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ORIGINAL INVESTIGATIONS

Post-Approval U.S. Experience With Left Atrial Appendage Closure for Stroke Prevention in Atrial Fibrillation

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ABSTRACT

BACKGROUND Left atrial appendage closure (LAAC) was approved by the U.S. Food and Drug Administration (FDA) as a stroke prevention alternative to warfarin for patients with nonvalvular atrial fibrillation. However, clinical decision-making is confounded by the fact that although LAAC attenuates the anticoagulant-related lifetime risk of bleeding, implantation is associated with upfront complications. Thus, enthusiasm for LAAC as a treatment option has been appropriately tempered, particularly as the therapy is introduced beyond the clinical trial sites into general clinical practice.

OBJECTIVES This study evaluated the acute procedural performance and complication rates for all cases performed in the United States since FDA approval.

METHODS In the absence of a formal national clinical registry since regulatory approval in March 2015, we obtained procedural data on implantation procedures. Every LAAC procedure requires the presence of a manufacturer clinical specialist and for procedural parameter and periprocedural complication data to be collected using a standardized process and forms.

RESULTS In 3,822 consecutive cases, implantation was successful in 3,653 (95.6%), with a median procedure time of 50 min (range 10 to 210 min). Implanting physicians performing these procedures (n = 382) included 71% new, nonclinical trial implanters, who performed 50% of the procedures. Procedural complication rates included 39 pericardial tamponades (1.02%) (24 treated percutaneously, 12 surgically, and 3 fatal); 3 procedure-related strokes (0.078%); 9 device embolizations (0.24%) (6 requiring surgical removal); and 3 procedure-related deaths (0.078%).

CONCLUSIONS Despite a large fraction of previously inexperienced operators, in the real-world post-FDA approval experience of LAAC, procedural success was high and complication rates were low. (J Am Coll Cardiol 2017;69:253–61)

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

FDA = U.S. Food and Drug Administration

LAA = left atrial appendage

LAAC = left atrial appendage closure

TEE = transesophageal echocardiography

In March 2015, the U.S. Food and Drug Administration (FDA) approved left atrial appendage closure device (LAAC) to reduce the risk of stroke in patients with nonvalvular atrial fibrillation (AF) (1). Approval was based primarily on 2 pivotal randomized clinical trials of device versus warfarin anticoagulation: PROTECT-AF (Watchman Left Atrial Appendage System for Embolic PROTECTion in Patients With Atrial Fibrillation) and PREVAIL (Prospective Randomized Evaluation of the Watchman LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy) (2–5). Together, those trials demonstrated that the device was noninferior to warfarin for the primary composite endpoint of stroke, systemic embolism, or cardiovascular death. Furthermore, device implantation was associated with an approximately 80% reduction in hemorrhagic strokes and a >50% reduction in cardiovascular death (2–6).

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In February 2016, the U.S. Centers for Medicare & Medicaid Services finalized its coverage decision, requiring all patients undergoing LAAC to be included into a prospective national registry (7). However, the first such LAAC registry was only certified in August 2016; accordingly, the majority of LAAC procedures performed since FDA approval have not been included into any national registry (8). This is important because it would be expected that the highest complication rate with a novel technology/technique such as LAAC would occur at its initial introduction into clinical practice.

Despite the absence of a prospective registry from the time of FDA approval, we were nonetheless able to collect procedural data on all LAAC procedures since approval. In brief, the manufacturer required a clinical specialist be present at all cases and for procedural parameters and major complications to be collected and reported using a standardized process and forms. Herein, we report the comprehensive procedural outcomes and acute procedure-related complication data for consecutive LAAC cases since FDA approval.

