which patients are suitable candidates for procedures using this device.
- Aspirin (eg, 81 mg or 325 mg) or an alternative antiplatelet/anticoagulant is recommended to be started at least 24 hours prior to the procedure. Cephalosporin therapy is optional.
- Maintain a recommended minimum active clotting time (ACT) of 200 seconds prior to device insertion and throughout the procedure.
- If TEE is used, the patient's esophogeal anatomy must be adequate for placement and manipulation of the TEE probe.
- Patients requiring multiple devices and/or concomitant catheterization procedures might require prolonged fluoroscopy times and multiple cineangiograms. The risks of radiation exposure (eg, increased cancer risk) should be discussed in detail with the patient or family and alternatives which do not involve radiation exposure should be reviewed.

Post-implant

- Patients should be treated with antiplatelet/anticoagulation therapy (such as aspirin) for 6 months post-implant. The decision to continue antiplatelet/anticoagulation therapy beyond 6 months is at the discretion of the physician.
- Endocarditis prophylaxis should be followed according to the American Heart Association recommendations.
- Any patient who has a residual shunt should undergo an echocardiographic evaluation of the residual shunt every 6 months until complete closure of the defect has been confirmed.
- Patients should be instructed to avoid strenuous activity for 1 month. Strenuous activities such as contact sports prior to 1 month after implant may cause the device to dislodge and embolize.

Use in Specific Populations

- Pregnancy - Care should be taken to minimize the radiation exposure to the fetus and the mother.
- Nursing mothers - There has been no quantitative assessment of the presence of leachables from the device/procedure in breast milk, and the risk to nursing mothers is unknown.

MR Conditional[1]

Through non-clinical testing, AMPLATZER™ devices have been shown to be MR Conditional. A patient with an implanted AMPLATZER™ device can be scanned safely immediately after placement of the device under the following conditions:

- Static magnetic field of 3 tesla or less
- Spatial gradient magnetic field of 720 G/cm or less
- Maximum MR system-reported, whole-body-averaged specific absorption rate (SAR) of 3 W/kg for 15 minutes of scanning

During testing, the device produced a clinically non-significant temperature rise at a maximum MR system-reported, whole-body-averaged specific absorption rate (SAR) of 3 W/kg for 15 minutes of scanning in a 3-tesla MR system using a transmit/receive body coil.

MR image quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the device. Therefore, optimization of MR imaging parameters to compensate for the presence of this device may be necessary.

**Potential Adverse Events**

Potential adverse events may occur during or after a procedure using this device may include, but are not limited to:

- Air embolus
- Allergic drug reaction
- Allergic dye reaction
- Anemia
- Anesthesia reactions
- Apnea
- Arrhythmia
- Arterial pulse loss
- Atelectasis
- Bacterial endocarditis
- Blood loss requiring transfusion
- Brachial plexus injury
- Cardiac arrest
- Device embolization
- Device fracture
- Fever
- Headache/migraine
- Heart block
- Hypotension
- Myocardial infarction
- Perforation of the vessel or myocardium
- Peripheral embolism
- Stridor
- Stroke
- Subaortic stenosis
- Thrombus formation on device

1. MR Conditional as defined in ASTM F 2503-05.

- Cardiomyopathy
- Chest pain
- Cyanosis
- Death
- Vascular access site injury
- Venous thrombosis
- Vomiting

**Clinical Studies**

***Clinical Summary***

The AMPLATZER™ Muscular VSD Occluder was evaluated in a prospective, multi-center, non-randomized, controlled investigation to evaluate muscular VSD closure. The original study included patients receiving primary treatment of VSD without establishment of a prospective statistical plan (ie, sample size, hypotheses) to establish safety and effectiveness. Of these consecutively enrolled patients, the clinical data presented below comprises a subset of patients retrospectively established by an independent review board to be “high risk.” Safety and effectiveness hypotheses were also retrospectively established.

***Deaths***

There were 2 reported deaths during the clinical trial in the High Risk patient population; both deaths were adjudicated by the Data Safety Monitoring Board (DSMB) as major adverse events.

A 3-year-old female with multiple muscular ventricular septal defects underwent 3 cardiac catheterizations. Five coils and 5 AMPLATZER™ Muscular VSD Occluders were implanted during the first and third procedures. During the second procedure, an attempt was made to implant an AMPLATZER™ Muscular VSD Occluder, which was unsuccessful. Seven months after the third procedure, she died suddenly. An independent DSMB adjudicated this death as a major adverse event, but was unable to determine if the death was related to the procedure or the device.

A 7-month-old male with a large muscular ventricular septal defect and pulmonary hypertension underwent cardiac catheterization for device closure of the defect. During the procedure, a device was attempted that was too small. The physician encountered difficulties in removing the device and ultimately inadvertently pulled the 10-Fr delivery sheath out of the right internal jugular vein, resulting in bleeding, hypotension, and cardiac arrest requiring resuscitation. The next day it was noted that the patient had suffered cerebral injury as a result of the procedural complications. The patient died 3 weeks post-procedure. An independent DSMB adjudicated this death as a procedure related major adverse event.

