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Results of the U.S. Food and Drug Administration Continued Access Clinical Trial of the GORE HELEX Septal Occluder for Secundum Atrial Septal Defect

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ABSTRACT

OBJECTIVES This report describes the immediate, 1-, and 5-year follow-up results of the U.S. Food and Drug Administration Continued Access clinical trial of the GORE HELEX Septal Occluder (W. L. Gore & Associates, Inc., Flagstaff, Arizona) for closure of secundum atrial septal defect.

BACKGROUND The trial was conducted between May 2003 and August 2006 to allow continued enrollment in a trial of the investigational device during review of data from the Pivotal Trial. Devices with hydrophilic coating on the expanded polytetrafluoroethylene to improve echocardiographic visualization were first used in this trial.

METHODS A total of 137 devices were implanted in 137 patients at 13 US institutions. Evaluations were scheduled at 1, 6, and 12 months for the initial trial and at 36 and 60 months for a later extension of the trial in those who consented to longer term evaluations.

RESULTS Twelve-month follow-up was completed on 122 of 126 patients with implantations, and 5-year follow-up on 83 of 95 patients who agreed to the trial extension. The overall clinical success rate was 96.7%, and the major adverse event rate 3.6%. Wire frame fractures were seen in 11.7% of patients with no clinical symptoms. A trivial, clinically insignificant leak was seen, or could not be ruled out, in 26.6% of patients at the 5-year evaluation, but no clinically significant leaks were seen. No patient experienced an erosion or sudden catastrophic event.

CONCLUSIONS The immediate, 1-, and 5-year follow-up outcomes of the Continued Access clinical trial continue to demonstrate that the GORE HELEX Septal Occluder is a safe and effective transcatheter occluder for repair of ostium secundum atrial septal defect. (J Am Coll Cardiol Intv 2014;7:905–12) © 2014 by the American College of Cardiology Foundation.

The GORE HELEX Septal Occluder (HELEX) (W.L. Gore and Associates, Inc., Flagstaff, Arizona) was developed for closure of secundum atrial septal defects (ASDs) in the early 1990s. Successful animal evaluations (1) were soon followed by the first human implantation by Wilson in Scotland in 1999 (2). A feasibility study was launched in the United States in April 2000, and a pivotal study was initiated in 2001. This was followed by the Continued Access study initiated in May 2003. The device was

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ABBREVIATIONS AND ACRONYMS

ASD = atrial septal defect

ePTFE = expanded polytetrafluoroethylene

HELEX = GORE HELEX Septal Occluder

modified with the addition of a hydrophilic coating on the Gore-Tex to improve echocardiographic visualization for the Continued Access study.

The HELEX is a circular double-disk device composed of a single flexible nitinol wire frame helically shaped and draped with a thin membrane of expanded polytetrafluoroethylene (ePTFE). The device is repositionable during its deployment and is retrievable even after initial release from the delivery system by a retrieval chord or string that tethers the occluder to the delivery system until final release.

METHODS

The Continued Access trial was begun in May 2003 at 13 clinical centers (Table 1).

Each center obtained approval from its institutional review board. Informed consent (and assent where applicable) was obtained by the principal investigator from each patient. The trial was approved by the U.S. Food and Drug Administration and was sponsored by W.L. Gore and Associates, Inc., the manufacturer of the device.

Inclusion criteria were an ostium secundum ASD with a balloon occlusion diameter of ≤22 mm, right heart volume overload on echocardiography or as indicated by a Q_p/Q_s ≥1.5:1, adequate rim in ≥75% of the circumference of the defect, and femoral venous access suitable to accommodate the 9-French delivery system. Exclusion criteria included significant comorbidity with anticipated cardiac surgery or catheter intervention, uncontrolled arrhythmia, arrhythmias requiring electrophysiological study, systemic or inherited conditions that would significantly increase patient risk of major morbidity or mortality during the term of the study, history of stroke, pregnancy or lactation, contraindications to antiplatelet therapy, pulmonary artery hypertension with greater than half systemic pulmonary artery pressure or resistance index ≥5 Wood units, significant atrial septal aneurysm, the presence of multiple defects requiring >1 device, and atrial septal thickness >8 mm.