METHODS

THE LAAC DEVICE. The Watchman device (Boston Scientific, Inc., Natick, Massachusetts) has been previously described (9). In brief, the device is a self-expanding nickel titanium structure available in 5 sizes to accommodate a variety of left atrial appendage (LAA) dimensions. The left atrial surface is covered by a permeable polyester fabric and affixed to the LAA ostium by anchors to minimize the possibility of embolization. Implantation is performed via a transseptal approach using pre-shaped guiding sheaths. Periprocedural medical therapy recommended by the FDA Instructions for Use includes heparin during implantation, then aspirin 81 mg and warfarin for 45 days post-procedure, at which time a transesophageal echocardiogram (TEE) is performed. Assuming residual peridevice flow ≤5 mm, warfarin is discontinued and the patient is treated with aspirin and clopidogrel 75 mg daily until 6 months, at which time clopidogrel is discontinued. After this, patients are advised to continue aspirin indefinitely.

IMPLANTATION. LAAC procedures to date have been performed by either interventional cardiologists or electrophysiologists or both. Based on the education plan formulated jointly by the FDA and the manufacturer, all new implanting physicians fulfilled prespecified conditions, including the knowledge base of stroke prevention in nonvalvular AF, information about therapeutic alternatives, results of the Watchman trials and registries, previous transseptal puncture experience, implantation case review, simulator training, and attendance at a physician training event. Manufacturer recommendations for patient selection, pre-procedural testing, and adjunctive peri-implant and initial post-implant medication were provided to each implanting physician and discussed before each implant. Implants were typically performed with guidance by multiplanar and/or 3-dimensional TEE imaging as well as angiography to determine LAA dimensions and anatomy, exclude the presence of thrombus, assess adequacy and stability of implantation, and ascertain any complications.

DATA ACQUISITION AND ANALYSIS. In the previously reported PROTECT-AF and PREVAIL randomized

and has been a consultant for Boston Scientific. Nicole T. Gordon is an employee of Boston Scientific. Dr. Holmes and Mayo Clinic have a financial interest in technology related to this research; that technology has been licensed to Boston Scientific. Dr. O'Neill has reported that he has no relationships relevant to the contents of this paper to disclose. Drs. Reddy and Holmes contributed equally to this work. Matthew J. Price, MD, served as Guest Editor for this paper.

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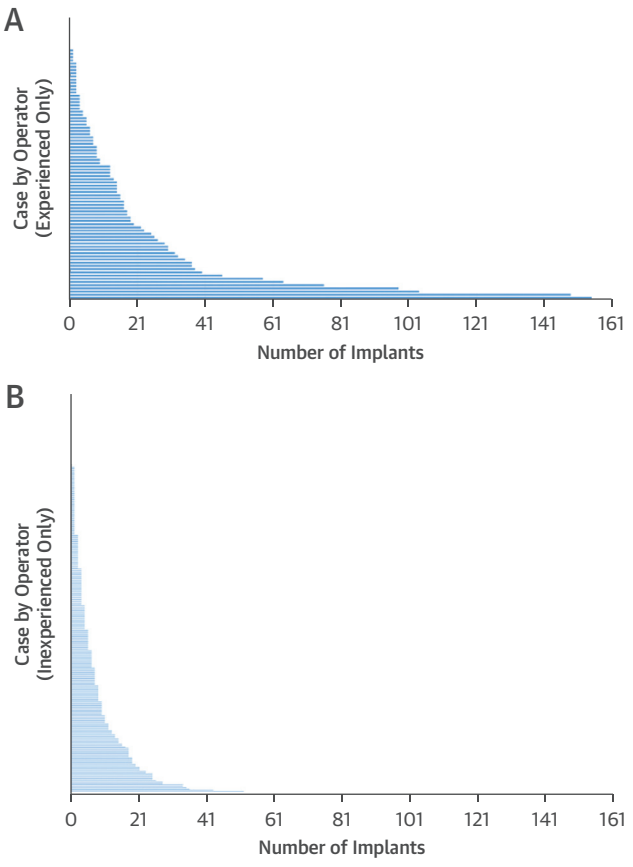
trials and the 2 companion registries, CAP (Continued Access to PROTECT-AF) and CAP2 (Continued Access to PREVAIL), the Watchman-specific mandated protocols for patient selection, procedural performance, and follow-up were reported (2-6). Standardized definitions were used as previously reported, and these protocols were followed in this current dataset. During procedures, all implants were mandated to be performed with a trained clinical specialist in attendance, and this Boston Scientific-employed individual was required to document the device characteristics, procedural performance, and release criteria measurements on a standardized form in an online database. Implant success was defined as confirmation of the device-specified release criteria and successful device release. If the initial placement criteria were not met, the device could be partially recaptured into the access sheath and repositioned unless the initial device was deployed too proximal relative to the appendage ostium, in which case full recapture was required and a new device used. An adequate seal was defined as a residual leak ≤5 mm observed by TEE. Major procedural complications were reported through the manufacturer's complaint handling system, and de-identified patient data were part of the required regulatory mandatory device reporting filing submitted to the FDA. There was information on major complications, such as pericardial effusion, need for urgent cardiac surgery, stroke, and device embolization within 24 h of implantation. Although there was no core laboratory, events were reviewed by the sponsor's medical safety group, which included the manufacturer medical officer, and independently further reviewed by 2 of the authors: an electrophysiologist (V.Y.R.) and an interventional cardiologist (D.R.H.). An event was defined as procedure related if it occurred during or within 7 days of the procedure and the reviewers concurred that the event was likely related to the device/procedure. If the information was insufficient, the conservative position (assuming procedure related) was taken.