***Observed Adverse Events***

Table 1. presents the major and minor adverse events, per patient and per procedure, observed in the High Risk patient population. As the sample size was limited, the unadjusted 95% confidence interval upper bound for any major adverse event was 60.25% per patient and 55.83% per procedure.

**Table 1. Major and Minor Adverse Events**

| Adverse Event Type | Adverse Event per Patient (%) | 95% Upper Confidence Bound[a] | Adverse Event per Procedure (%) | 95% Upper Confidence Bound |
|---|---|---|---|---|
| **MAJOR Adverse Event Type** | | | | |
| Hematoma[b] | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Hypotension[b] | 5/41 (12.2%) | 26.20% | 5/51 (9.8%) | 21.41% |
| Bradycardia[b] | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Arterial pulse loss | 2/41 (4.9%) | 16.53% | 2/51 (3.9%) | 13.46% |
| Blood transfusion | 2/41 (4.9%) | 16.53% | 2/51 (3.9%) | 13.46% |
| Subaortic stenosis | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Cardiomyopathy | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Delivery system failure | 2/41 (4.9%) | 16.53% | 2/51 (3.9%) | 13.46% |
| Death | 2/41 (4.9%) | 16.53% | 2/51 (3.9%) | 13.46% |
| Stroke | 2/41 (4.9%) | 16.53% | 2/51 (3.9%) | 13.46% |
| Blood loss | 4/41 (9.8%) | 23.13% | 4/51 (7.8%) | 18.88% |

**Table 1. Major and Minor Adverse Events**

| Adverse Event Type | Adverse Event per Patient (%) | 95% Upper Confidence Bound[a] | Adverse Event per Procedure (%) | 95% Upper Confidence Bound |
|---|---|---|---|---|
| Device embolization | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Paroxysmal ventricular tachycardia[b] | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Third-degree heart block | 2/41 (4.9%) | 16.53% | 2/51 (3.9%) | 13.46% |
| Cardiac perforation | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Hemostasis and coagulation disorders | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Anemias caused by blood loss | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Device collapse | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Cardiac arrest | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| **Any Major Adverse Event** | **18/41 (43.9%)** | **60.25%** | **21/51 (41.2%)** | **55.83%** |
| **MINOR Adverse Event Type** | | | | |
| Hematoma[b] | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Hypotension[b] | 2/41 (4.9%) | 16.53% | 2/51 (3.9%) | 13.46% |
| Bradycardia[b] | 2/41 (4.9%) | 16.53% | 2/51 (3.9%) | 13.46% |
| Atelectasis | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Venous thrombosis | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Atrial flutter | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Stridor | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Paroxysmal ventricular tachycardia[b] | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Cyanosis | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Edema | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Premature ventricular contraction | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Fever | 1/41 (2.4%) | 12.86% | 3/51 (5.9%) | 16.24% |
| Second-degree heart block Mobitz Type 2 | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| Vomiting | 1/41 (2.4%) | 12.86% | 1/51 (2.0%) | 10.45% |
| **Any Minor Adverse Event** | **10/41 (24.4%)** | **40.30%** | **13/51 (25.5%)** | **39.63%** |
| **Any Major or Minor Adverse Event** | **22/41 (53.7%)** | **69.34%** | **28/51 (54.9%)** | **68.87%** |

a. Confidence intervals are unadjusted for multiple comparisons.
b. An independent data safety monitoring board reviewed and adjudicated all adverse events, and, depending on the severity and/or time of occurrence, the same type of event could be classified as either a major or minor adverse event.

***Study Purpose***

The primary purpose of this evaluation was to retrospectively determine if the AMPLATZER™ Muscular VSD Occluder is reasonably safe and effective for the treatment of congenital muscular ventricular septal defects in patients with complex ventricular septal defect of significant size to warrant closure, and who are considered to be at high risk for standard transcatheter closure based on anatomical conditions, and/or based on overall medical condition.

Primary effectiveness was evaluated at 12 months post-implant. Successful closure of the defect was defined as less than or equal to a 2-mm residual shunt. Effectiveness was also evaluated at 24 hours (acutely), 1 month, 6 months, and 24 months post-implant.

In addition, patients were classified according to the Clinical Status Scale pre-procedure, and at 6 months and 12 months post-procedure.

Safety was assessed following device placement attempt through the follow-up period by collecting all adverse events that occurred among all consented patients.

***Study Design***

This study was a prospective, non-randomized, multi-center clinical investigation. A total of 11 investigational centers received IRB approval and enrolled patients in the High Risk subset.