For the Continued Access study, a diagnostic catheterization was performed for determination of shunt and resistances. Stop-flow balloon sizing was performed in standard fashion. Although current recommendations are to use a device 2 times the stop-flow diameter, ratios as low as 1.6 times the stop-flow diameter were allowed in this study. The selected device was loaded into the delivery catheter per manufacturer's instructions. The delivery catheter was then introduced into a short 9-French sheath. The delivery catheter was advanced under fluoroscopic guidance across the ASD. The device was configured with 1 disk on either side of the septum using fluoroscopic and either transesophageal or intracardiac echocardiographic guidance. A detailed description of the implantation procedure was previously published (3).

Pre-procedure evaluation included history and physical, electrocardiogram, and transthoracic echocardiogram. The same evaluations were performed pre-hospital discharge and again at 1, 6, 12, 36, 48, and 60 months post-implantation. Fluoroscopy of the device was performed at 6, 12, and 60 months to assess for wire frame fracture.

OUTCOME MEASURES. The primary endpoint of the Continued Access study was clinical success, a composite variable evaluating safety and efficacy, at

TABLE 1 Patient Enrollment by Site

Site	City	Investigator(s)	Device Count
Advocate Hope Children's Hospital	Oak Lawn/Chicago	Alexander Javois, MD	23 (16.8)
Children's Health Care Egleston–Emory	Atlanta	Robert Vincent, MD	5 (3.6)
Children's Hospital and Regional Medical Center	Seattle	Thomas Jones, MD	21 (15.3)
Children's Hospital of Iowa	Iowa City	Thomas Fagan, MD	12 (8.8)
Children's Hospital of Oakland	Oakland	Ziad Saba, MD	3 (2.2)
Children's Hospital of Philadelphia	Philadelphia	Jonathan Rome, MD	24 (17.5)
Children's Hospital of San Diego	San Diego	Frank Ing, MD	6 (4.4)
Children's Hospital Los Angeles	Los Angeles	Sarah Bedran, MD	2 (1.5)
Cleveland Clinic Foundation	Cleveland	Larry Latson, MD	12 (8.8)
Denver Children's Hospital	Denver	Kak-Chen Chan, MD	1 (0.7)
Duke University Medical Center	Durham	J. Rhodes/J. Delaney, MD	11 (8.0)
Miami Children's Hospital	Miami	Evan Zahn, MD	16 (11.7)
University of Texas Southwestern Medical Center	Dallas	Thomas Zellers, MD	1 (0.7)
Total no. of subjects implanted			137

Values shown are number (%).

12 months. It was defined as 1) all atrial defects either completely occluded or any possible residual shunt judged to be clinically insignificant, 2) the absence of repeat procedure to the target ASD, and 3) the absence of major complication(s). Secondary endpoints included the individual component variables of safety and efficacy. Safety outcomes for the study included assessment of all device-related and procedure-related adverse events through the 12-month follow-up. Determinations of major versus minor adverse events were adjudicated by the Data and Safety Monitoring Board. The Data and Safety Monitoring Board comprised 4 uninvolved physicians (2 cardiac surgeons and 2 interventional cardiologists) and a biostatistician. Major complications were defined as events related to the device or procedure that resulted in readmission to the hospital or permanent damage or deficit. Specific types of events were pre-designated to be recorded as major adverse events. These included additional intervention such as a pericardial or pleural drainage tube, new arrhythmia requiring intervention, device embolization, endocarditis, fracture of the device resulting in surgery and/or clinical sequelae, perforation of cardiovascular structures by the device or delivery system, a thrombotic/thromboembolic event resulting in clinical sequelae, permanent loss of arterial pulse, retroperitoneal bleed or groin hematoma, transfusion, or repeat procedure to the target defect. Events to be classified as minor adverse events included device fracture resulting in no clinical sequelae, noncomplicated pleural or pericardial effusion that resolved without intervention or with nonsteroidal anti-inflammatory drugs and diuretics, transient pain or weakness due to peripheral nerve stretching while under anesthesia, arrhythmias requiring no extended pacing or medication, temporary loss of arterial pulse, superficial hematoma, migraines, transfusion, and fever.