For this analysis, specific metrics of the procedure were compared with the results obtained in the previous FDA clinical trials (PROTECT-AF, PREVAIL, CAP, and CAP2) as well as the recent European registry EWOLUTION (Registry on Watchman Outcomes in Real-Life Utilization) (2-6,10,11). Because our present dataset did not include patient demographics or follow-up outcomes data as part of a prospective clinical registry, specific institutional review board approvals were not required outside of the center-mandated informed consent.

FIGURE 1 Procedure Volume by Operator



Numbers of procedures performed by each operator separated by experienced **(A)** and inexperienced **(B)** operator cohorts. Each **horizontal bar** represents a single operator, and the magnitude of its rightward extension indicates the number of procedures performed by that particular operator.

RESULTS

PROCEDURAL PERFORMANCE. Between March 2015 and May 2016, a total of 3,822 consecutive patients underwent device implantation by 382 operating physicians at 169 U.S. centers. The operators included those who had previously performed LAAC procedures as part of clinical trials (29%) as well as "naive" operators (71%) who had not previously performed any procedures before FDA approval (Figure 1). This physician group performed 50% of all the procedures in the 3,822-patient cohort.

The procedure was successfully performed in 3,653 of 3,822 patients (95.6%) (Table 1). Median procedure time was 50 min (range 10 to 210 min). The average number of devices used per case was 1.38 (range 1 to 6).

TABLE 1 Outcomes in the Post-FDA Approval Experience

	Post-FDA Approval Experience
Procedural parameters	
No. of procedures	3,822
Implantation success	3,653 (95.6)
Procedure duration, min	
Median	50
IQR (1st)	36
IQR (3rd)	66
Devices used per procedure	1.38
Complications	
Pericardial tamponade	39 (1.02)
Treated with pericardiocentesis	24 (0.63)
Treated surgically	12 (0.31)
Resulted in death	3 (0.078)
Pericardial effusion, no intervention	11 (0.29)
Procedure-related stroke	3 (0.078)
Device embolization	9 (0.24)
Removed percutaneously	3
Removed surgically	6
Death	
Procedure-related mortality	3 (0.078)
Additional mortality within 7 days	1 (0.026)

Values are n or n (%), unless otherwise indicated.
FDA = U.S. Food and Drug Administration; IQR = interquartile range.

During the procedure, a partial recapture on the final device was required in 23% of cases. In this subset of patients requiring recapture, the average number of recaptures per procedure was 1.49. The device sizes used during the procedures were as follows: 21-mm device in 10.2%, 24-mm device in 25.5%, 27-mm device in 32.7%, 30-mm device in 19.1%, and 33-mm device in 12.5%. The average LAA ostial sizes (in millimeters) and final device compressions for the various implanted devices were 21-mm device—17.0, 19%; 24-mm device—19.3, 20%; 27-mm device—21.2, 21%; 30-mm device—23.3, 22%; and 33-mm device—25.5, 23%. Of note, the average device compression in this cohort, 21%, was slightly higher than recommended by the manufacturer instructions for use (10% to 20%).