***Patient Demographics***

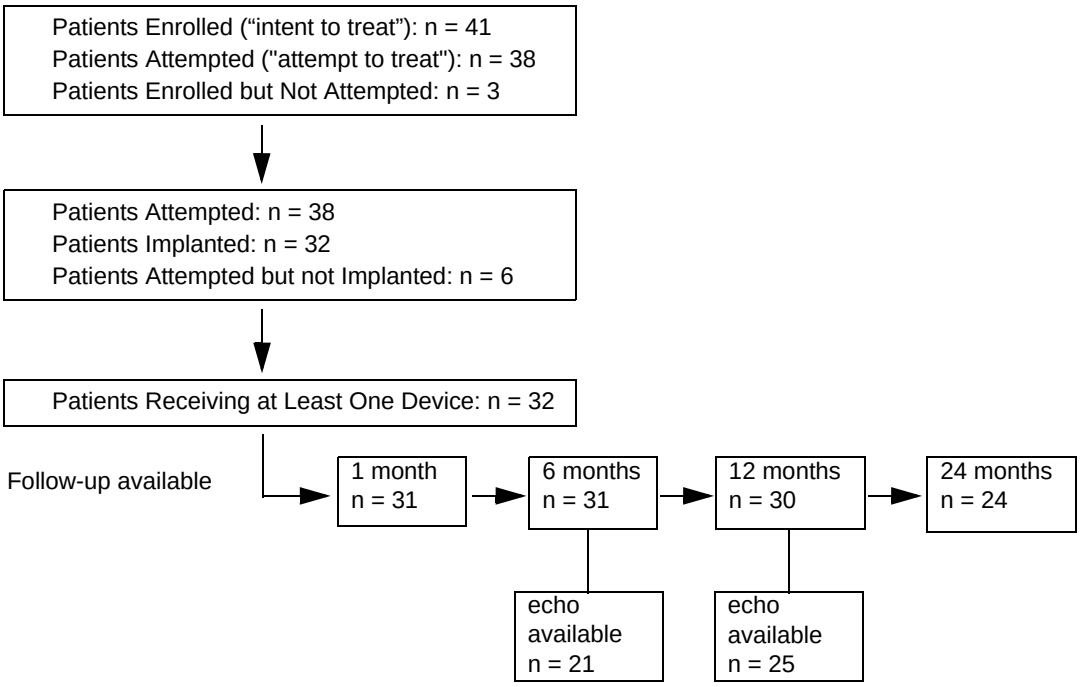
A total of 41 high risk patients were consented to participate in the clinical study and undergo transcatheter VSD closure with the AMPLATZER™ Muscular VSD Occluder. Of the 41 patients, 3 patients were classified as “intent to treat” patients in which the patient signed the informed consent but the patient was not exposed to the investigational device. The remaining 38 patients underwent a cardiac catheterization procedure and an attempt to place the AMPLATZER™ Muscular VSD Occluder. Six of the 38 patients were “attempt to treat” patients in that a device was not successfully implanted during any procedure. The mean age of the 41 patients was 3.2 years (range 0.1 to 49.0 years) and 21 (55.2%) of the patients were male.

***Study Protocol***

Physical examinations and Doppler transthoracic echocardiograms (TTE) were performed pre-implant procedure and at follow-up. Clinical follow-up testing was required at hospital discharge, and at 1 month, 6 months, 12 months, and 24 months post-procedure. All reported adverse events were reviewed and adjudicated by an independent data safety monitoring board (DSMB). Adverse events were adjudicated according to severity (major, minor, observation), using definitions determined by the DSMB. Adverse event relationship to device and procedure, and whether the event was anticipated or not, was also determined by the DSMB. The ventricular septal defect(s) shunt status was evaluated at 1-month, 6-month, 12-month, and 24-month follow-up intervals using TTE and was classified according to degree: none, trivial (less than 1 mm), small (1–2 mm), moderate (greater than 2–4 mm), and large (greater than 4 mm). Of the 31 patients seen for the 6-month follow-up, an independent echo board reviewed tapes for 21 (67.7%) patients. Of the 30 patients who were seen at the 1-year follow-up visit, 25 (83.3%) patients had echo tapes reviewed by the board.

***Principal Safety and Effectiveness Results***

The following tables describe the principal safety and effectiveness results of the AMPLATZER™ Muscular VSD device in high-risk patients. Of the 41 high risk patients enrolled in the study, there were 3 “intent to treat” patients who signed the consent but were not exposed to the device. The remaining 38 patients underwent a cardiac catheterization during which device placement was attempted. Of these 38 patients, 6 patients were “attempt-to-treat” patients, meaning device placement was not successful at any time during the clinical trial. Two additional patients had an “attempt to treat” procedure, but at some point during the clinical trial also had a procedure with successful device placement. The following flow diagram depicts patients enrolled, patients who received at least 1 device, and the number of patients who were seen at each follow-up interval.




The Acute Effectiveness table is broken down by patient, procedure, and finally, by device. The data is also provided by patients attempted and also all consented patients.

Technical success by patient is defined as the number of patients who experienced only successful procedures, meaning that the patient did not have any procedures in which they left the catheterization lab without device placement. Acute procedure success by patient is defined as the number of patients who had a shunt less than or equal to 2 mm immediately post-procedure.

The second portion of the following table describes the results by procedure. Technical success by procedure was defined as the number of successful procedures. The acute procedure success was defined as procedures in which there was less than or equal to a 2-mm residual shunt immediately post-procedure.

The last analysis was by device. Acute results by device were the number of devices successfully implanted. The acute procedure success closure results by device is the number of devices with a less than or equal to a 2-mm residual shunt immediately post-procedure.