Efficacy outcome included assessment of defect closure at each of the follow-up visits and was evaluated in terms of residual shunt. A description of residual defect was determined by the principal investigator at each site, but final determination for endpoints was by an echocardiography core laboratory. Residual shunt was categorized as clinically significant, clinically insignificant, or completely occluded. Device artifact and technical factors made precise measurement of residual shunt size with a single number untenable. Clinically significant leak was defined as any of the following: 1) residual left-to-right shunt with evidence of right heart volume overload that would likely require repeat intervention as judged by the echocardiographer; 2) a $Q_p/Q_s \geq 1.5{:}1$ as measured by cardiac catheterization; 3) clinical sequelae related to the leak; and 4) hemodynamically significant, defined as failure to meet the criteria for hemodynamically insignificant. Clinically insignificant leak was defined as a definite or possible small leak associated with all of the following criteria: 1) normalization of ventricular septal motion; 2) noticeable variation in right ventricular end-diastolic dimension with respiration; 3) significant decrease in right ventricular size as determined by comparison of equivalent images of the right ventricle before and after device placement evaluating for decrease in the M-mode echocardiographic measurement of the right ventricle and no diastolic flattening of the ventricular septal contour in the short-axis view; and 4) the apparent effective diameter of any residual leak or leaks as determined by evaluation of both 2-dimensional echocardiographic and color Doppler views judged to be approximately ≤ 3 mm and clearly <6 mm. There could be no clinical sequelae for a small leak to be considered an insignificant leak.

STATISTICAL ANALYSIS. Statistics presented are descriptive. No statistical tests of hypotheses were conducted.

RESULTS

A total of 137 patients underwent successful implantation at 13 sites between May 2003 and August 2006. Patient, ASD, and HELEX device characteristics are provided in Table 2. Implantation and follow-up compliance for these 137 patients are shown in Table 3. Of the 137 patients who underwent device implantation, 11 were lost to follow-up at 1 year. Of the remaining 126 patients, 122 (96.8%) completed the 12-month evaluation. At 5 years, 83 of 95 of the patients (87.4%) who consented to the extended study completed the evaluation (42 patients withdrew from the study or were lost to follow-up).

Clinical success, a composite of safety and efficacy, at 12 months was high at 96.7%. Major adverse events are detailed in Table 4. Most events were seen within the first 30 days of implantation. Beyond that time, events were mostly incidental device wire frame fracture without clinical significance. Five major adverse events were seen: 2 device embolizations, both on day 1, that were successfully retrieved by transcatheter technique; 1 wire frame fracture incidentally discovered at 61 days post-implantation with the device retrieved by transcatheter technique; 1 wire frame fracture associated with an echocardiographic finding suggesting 2 additional ASDs and so the device was removed on day 1,175 with surgical

TABLE 2 Patient Demographic Characteristics

	Device Count
No. of subjects who underwent implantation	137
Sex	
Male	54 (39.4)
Female	83 (60.6)
Subject ethnicity	
White or Caucasian	92 (67.2)
Black or African American	8 (5.8)
Hispanic or Latino	17 (12.4)
Asian	7 (5.1)
Other	10 (7.3)
Unknown	3 (2.2)
Patient age, yrs	
No.	137
Mean (SD)	9.5 (10.4)
Median	5.8
Range	0.8–58.4
Weight, kg	
No.	137
Mean (SD)	30.7 (22.7)
Median	19.7
Range	6.9–114.0
Body surface area	
No.	137
Mean (SD)	0.98 (0.48)
Median	0.79
Range	0.33–2.40
Defect size from balloon sizing, mm	
No. of patients	134*
Mean (SD)	13 (3.0)
Median	13.0
Range	5–22.0

Values shown are number (%) unless otherwise indicated. *The balloon sizing for 3 subjects was not recorded/documented at the time of implantation.

closure of all defects; and 1 unrelated death on day 820 (graft-versus-host disease after bone marrow transplantation).