PROCEDURE-RELATED COMPLICATIONS. Agreement during event categorization was 100% among both adjudicating authors and the manufacturer medical officer. The most prevalent complication was pericardial effusion requiring intervention in 39 patients (1.02%) (Table 1). In two-thirds of these instances (n = 24), the effusions were successfully drained percutaneously; the remaining (n = 12) required surgery, and 3 patients did not survive (see below). An additional 11 patients (0.29%) developed pericardial effusions that did not require intervention but instead only conservative management.

Three strokes (0.08%) and 3 deaths (0.08%) were attributed to the procedure. Two of the strokes presented with symptoms consistent with ischemic stroke (inability to use arm and right-sided weakness). The other stroke presented the day after the procedure, and a head computed tomographic scan revealed a hemorrhagic bleed. All 3 deaths were secondary to pericardial effusions related to LAA perforation by the device. One patient died during pericardiocentesis before surgery could be performed, 1 died during surgery, and 1 died 2 days after surgical repair. In addition, 1 patient died within 7 days of the procedure from a pulmonary embolism unrelated to the device. There were 9 instances (0.24%) of device embolization (Table 2); two-thirds of these (n = 6) required surgical removal, whereas the remaining third (n = 3) were removed percutaneously. All but 1 of the device embolizations were identified either during the procedure (n = 5) or while the patient was recovering in the hospital (n = 3). The last embolization was discovered during the routine 45-day TEE; this device was percutaneously removed within 24 h.

DISCUSSION

This initial post-FDA approval U.S. clinical experience with LAAC using the Watchman device in 3,822 consecutive patients implanted by 382 physicians revealed that: 1) procedural success was excellent at approximately 95%, with an acceptable average procedure duration of approximately 50 min; 2) approximately one-half of the procedures were performed by operators without previous implant experience; and 3) complication rates were favorable, with pericardial tamponade, procedure-related stroke, and mortality rates of only approximately 1%, 0.08%, and 0.08%, respectively.

For nonvalvular AF, both the LAAC randomized controlled trials (PROTECT-AF and PREVAIL) and their accompanying registries (CAP and CAP2), which together included nearly 2,000 patients receiving the device (Table 3), have been concordant in demonstrating the noninferiority of the LAAC device to warfarin for stroke or systemic embolism and its superiority in reducing hemorrhagic stroke, cardiovascular mortality, and nonprocedure-related bleeding (2–6,10,12). In addition, the device has been found to result in improved quality of life (13). In a detailed cost-effectiveness analysis that incorporated the economic impact of strokes as a function of their resulting level of disability, LAAC demonstrated *dominance* over both warfarin and the class of

TABLE 2 Device Embolization Details

Device Size, mm	Method of Removal	Notes
21	Percutaneous snare	Lower abdominal aorta/ retrograde arterial removal
21	Percutaneous snare	Lodged in abdominal aorta, identified at 45-day TEE visit
33	Surgical	Left ventricle
33	Surgical	N/A
30	Surgical	Left ventricle
24	Percutaneous snare	Retrieved during procedure, then a second device was successfully placed
27	Surgical	Device entangled in mitral valve
27	Surgical	N/A
27	Surgical	Device entangled in aortic valve/left ventricular outflow tract

N/A = not available; TEE = transesophageal echocardiography.

nonwarfarin oral anticoagulants (14,15). Accordingly, LAAC with the device has become an important stroke prevention therapeutic alternative, particularly for patients who are poor candidates for long-term oral anticoagulation (16).

The efficacy data are compelling, but it is important to recognize that significant procedural complications have been reported (10). In PROTECT-AF, although there was no procedure-related mortality, there was a relatively high rate of other complications, including cardiac tamponade in 4.3%, procedure-related stroke in 1.15%, and device embolization in 0.6% (**Table 4**) (2,5,10). Overall, complication rates improved over the course of subsequent FDA Watchman trials, particularly the high rates of pericardial tamponade and procedure-related stroke (**Table 4**, **Central Illustration**) (10). Of course, this improvement occurred in the context of the strictly controlled environment of FDA clinical trials. On the other hand, there has been some experience of "real-world" use of LAAC outside the United States.