**Table 2. Acute Effectiveness**

| Acute Results Effectiveness | All Attempted Patients[a] | All Consented Patients[b] |
|---|---|---|
| **Acute Results by Patient** | | |
| Technical Success[c] | 30/38 (79.0%) | 30/41 (73.2%) |
| Acute Procedure Success[d] | 29/38 (76.3%) | 29/41 (70.7%) |
| **Acute Results by Procedure** | | |
| Technical Success[e] | 39/47 (83.0%) | 39/51 (76.5%) |
| Acute Procedure Success[f] | 38/47 (80.9%) | 38/51 (74.5%) |
| **Acute Results by Device** | | |
| Technical Success[g] | 65/82 (79.3%) | -- |
| Acute Procedure Success Closure Results[h] | 64/82 (78.1%) | -- |

a. Acute results for all attempted patients.

b. Acute results for all consented patients.
c. Number of patients who experienced only successful procedure(s), 2 of the 8 technical-failure patients had both successful and unsuccessful procedure(s). Patients who did not receive the device are included in the denominator.
d. Number of patients who had a shunt of less than or equal to 2 mm immediately post-procedure.
e. Number of successful procedures.
f. Number of procedures in which there was a shunt less than or equal to 2 mm immediately post-procedure.
g. Number of devices successfully implanted.
h. Number of devices for which the shunt was less than or equal to 2 mm immediately post-procedure.

Closure by follow-up period is reported both by Echo Board adjudication and by investigator. An independent Echo Board reviewed the 6-month and 12-month echocardiograms for a majority of the patients seen for each follow-up interval. They determined if there was residual shunting, and if so, to what degree.

Closure is also reported as assessed by investigator for patients seen at the specific follow-up interval, for all attempted patients, and lastly for all patients. Closure success is defined as patients who had a shunt of less than or equal to 2 mm at the specific follow-up interval.

**Table 3. Closure by Follow-up Period – Effectiveness**

| **Closure Success Defined as ≤ 2 mm Shunt at Follow-Up Interval** | | |
|---|---|---|
| **Success by Echo Board Adjudication[a]** | **Results** | **95% Confidence Intervals[b]** |
| 6-month Success | 20/21 (95.2%) | (76.2%; 99.9%) |
| 12-month Success | 25/25 (100.0%) | (86.3%; 100.0%) |
| **Success by Investigator Assessment – Patients Seen[c]** | | |
| 1-month Success | 30/31 (96.8%) | (83.3%; 99.9%) |
| 6-month Success | 29/31 (93.6%) | (78.6%; 99.2%) |
| 12-month Success | 28/30 (93.3%) | (77.9%; 99.2%) |
| 24-month Success | 24/24 (100.0%) | (85.8%; 100.0%) |
| **Success By Investigator Assessment – All Attempted Patients[d, e]** | | |
| Acute Procedure Success | 29/38 (76.3%) | (59.8%; 88.7%) |
| 1-month Success | 30/38 (79.0%) | (62.7%; 90.5%) |
| 6-month Success | 29/38 (76.3%) | (59.8%; 88.6%) |
| 12-month Success | 28/38 (73.7%) | (56.9%; 86.6%) |
| 24-month Success | 24/38 (63.2%) | (46.0%; 78.2%) |
| **Success By Investigator Assessment – All Consented Patients[f, g]** | | |
| Acute Procedure Success | 29/41 (70.7%) | (54.5%; 83.9%) |
| 1-month Success | 30/41 (73.2%) | (57.1%; 85.8%) |
| 6-month Success | 29/41 (70.7%) | (54.5%; 83.9%) |
| 12-month Success | 28/41 (68.3%) | (51.9%; 81.9%) |
| 24-month Success | 24/41 (58.5%) | (42.1%; 73.7%) |

a. Number of patients who had their follow-up Echo reviewed by the Echo Board and had a shunt of less than or equal to 2 mm at follow-up interval
b. Confidence intervals are unadjusted for multiple comparisons.
c. Number of patients who were seen at follow-up interval, whether or not they had shunt evaluated, and had a shunt of less than or equal to 2 mm at follow-up interval. Patients who were not seen but had a shunt greater than 2 mm at last follow-up interval are included in the denominator.
d. Number of patients who had an attempted procedure and had a shunt of less than or equal to 2 mm at follow-up interval.
e. The 6 patients who did not have a device implanted are included in the denominator.
f. Number of patients who had a shunt of less than or equal to 2 mm at follow-up interval
g. The 6 patients who did not have a device implanted and the 3 patients who were never exposed to a device are included in the denominator (ie, intent to treat).

In addition to Closure by Follow-up Period, a Composite Success parameter was calculated to comprehensively evaluate both the safety and effective performance of the device at the 1-month and 12-month follow-up intervals.

Composite success was defined as patients in which device placement was attempted who did not experience technical failure, a major adverse event, or major shunt at the respective follow-up visit. Patients who were technical successes and did not have a major adverse event at the specific follow-up interval and did not have the shunt evaluated at the follow-up interval, but were classified as a failure at the shunt evaluation at their last follow-up interval were classified as composite failures. Technical success patients with no major adverse event at the specific follow-up interval who did not have the shunt evaluated at the follow-up interval, but were classified as a successful closure at the shunt evaluation at their last follow-up interval were classified as missing.

**Table 4. Composite Results**

| Composite Results | Results | 95% Confidence Intervals[a] |
|---|---|---|
| 1-month Composite Results | 20/36 (55.6%) | (38.1%; 72.1%) |
| 12-month Composite Results | 14/32 (43.8%) | (26.4%; 62.3%) |

a. Confidence intervals are unadjusted for multiple comparisons.