Wire frame fracture data are shown in Table 5. A fracture was discovered in 8.5% of patients who underwent fluoroscopic evaluation in the first 12 months and in 5.2% of patients from 13 to 60 months. No fractures were seen in 15- and 20-mm devices. There was an increasing incidence of fracture as device size increased: 2.1% of 25-mm devices, 26.7% of 30-mm devices, and 45.5% of 35-mm devices. The majority (10/14) of fractures were noted within the first 12 months. Thirteen of 14 fractures were incidentally discovered at scheduled fluoroscopic evaluations. The one fracture detected outside the scheduled fluoroscopic evaluation was found in a device noted to have excessive mobility of the right atrial disk on routine echocardiography. All other fractures were discovered incidentally, and no fracture was associated with any clinical signs. Two patients with fractures underwent treatment; 1 demonstrated increased mobility and 1 had a persistent large shunt with additional defects. Both were removed electively. There were no apparent clinical sequelae related to the other fractures, consistent with the experience reported in the pivotal study (4).

Residual shunting data are shown in Table 6. The echocardiographic core laboratory was instructed to classify studies in which all ideal views were not obtainable (could not definitely rule out a leak) into the appropriate clinically significant or insignificant leak category. This policy was used to ensure that the

TABLE 3 Patient Follow-up Compliance by Interval

Device Training	Pre-discharge	1 Month	6 Months	12 Months	36 Months	60 Months
Total no. of patients*	137	137	137	137	137	137
Patients who discontinued before interval	0	3	9	11	33	42
Patients not reached at start of interval	0	0	0	0	0	0
Patients available for interval follow-up†	137	134	128	126	104	95
No. with follow-up evaluation	136 (99.3)	121 (90.3)	112 (87.5)	122 (96.8)	72 (69.2)	84 (88.4)
Transthoracic or transoesophageal echocardiography	136 (99.3)	121 (90.3)	111 (86.7)	122 (96.8)	71 (68.3)	83 (87.4)
Electrocardiography completed	125 (91.2)	117 (87.3)	106 (82.8)	118 (93.7)	69 (66.3)	82 (86.3)
Fluoroscopy completed‡	0 (0.0)	0 (0.0)	95 (74.2)	109 (86.5)	4 (3.8)	74 (77.9)
No. with visit pending§	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
No. without follow-up evaluation	1 (0.7)	13 (9.7)	16 (12.5)	4 (3.2)	32 (30.8)	11 (11.6)
Discontinued in interval before visit‖	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.8)	3 (2.9)	2 (2.1)
Interval visit was outside window	0 (0.0)	0 (0.0)	0 (0.0%)	0 (0.0)	1 (1.0)	3 (3.2)
Missed visit¶	0 (0.0)	13 (9.7)	16 (12.5)	3 (2.4)	28 (26.9)	6 (6.3)

Values shown are number (%). Percentages use patients available for interval follow-up as the denominator (unless otherwise noted). Follow-up windows are as follows: pre-discharge, days 0 to 2; 1 month, days 15 to 46; 6 months, days 151 to 244; 12 months, days 245 to 548; 36 months, days 913 to 1,276; 60 months, days 1,642 to 2,006. *Number of patients with a successful HELEX device placement. †Patients available for interval follow-up equal the total number of patients minus patients who discontinued before the interval and patients not reached at start of interval. ‡Fluoroscopy required at 6, 12, and 60 months. §Patients currently in study interval, but no visit reported at time of analysis. ‖Patients available for follow-up visit at start of interval, but discontinued in window and before visit. These patients are included in patients who discontinued before interval in next time interval. ¶Patients completed study interval window with no visit reported.