In the recently published prospective EWOLUTION registry, 1,021 consecutive patients underwent implantation in 47 centers in Europe, the Middle East, and Russia (11). The patient cohort had a high risk for stroke (CHA_2DS_2-VASc score = 4.5 ± 1.6) and a moderate-to-high bleeding risk (HAS-BLED score = 2.3 ± 1.2), and the documented procedural success of device implantation was 98.5%. Complication rates were favorable: cardiac tamponade occurred in 0.29%, procedure-related stroke in 0.078%, device embolization in 0.24%, and procedure-related mortality rate in 0.078 (**Tables 3 and 4**) (11). Other LAAC devices have also been evaluated in registries outside of the United States, although no randomized trials have been completed. Studying the most common other LAAC device, the retrospective Amplatzer cardiac plug registry included 1,047 patients from 22 European centers (17). Similar to EWOLUTION, this registry investigated Amplatzer device safety, feasibility, and efficacy in a real-world AF patient population. The cohort again had a high risk for stroke (CHA_2DS_2-VASc score = 4.5 ± 1.6) and bleeding (HAS-BLED score = 3.2 ± 1.2), and device implantation was successful in 97.3%. Major complications were site reported and occurred at rates similar to those reported for the device: cardiac tamponade in 1.24%, procedure-related stroke in 0.86%, device embolization in 0.77%, and procedure-related mortality in 0.76% (17).

It is in the background of these favorable outcomes from clinical trials and from registries outside of the United States that the present data hold significant interest. First, this dataset is notable for being comprehensive and inclusive of all Watchman implantation procedures since FDA approval in March 2015. This is particularly important because this captures the initial experience in the absence of a national registry as this technology is extended beyond the clinical trials to widespread clinical practice.

TABLE 3 Comparison of Procedural Parameters Across Watchman Studies

	PROTECT-AF	PREVAIL	CAP	CAP2	EWOLUTION	Post-FDA Approval	Aggregate Data*
No. of procedures	463	269	566	579	1,021	3,822	6,720
Implantation success, %	90.9	95.1	94.4	94.8	98.5	95.6	94.9
Procedure duration, min							
Median	51	52	46	55	N/A	50	50.8
IQR (1st)	37	40	34	39	N/A	36	
IQR (3rd)	71	73	62	80	N/A	66	
Devices used per procedure	1.6	1.5	1.4	1.4	1.07	1.38	1.39

*Aggregate data combined from PROTECT-AF, PREVAIL, CAP, CAP2, EWOLUTION, and the Post-FDA Approval Experience.

CAP = Continued Access to PROTECT-AF; CAP2 = Continued Access to PREVAIL; EWOLUTION = Registry on Watchman Outcomes in Real-Life Utilization; PREVAIL = Prospective Randomized Evaluation of the Watchman LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy; PROTECT-AF = Watchman Left Atrial Appendage System for Embolic PROTECTion in Patients With Atrial Fibrillation; other abbreviations as in **Tables 1 and 2**.