**Table 5. Major Adverse Events by Follow-up Period**

| **Major Adverse Events – Safety** | | |
|---|---|---|
| **Major Adverse Event by Patient** | **Results**[a,b] | **95% Confidence Interval**[c] |
| Major AEs at 24 Hours | 16/39 (41.0%) | (25.6%; 57.9%) |
| Major AEs at 1 Month | 16/39 (41.0%) | (25.6%; 57.9%) |
| Major AEs at 6 Months | 17/39 (43.6%) | (27.8%; 60.4%) |
| Major AEs at 12 Months | 18/39 (46.2%) | (30.1%; 62.8%) |
| Major AEs at 24 Months | 18/39 (46.2%) | (30.1%; 62.8%) |

a. The numerator depicts the number of consented patients who experienced a major adverse event at the specific follow-up interval.
b. The denominator includes the 38 attempted patients plus 1 "intent to treat" patient who experienced 2 major adverse events. The other 2 "intent to treat" patients did not experience a major adverse event and are not included in the denominator.
c. Confidence intervals are unadjusted for multiple comparisons.

Mortality results are reported in multiple ways and a range of assumptions are made regarding the outcome of patients due to unavailable follow-up data. For example, death is reported with the assumption that all consented patients, whether or not they were exposed to the device, who were not seen at a specific follow-up interval and never returned at a later date have died. This includes all “intent to treat” and “attempt to treat” patients who were discontinued immediately post-procedure.

**Table 6. Mortality Results – Safety**

| **Mortality of all attempted patients**[a] | **Results** | **95% Confidence Interval**[b] |
|---|---|---|
| Mortality at 24 Hours | 0/38 (0.0%) | |
| Mortality at 1 Month | 1/38 (2.6%) | (0.1%; 13.8%) |
| Mortality at 6 Months | 1/38 (2.6%) | (0.1%; 13.8%) |
| Mortality at 12 Months | 2/38 (5.3%) | (0.6%; 50.8%) |
| Mortality at 24 Months | 2/38 (5.3%) | (0.6%; 50.8%) |
| **Mortality of patients seen for follow-up**[c] | | |
| Mortality at 24 Hours | 0/33 (0.0%) | |
| Mortality at 1 Month | 1/33 (3.0%) | (0.1%; 15.8%) |

**Table 6. Mortality Results – Safety**

| | | |
|---|---|---|
| Mortality at 6 Months | 1/32 (3.2%) | (0.1%; 16.2%) |
| Mortality at 12 Months | 2/32 (6.3%) | (0.8%; 20.8%) |
| Mortality at 24 Months | 2/28 (7.1%) | (0.9%; 23.5%) |
| **Assumed Mortality of Patients Implanted with a Device**[d, e] | | |
| Mortality at 24 Hours | 0/32 (0.0%) | |
| Mortality at 1 Month | 1/33 (3.0%) | (0.1%; 15.8%) |
| Mortality at 6 Months | 1/33 (3.0%) | (0.1%; 15.8%) |
| Mortality at 12 Months | 4/33 (12.1%) | (3.4%; 28.2%) |
| Mortality at 24 Months | 6/33 (18.2%) | (7.0%; 35.5%) |
| **Assumed Mortality of All Consented Patients**[f, g] | | |
| Mortality at 24 Hours | 7/41 (17.1%) | (7.2%; 32.1%) |
| Mortality at 1 Month | 7/41 (17.1%) | (7.2%; 32.1%) |
| Mortality at 6 Months | 7/41 (17.1%) | (7.2%; 32.1%) |
| Mortality at 12 Months | 10/41 (24.4%) | (12.4%; 40.3%) |
| Mortality at 24 Months | 14/41 (34.2%) | (20.1%; 50.6%) |

a. Number of attempted patients with a known death at follow-up interval
b. Confidence intervals are unadjusted for multiple comparisons.
c. Number of patients seen for follow-up at follow-up interval with a known death
d. Number of patients with at least 1 successful procedure who were discontinued for any reason at follow-up interval and patients with no successful procedures who have died
e. Twelve-month and 24-month intervals include the 2 patients who were discontinued due to death and additional patients who were discontinued for other reasons but are assumed to have died.
f. Number of all consented patients who were not seen at the follow-up interval and never came back at a later date were assumed dead (ie, intent to treat)
g. One patient who died 3 weeks post-procedure was not evaluated at 24 hours post-procedure and is therefore assumed dead at the 24-hour follow-up interval.

**Table 7. Total Fluoroscopy Time per Patient**

| **Procedure variable** | | **Results** |
|---|---|---|
| Fluoro time (min.) | Mean ± s.d. (N)<br>[range] | 95.5 ± 93.7 (41)<br>[8.7, 573.0] |

**Table 8. Total Fluoroscopy Time per Procedure**

| **Procedure variable** | | **Results** |
|---|---|---|
| Fluoro time (min.) | Mean ± s.d. (N)<br>[range] | 76.8 ± 59.7 (51)<br>[8.7, 356.0] |

## Patient Information

Refer to the *Patient's Guide to Transcatheter Closure of a Ventricular Septal Defect using the AMPLATZER™ Muscular VSD Occluder System*.