TABLE 4 Number of Patients by Category of Major Adverse Events

	Days 0-30 Post-procedure	Day 31-Month 18 Post-procedure	Months 19-60 Post-procedure	Overall
No. of patients evaluable for safety	137	133	109	137
Patients with ≥1 major adverse event	2 (1.5)	1 (0.8)	2 (1.8)	5 (3.6)
Device related				
No. of patients	2 (1.5)	1 (0.8)	1 (0.9)	4 (2.9)
Cardiac	2 (1.5)	–	–	2 (1.5)
Embolization (post-procedure)	2 (1.5)	–	–	2 (1.5)
Device (HELEX Septal Occluder (W. L. Gore & Associates, Inc., Flagstaff, Arizona))	–	1 (0.8)	1 (0.9)	2 (1.5)
Device removal related to fracture	–	1 (0.8), unstable device	1 (0.9), additional defects	2 (1.5)
Other (not device or not procedure related)				
No. of patients	–	–	1 (0.9)	1 (0.7)
Other	–	–	1 (0.9)	1 (0.7)
Death s/p bone marrow transplantation	–	–	1 (0.9)	1 (0.7)

Values shown are number (%).
s/p = status post.

reported incidence of possible leaks could not be underestimated. No echocardiograms were deemed unsuitable for detecting larger leaks or requiring repeat evaluation. By definition, clinically insignificant leak indicated that right heart chamber sizes were normal and no further intervention was required. One clinically significant leak was seen at 12 months. Unfortunately, this patient was lost to further follow-up. In the cohort of patients who consented to 5-year follow-up, there were no residual significant leaks. No residual shunting was seen with the 15-mm device. With increasing device size, however, clinically insignificant leaks became more frequent. At 5-year follow-up, 21.1% of 20-mm devices, 26.7% of 25-mm, 26.3% of 30-mm, and 57.1% of 35-mm were found to have clinically insignificant leaks (Tables 7 and 8). The only residual clinically significant leak was seen in a patient with a 35-mm device. At 12 months, complete occlusion was seen in 70.1% and a clinically insignificant leak in 29.1%. The data were nearly identical at 5 years post-implantation with 58 of 79 patients (73.4%) with total occlusion and 21 of 79 (26.6%) with a clinically insignificant leak (Table 6).

TABLE 5 Summary of Wire Frame Fractures: Overall and by Device Size (mm)

	Overall	15	20	25	30	35
Patients with successful delivery	137	5	31	55	32	14
6-Month follow-up visit	114	5	24	46	29	10
Fluoroscopy completed*	98	5	19	38	26	10
Patients with fracture(s)*†	7 (7.1)	0	0	1 (2.6)	4 (15.4)	2 (20.0)
12-Month follow-up visit	122	5	27	48	29	13
Fluoroscopy completed	109	4	26	42	26	11
Patients with fracture(s)†	3 (2.8)	0	0	0	1 (3.8)	2 (18.2)
6- or 12-Month follow-up visit	128	5	29	51	30	13
Fluoroscopy completed*	118	5	27	46	29	11
Patients with fracture(s)*†	10 (8.5)	0	0	1 (2.2)	5 (17.2)	4 (36.4)
Post-12-month follow-up visit	109	5	25	42	26	11
Fluoroscopy completed*	77	4	20	24	22	7
Patients with fracture(s)*†	4 (5.2)	0	0	0	3 (13.6)	1 (14.3)
Overall	129	5	30	51	30	13
Fluoroscopy completed*	120	5	27	47	30	11
Patients with fracture(s)*†	14 (11.7)	0	0	1 (2.1)	8 (26.7)	5 (45.5)

Values shown are number or number (%). *Includes 2 fractures identified before 6-month follow-up. †Denominator for percentage is number of subjects completing fluoroscopy.