TABLE 4 Comparison of Procedural Complications Across Watchman Studies

	PROTECT-AF	PREVAIL	CAP	CAP2	EWOLUTION	Post-FDA Approval	Aggregate Data*
Pericardial tamponade	20 (4.3)	5 (1.9)	8 (1.4)	11 (1.9)	3 (0.29)	39 (1.02)	86 (1.28)
Treated with pericardiocentesis	13 (2.8)	4 (1.5)	7 (1.2)	N/A	2 (0.20)	24 (0.63)	67%
Treated surgically	7 (1.5)	1 (0.4)	1 (0.2)	N/A	1 (0.10)	12 (0.31)	29%
Resulted in death	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (0.078)	4%
Pericardial effusion, no intervention	4 (0.9)	0 (0)	5 (0.9)	3 (0.5)	4 (0.39)	11 (0.29)	27 (0.40)
Procedure-related stroke	5 (1.15)	1 (0.37)	0 (0)	2 (0.35)	1 (0.10)	3 (0.078)	12 (0.18)
Device embolization	3 (0.6)	2 (0.7)	1 (0.2)	0 (0)	2 (0.20)	9 (0.24)	17 (0.25)
Removed percutaneously	1	0	0	0	1	3	29%
Removed surgically	2	2	1	0	1	6	71%
Death							
Procedure-related mortality	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	3 (0.078)	4 (0.06)
Additional mortality within 7 days	0 (0)	0 (0)	0 (0)	1 (0.17)	3 (0.29)	1 (0.026)	5 (0.07)

Values are n (%) or n unless otherwise indicated. *Aggregate data combined from PROTECT-AF, PREVAIL, CAP, CAP2, EWOLUTION, and the Post-FDA Approval Experience.
Abbreviations as in Tables 1 to 3.

Second, despite the limitations imposed on this study by the absence of patient-level clinical characteristics, both the total number of patients studied (n = 3,822) and the number of implanting operators (n = 382) are larger than the combined experience of all the FDA trials and the EWOLUTION registry. In this context, the first important finding in our dataset was the high rate of successful device implantation. Not surprisingly, implantation success had been lowest in the initial PROTECT-AF trial at approximately 91% and improved to approximately 95% in the subsequent FDA trials, culminating in a 98.5% implant success rate in EWOLUTION (Table 3). In comparison, the 95.6% success rate in the current post-approval experience, which included a large proportion of naive operators, is quite favorable. The procedure proved to be efficient with procedural times approximating 1 h. Also, the number of devices used per case, 1.38, similarly compares favorably with the FDA clinical trial outcomes (Table 3).

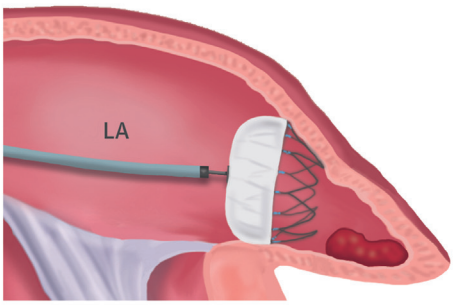
Finally, the most critical findings of these data relate to patient safety. In the FDA clinical trials, the most frequent major procedural complication was pericardial tamponade (10). In the current post-FDA approval experience, pericardial tamponade occurred in only about 1% of patients, a rate that is favorable in comparison to the FDA clinical trials (Table 4). Although this rate is higher than the 0.39% tamponade rate observed in EWOLUTION, it is important to recognize that the device has only been approved in the United States since 2015. In contrast, the Watchman device and other LAAC devices have been commercially available in Europe since 2009. Greater experience with LAAC was likely the reason for the lower overall rate of complications in EWOLUTION. One would expect a similar continued reduction of the procedure-related adverse event rate over time in the United States.

Furthermore, the majority, approximately two-thirds of these tamponades, could be treated percutaneously without the need for cardiac surgery, both in the current post-approval experience and in the aggregate Watchman LAAC outcomes (Table 4). Also, an additional 0.29% of the cohort demonstrated pericardial effusion requiring no intervention. Whether these are related to atrial microtears that self-sealed or simply are unrecognized effusions present before the implantation procedure is unknown. Because patients did not undergo routine transthoracic echocardiography the next day, it is possible that the true rate of asymptomatic effusion was underestimated. Finally, it is worth comparing this cardiac tamponade rate with that of another left atrial cardiovascular procedure, catheter ablation of AF. Despite this being a more mature therapy performed annually in >300,000 patients globally, the pericardial tamponade rate during AF ablation was 1.31% in a worldwide survey of 20,835 procedures (18) and 1.52% in an analysis of the 93,801 ablation procedures performed between 2000 and 2010 as identified in the national inpatient sample (19).