### How Supplied

The AMPLATZER™ Muscular VSD Occluder is packaged separately from the AMPLATZER™ TorqVue™ Delivery System. Refer to Table 9. for recommended delivery system sizes.

**Table 9. Device Specifications**

| Device Order Number | Device Size at waist (mm) | Left and Right Ventricle Disc Diameter (mm) | Length of Connecting Waist (mm) | TorqVue™ Delivery System (French) | |
|---|---|---|---|---|---|
| | | | | 45° | 180° |
| 9-VSD-MUSC-004 | 4 | 9 | 7 | 6 | 5 |
| 9-VSD-MUSC-006[a] | 6 | 14 | 7 | 6 | 6 |
| 9-VSD-MUSC-008[a] | 8 | 16 | 7 | 6 | 6 |
| 9-VSD-MUSC-010[a] | 10 | 18 | 7 | 6 | 6 |
| 9-VSD-MUSC-012[a] | 12 | 20 | 7 | 7 | 7 |
| 9-VSD-MUSC-014[a] | 14 | 22 | 7 | 8 | 8 |
| 9-VSD-MUSC-016 | 16 | 24 | 7 | 8 | 8 |
| 9-VSD-MUSC-018 | 18 | 26 | 7 | 9 | 9 |

a. The device specifications for the 006–014 devices were modified after the clinical trial was completed. The devices used during the clinical trial utilized a right ventricular disc that was 2 mm smaller than the left ventricular disc. The marketed devices have equal disc diameters.

### AMPLATZER™ TorqVue™ Delivery System

The AMPLATZER™ Muscular VSD Occluder is implanted with either a 45° or a 180° AMPLATZER™ TorqVue™ Delivery System (Figure 2).

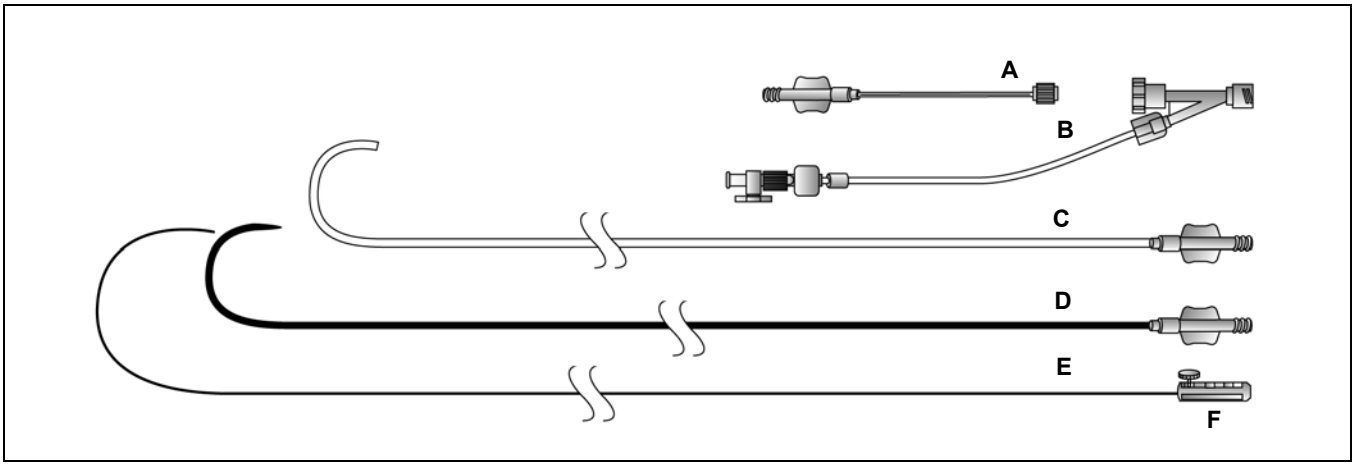



**Figure 2. AMPLATZER™ TorqVue™ Delivery System.**

A. Loader – introduces a device into the delivery sheath
B. Hemostasis valve with extension tube and stopcock – allows flushing of the delivery system and controls back bleeding
C. Delivery sheath – provides a pathway through which a device is delivered
D. Dilator – eases penetration of tissue
E. Delivery cable (optional) – attaches to a device for controlling its movement through the delivery sheath
F. Plastic vise (optional) – attaches to the delivery cable, serving as a “handle” for detaching (unscrewing) the delivery cable from a device

The delivery system selected is based on physician preference for sheath placement (Table 10).

**Table 10. Delivery System Selection**

| If preferred sheath placement is: | Select a: |
|---|---|
| Middle of the LV | 45° delivery system |
| Ascending aorta | 180° delivery system |

**Directions for Use**

The AMPLATZER™ Muscular VSD Occluder is implanted percutaneously by catheter technique (right- or left-sided approach). The approach depends on the location of the muscular ventricular septal defect. Generally, defects in the upper portion of the septum can be approached from the femoral vein, whereas low defects may be easier to close with a transjugular approach.