TABLE 6 Residual Defect Status

	12 Months (Days 245-548)	24 Months Optional (Days 549-912)	36 Months (Days 913-1,276)	48 Months Optional (Days 1,277-1,641)	60 Months (Days 1,642-2,006)
Patients with successful delivery	137	137	137	137	137
Patients with core laboratory review	117	16	65	20	79
Completely occluded	82 (70.1)	8 (50.0)	52 (80.0)	12 (60.0)	58 (73.4)
Clinically insignificant leak	34 (29.1)	8 (50.0)	13 (20.0)	8 (40.0)	21 (26.6)
Clinically significant leak	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Patients missing core laboratory review	20	121	72	117	58
Discontinued study before evaluation	12 (60.0)	28 (23.1)	35 (48.6)	37 (31.6)	44 (75.9)
Core laboratory review not completed	8 (40.0)	93 (76.9)	37 (51.4)	80 (68.4)	14 (24.1)

Values shown are number or number (%).

Clinical success endpoints at 12, 36, and 60 months are shown in Table 9. At 5 years, 54 of 137 patients were not participating in the extended trial or were lost to follow-up. Protocol-scheduled follow-up was extended from 1 year post-procedure to 5 years post-procedure as a separately consented study at the time of U.S. Food and Drug Administration approval. Many subjects chose not to continue participation in the extended follow-up. Of the remaining 83 patients, 79 (95.2%) met criteria for clinical success.

DISCUSSION

Compared with the Pivotal Study of the HELEX (5), Continued Access study patients were younger (9.5 years vs. 12.4 years) and smaller (30.7 kg vs. 35.6 kg). All investigators reported higher confidence in placing the new hydrophilically coated device due to improved echocardiographic imaging. The hydrophilic coating on the ePTFE enhanced ultrasound penetration of the device with markedly less echocardiographic reflection artifact (6). The smaller patient size in the Continued Access study is likely a result of better device visualization as well as enhanced learning curve over time.

Overall, only 4 device-related major adverse events were detected: 2 embolizations within 24 h of implantation (successfully retrieved in the catheter laboratory and subsequently closed by transcatheter technique) and 2 device fractures resulting in removal. The fractured device removed in the catheter laboratory at 61 days demonstrated an excessively mobile right atrial disk. Despite complete closure of the ASD, it was thought that the long-term outcome of this device was uncertain, and so the decision was made to remove it. The second device was removed because there were 2 additional ASDs that required treatment that would be best addressed surgically (protocol did not allow additional devices). None of these 4 major adverse events resulted in clinical manifestations (all patients were asymptomatic before the decision to intervene).

STUDY LIMITATIONS. First, this study was not designed for comparison with other devices or techniques, nor was it designed as a randomized

TABLE 7 Residual Defect Status: 12-Month Echocardiography Core Laboratory Review

	Device Size, mm				
	15	20	25	30	35
No. of patients with successful delivery	5	31	55	32	14
No. of patients with core laboratory review	5	26	47	27	12
Completely occluded	4 (80.0)	18 (69.2)	32 (68.1)	23 (85.2)	5 (41.7)
Clinically insignificant leak	1 (20.0)	8 (30.8)	15 (31.9)	4 (14.8)	6 (50.0)
Clinically significant leak	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
Patients missing core laboratory review	0	5	8	5	2
Discontinued study before evaluation		2 (40.0)	6 (75.0)	3 (60.0)	1 (50.0)
Core laboratory review not completed		3 (60.0)	2 (25.0)	2 (40.0)	1 (50.0)

Values shown are number or number (%).

TABLE 8 Residual Defect Status: 60-Month Echo Core Lab Review

	Device Size, mm				
	15	20	25	30	35
Patients with successful delivery	5	31	55	32	14
Patients with core laboratory review	4	19	30	19	7
Completely occluded	4 (100.0)	15 (78.9)	22 (73.3)	14 (73.7)	3 (42.9)
Clinically insignificant leak	0 (0.0)	4 (21.1)	8 (26.7)	5 (26.3)	4 (57.1)
Clinically significant leak	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Patients missing core laboratory review	1	12	25	13	7
Discontinued study before evaluation	1 (100.0)	8 (66.7)	22 (88.0)	8 (61.5)	5 (71.4)
Core laboratory review not completed	0 (0.0)	4 (33.3)	3 (12.0)	5 (38.5)	2 (28.6)

Values shown are number or number (%).

evaluation. Second, the study has relatively small numbers so it is not powered to detect small differences in the outcome parameters. Third, exclusion criteria may not reflect the entire population in which devices may be used after approval.