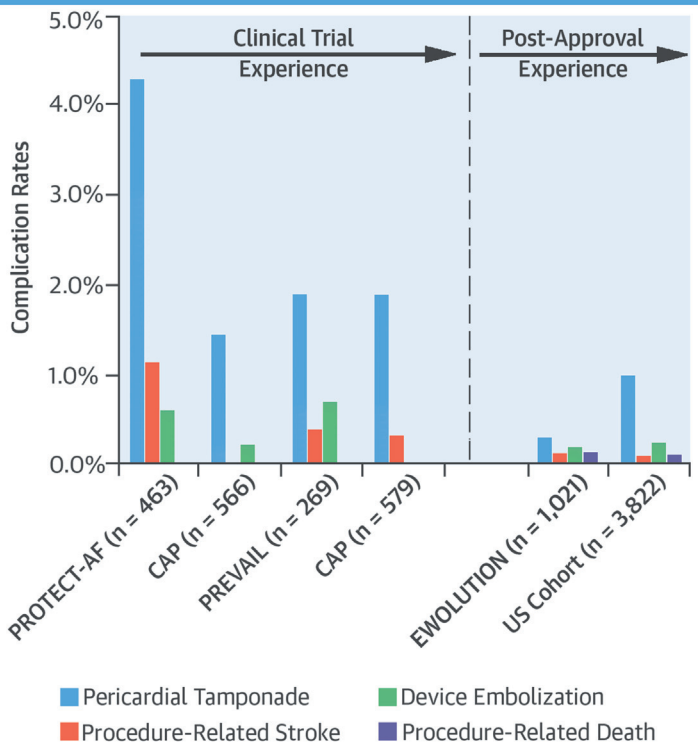
Procedure-related stroke, presumably related to inadvertent embolization of air or clot from the transseptal sheath, was an important issue in PROTECT-AF, occurring in 1.15% of patients. These procedure-related strokes were the difference between noninferiority and superiority at the time of the first reported analysis (2,3). However, with enhanced physician training, this rate has dramatically declined such that the rate in the present post-approval experience rate was <0.1%. Furthermore, of the 3 procedure-related strokes that occurred, 1

CENTRAL ILLUSTRATION **Major Complication Rates Across Watchman Clinical Studies**

Major Complication Rates Across Watchman Clinical Studies



Procedural Parameters	Aggregate Clinical Data
Number of Procedures	6,720
Implantation Success, %	94.9%
Complication Rates	
Pericardial Tamponade	1.24%
Procedure-Related Stroke	0.18%
Device Embolization	0.25%
Procedure-Related Death	0.06%



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(Top left) Placement of the Watchman device to sequester the left atrial appendage from the systemic circulation. **(Bottom left)** Table summarizing the aggregate procedural parameter outcomes and complication rates after combining the >6,000 patients receiving the device in the FDA clinical trials (PROTECT-AF, PREVAIL, CAP, and CAP2) and the post-approval studies (EWOLUTION and the present post-FDA approval U.S. cohort). **(Right)** Graph comparing the complication rates of the 4 major procedure-related complications (pericardial tamponade, procedure-related stroke, device embolization, and procedure-related death) across the various Watchman clinical studies. CAP = Continued Access to PROTECT-AF; CAP2 = Continued Access to PREVAIL; EWOLUTION = Registry on Watchman Outcomes in Real-Life Utilization; FDA = U.S. Food and Drug Administration; PREVAIL = Prospective Randomized Evaluation of the Watchman LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy; PROTECT-AF = Watchman Left Atrial Appendage System for Embolic PROTECTion in Patients With Atrial Fibrillation.

patient presented the next day with a cranial bleed identified on computed tomographic imaging, raising the possibility that this was actually a hemorrhagic stroke, perhaps related to oral anticoagulation. Similarly, the device embolization rate is also lower at 0.24%, translating to 1 embolization per 425 patients. As previously reported, the majority were recognized either at the time of the procedure or before hospital discharge (20). However, because comprehensive follow-up TEE data was not available, it is possible that not all asymptomatic embolizations were identified. It is also important to recognize that approximately two-thirds of these embolized devices could not be removed percutaneously and required open surgical removal. This was true for both the post-approval cohort and the aggregate Watchman LAAC cohort (Table 4).