***Catheter Technique***

1. Perform procedure under either general or conscious sedation.
2. Give patient a dose of an appropriate antibiotic during the catheterization procedure.
3. Obtain access in the femoral artery, femoral vein, and/or right internal jugular vein.
4. Administer heparin to achieve a recommended activated clotting time of greater than 200 seconds throughout the procedure.
5. Perform routine right and left heart catheterization. Assess the pulmonary vascular resistance.
6. Perform angiography to define the location, size, and number of VSD(s).
7. Use transesophageal echocardiography (TEE) to provide additional imaging of the VSD(s) and to assist with delivery system and device placement.
8. Select a device up to 2 mm larger than the VSD(s) size as assessed by TEE or angiography at end-diastole (the bigger of the 2 diameters).
9. Access the VSD(s) with a guidewire using either venous (Figure 3) or arterial approach (Figure 4). The venous approach may be from either the inferior vena cava or the superior vena cava (arteriovenous loop), depending on the location of the VSD.

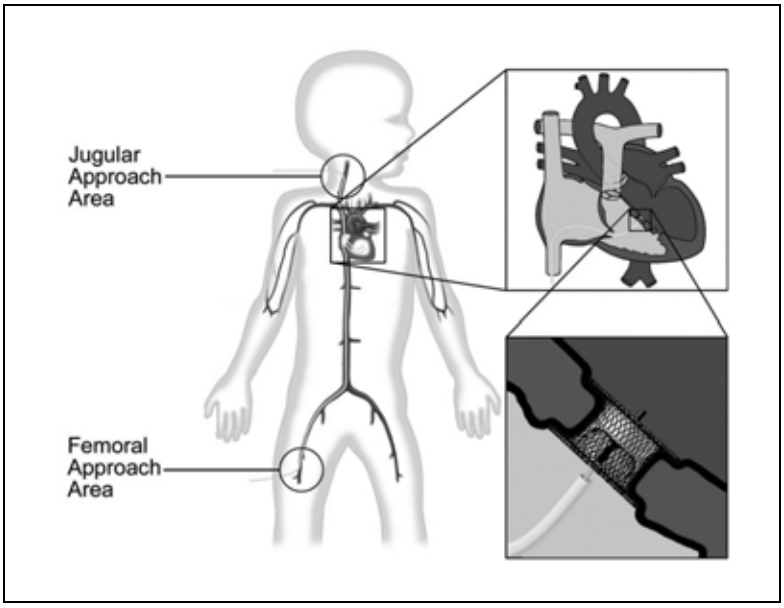



**Figure 3. Right-sided Approach.**

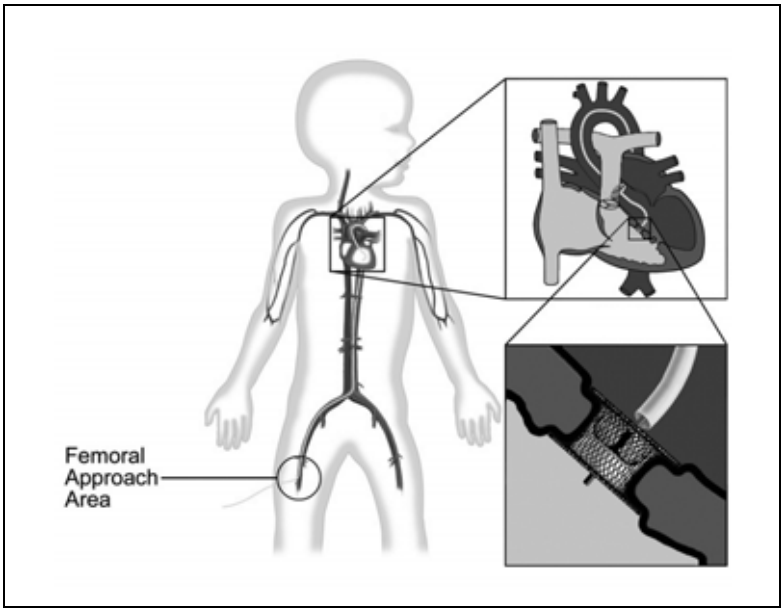



**Figure 4. Left-sided Approach.**

10. Advance the delivery sheath and dilator over the guidewire until the tip of the dilator crosses the VSD.
11. Remove the dilator.
12. Advance the guidewire into the apex of the ventricle and position the tip of the delivery sheath in the body of the ventricle.
13. Pass the delivery cable through the loader and attach the AMPLATZER™ Muscular VSD Occluder to the tip of the delivery cable by rotating the device clockwise until secure. To ensure proper occluder release, rotate the device counterclockwise 1/8 of a turn.
14. Immerse the device and loader in sterile saline solution and retract the device into the loader.
15. Slowly remove the guidewire and allow for back-bleeding to purge air from the system.
16. Connect the loader to the delivery sheath.
17. Transfer the device from the loader into the delivery sheath, and without rotation, advance the device to the tip of the delivery sheath.
18. Use TEE and angiography as a guide during each step of device deployment.
19. Retract the delivery sheath slowly until the distal disc is deployed.
20. Pull the entire assembly (delivery cable and delivery sheath) into the VSD.
21. Retract the sheath to deploy the waist of the device in the defect.
22. Once position is confirmed (Figure 5), retract the sheath to deploy the proximal disc.