CONCLUSIONS

This report focuses on both the short- and long-term safety and efficacy data for the U.S. FDA Continued Access Clinical Trial of the HELEX. More than 96% of patients with successful implantation met the primary endpoint of clinical success with no more than a trivial residual shunt, normalization of right ventricular size, and no major adverse event. In particular, there were no erosions, perforations, allergic reactions, or arrhythmias requiring treatment. The major adverse events seen were 2 early asymptomatic device embolizations treated by transcatheter retrieval and 2 elective removals of devices from the atrial septum (1 possible device instability and 1 associated with additional defects).

One patient had a clinically significant residual shunt at intermediate follow-up, and no clinically significant leaks were seen in patients who consented to follow-up for 5 years. Although this Continued Access study included patients with implantation procedures using a device-to-defect ratio as small as 1.6:1 and defects as large as 22 mm, subsequent analysis of combined data from the Feasibility, Pivotal, and Continued Access Studies of the HELEX have shown that the small residual leaks are more likely to occur with device size-to-defect size ratios <2:1 and in patients with defects >18 mm (7). Based on those findings, current instructions for use recommend device size-to-defect size ratios ≥2:1 and limitation of use to defects ≤18 mm.

Wire frame fractures were seen in 11.7% of patients, but all were asymptomatic, with 92% being detected only by radiographic evaluation including fluoroscopy. It has become evident that simple detection of a wire frame fracture does not require additional treatment or investigation; thus, fluoroscopic evaluations are no longer recommended in the instructions for use. No change in follow-up has been recommended for simple detection of a wire frame fracture, but abnormal mobility of a portion of the device as seen on echocardiography warrants radiographic evaluation and close follow-up. Embolization of a portion of the device has not been observed, likely because the entire wire frame except for the locking mechanism is ensheathed by an ePTFE membrane. In the worldwide experience with the HELEX, there have been 2 patients reported with asymptomatic perforations of a mitral valve leaflet discovered by echocardiography (4,8). The recommended schedule of echocardiographic evaluations appears to be adequate for evaluation of this possibility. To date, there have been no reported cases of late sudden catastrophic events (such as erosion) associated with the HELEX. The shape and

TABLE 9 Clinical Success Endpoint Through 12-Month Follow-up

	12 Months	36 Months	60 Months
Evaluable patients with successful delivery	137	137	137
Clinical success endpoint			
Patients evaluated	120	69	83
Clinical success	116 (96.7)	65 (94.2)	79 (95.2)
Clinical failure	4 (3.3)	4 (5.8)	4 (4.8)
Major device/procedure adverse event	3 (2.5)	4 (5.8)	4 (4.8)
Adverse event			
Significant leak on final core laboratory evaluation	1 (0.8)	0 (0.0)	0 (0.0)
Patients not evaluated	17	68	54
Lost to follow-up before evaluation	9	32	40
Final defect evaluation missing	8	36	14

Values shown are number or number (%).

relative "softness" of this device likely contribute to this excellent safety record. The larger the device, the more likely it was that a wire frame fracture would develop.

A relatively high incidence of clinically insignificant residual leak (or inability to rule out a trivial leak) was seen at 1 year and persisted at 5-year follow-up. Because right heart chamber dimensions normalized, patients with these leaks were considered to be similar to the ~20% of the normal population who can be shown to have a patent foramen ovale or small interatrial communication by careful echocardiographic evaluation. No changes in antiplatelet treatment or endocarditis prophylaxis precautions have been recommended for patients with possible or definite insignificant leaks. Recommended changes for device size-to-defect size ratio and maximal ASD size will likely result in a lower incidence of such possible trivial leaks.

Immediate, 1-, and 5-year follow-up of the multicenter trial indicates that the device is a safe and effective alternative to the repair of an ostium secundum ASD.

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