Finally, procedure-related mortality has been infrequent throughout the Watchman LAAC experience (Table 4). In the aggregate Watchman LAAC experience, procedure-related mortality was only 0.06%, which translates to only 1 death per 1,680 patients (Table 4). Interestingly, all 3 deaths in the post-FDA approval experience occurred in patients who sustained pericardial tamponade. This is similar to catheter ablation of AF, wherein the most common cause of procedure-related mortality was also pericardial tamponade (21). Thus, although the overall safety outcomes are favorable and pericardial tamponade rates are overall decreasing, this complication

nonetheless can be deadly. Hopefully, future technology improvements will further decrease cardiac tamponade rates (22).

These favorable complication rates are all the more remarkable when one considers that 71% of the operators were newly implanting physicians, and these physicians performed 50% of the procedures. Because this was not an institutional review board-approved clinical study with available patient-level data linked to complications, it was not possible to compare the complication rates of experienced operator to those of inexperienced operators. However, even if one made the implausible assumption that all of the complications occurred only with the inexperienced operators, the complication rates for pericardial tamponade, procedure-related stroke, device embolization, and procedure-related mortality still would have been only 2.0%, 0.16%, 0.48%, and 0.16%, respectively. Compared to the clinical trials, even these putative rates would be reasonable for an initial introduction of a first-in-class procedure such as LAAC. Together, these outcomes suggest that the FDA-mandated clinical education program instituted by the manufacturer has been successful in transferring to new operators the various procedural lessons from the years of clinical trials.

STUDY LIMITATIONS. Although information was entered by trained clinical specialists, this dataset lacks the structured oversight of a clinical trial, with no source verification, no core laboratory for procedural testing and assessment, and no informed consent for collection of patient characteristics or follow-up outcomes. Operators were not required to report procedure-related adverse events that were recognized beyond the procedural period itself (when the clinical specialist was not present); therefore, complication rates may be underestimated compared to that observed in the clinical trials. Complication data were site reported and were submitted to the FDA by the manufacturer as part of the required regulatory mandatory device reporting filings. These were all independently reviewed by 2 of the investigators (V.Y.R., D.R.H.) with complete concordance of attribution of causation of any of the events. Mitigating against these limitations was the presence of well-trained clinical specialists during the cases and an adjudication oversight process. Patient demographics were not collected as part of the standardized implant form because a national registry with informed consent had not yet been established for this cohort. However, clinical demographic data for all consecutive post-approval implant patients were obtained from several of the authors' centers (V.Y.R., S.K.D., D.N.G., R.P.H.) representing a total of 426 patients: age 76 ± 8 years, CHA_2DS_2-VASc score 4.0 ± 1.4, and HAS-BLED score 2.5 ± 1.0 (V.Reddy, October 2016, unpublished data). Although these patients represent only a fraction of the full 3,822-patient cohort, the characteristics of the patients in this cohort suggest that they are similar to the patients enrolled in the clinical trials.

CONCLUSIONS

Since the time of device approval by the U.S. FDA, clinical application of the Watchman LAA closure technology has been used in increasing numbers of patients. The data from this study indicate that in this real-world dispersion of this technology, procedural success rates remain high. Similarly, despite a large fraction of inexperienced operators performing approximately 50% of the procedures, major complication rates were low compared to earlier reported experiences in the clinical trials. Importantly, cardiac tamponade occurred in approximately 1% and procedure-related mortality occurred in <0.1% of patients.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: The LAAC device has emerged as a stroke prevention option for patients who are poor candidates for long-term oral anticoagulation. After FDA approval, nearly 70% of physicians implanting the device were previously inexperienced with the procedure, yet the reported rate of procedure-related complications has been relatively low, including an approximately 1% rate of pericardial tamponade.

TRANSLATIONAL OUTLOOK: Further studies are needed to characterize the patients for whom LAAC is most often selected and to define the efficacy of this therapeutic option for stroke prevention in clinical practice.

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