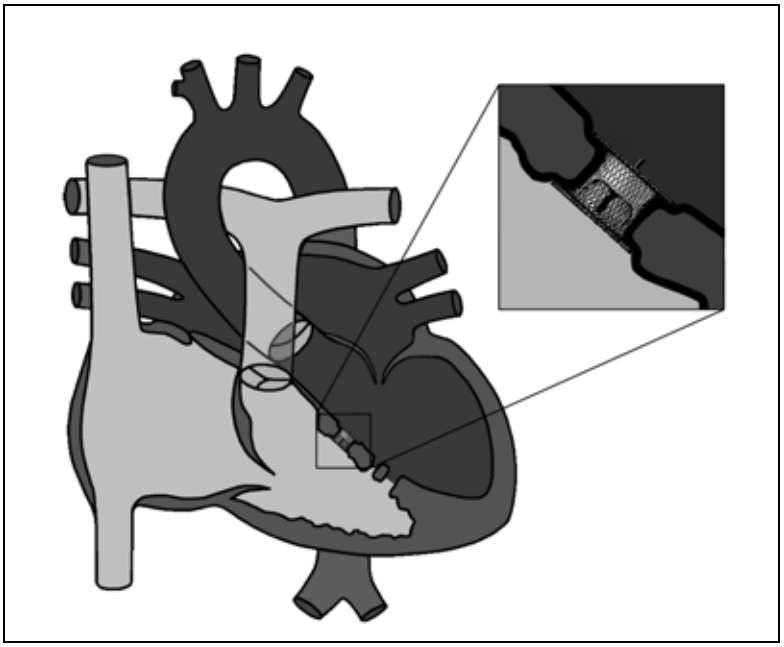


**Figure 5. Placement of the AMPLATZER™ Muscular VSD Occluder.**

23. If the position of the device is unsatisfactory:
    - Stabilize the delivery cable and re-advance the delivery sheath until the device is completely within the sheath.
    - Reposition the device and deploy it again, or remove the device from the patient.
24. If the device position is satisfactory:
    - Attach the plastic vise to the delivery cable, then release the device by rotating the delivery cable counterclockwise until it separates from the device.
    - Retract the delivery cable into the delivery sheath.
    - Remove the delivery cable and delivery sheath from the patient.
25. Complete a TEE evaluation to confirm device placement; assess for residual shunting, obstruction, or regurgitation induced by the device.
26. Perform an angiogram to assess for residual flow through the device.
27. Two doses of an appropriate antibiotic is recommended post-catheterization procedure at 8-hour intervals.

**Post-procedure Instructions**

- Temporary patient ID card – Go to www.amplatzer.com/tempIDcard to print the temporary patient identification card. Complete this card and give it to the patient.
- Registration form – An implant registration form is located in each device box. Complete the patient information section and send the form to AGA Medical Corporation.

**Disposal**

- The carton and IFU are recyclable. Dispose of all packaging materials as appropriate.
- Devices may be returned to AGA Medical for disposal. Contact your AGA Medical representative or returns@amplatzer.com for instructions.
- Use solid biohazard waste procedures to discard devices.

**Warranty**

AGA Medical Corporation warrants to buyer that, for a period equal to the validated shelf life of the product, this product shall meet the product specifications established by the manufacturer when used in accordance with the manufacturer's instructions for use and shall be free from defects in materials and workmanship. AGA Medical Corporation's obligation under this warranty is limited to replacing or repairing at its option, at its factory, this product if returned within the warranty period to AGA Medical Corporation and after confirmed to be defective by the manufacturer.

EXCEPT AS EXPRESSLY PROVIDED IN THIS WARRANTY, AGA MEDICAL CORPORATION DISCLAIMS ANY REPRESENTATION OR WARRANTY OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY AS TO MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

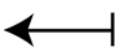
See the Terms and Conditions of Sale for further information.

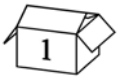
**State of California (USA) Only:**

WARNING: This product and its packaging have been sterilized with ethylene oxide. The packaging may expose you to ethylene oxide, a chemical known to the State of California to cause cancer or birth defects or other reproductive harm.

**Symbol Definitions**

The following symbols may appear on the device packaging:

| Symbol | Definition |
|---|---|
|  | Manufacturer |
|   | EU authorized representative |
|   | Reference number |
|   | Product serial number |
|   | Product lot number |
|  | Use by date<br>(Use on or before the last day of the expiration month noted on the product packaging.) |
|  | Do not reuse |
|   | Sterilized using ethylene oxide |
|  | Consult instructions for use |
|  | Keep dry |
|  | Do not use if package is damaged |
|   | Does not contain natural latex components |
|   | MR Conditional |
|  | Inner diameter |
|  | Outer diameter |
|  | Length |
|  | Usable length |

| | |
|---|---|
|  | Recommended delivery sheath/catheter dimensions |
| CE | Indication of conformity with the essential health and safety requirements set out in European Directives |
| ℞ ONLY | Federal law (USA) restricts this device to sale by or on the order of a physician (or properly licensed practitioner). |
|  | Quantity |
|  | Date of manufacture |
| **Muscular VSD Occluder** | Muscular VSD Occluder |