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Changes in Left Atrial Appendage Dimensions Following Volume Loading During Percutaneous Left Atrial Appendage Closure

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ABSTRACT

OBJECTIVES This study sought to determine whether volume loading alters the left atrial appendage (LAA) dimensions in patients undergoing percutaneous LAA closure.

BACKGROUND Percutaneous LAA closure is increasingly performed in patients with atrial fibrillation and contraindications to anticoagulation, to lower their stroke and systemic embolism risk. The safety and efficacy of LAA closure relies on accurate device sizing, which necessitates accurate measurement of LAA dimensions. LAA size may change with volume status, and because patients are fasting for these procedures, intraprocedural measurements may not be representative of true LAA size.

METHODS Thirty-one consecutive patients undergoing percutaneous LAA closure who received volume loading during the procedure were included in this study. After an overnight fast and induction of general anesthesia, patients had their LAA dimensions (orifice and depth) measured by transesophageal echocardiography before and after 500 to 1,000 ml of intravenous normal saline, aiming for a left atrial pressure >12 mm Hg.

RESULTS Successful implantation of LAA closure device was achieved in all patients. The average orifice size of the LAA at baseline was 20.5 mm at 90°, and 22.5 mm at 135°. Following volume loading, the average orifice size of the LAA increased to 22.5 mm at 90°, and 23.5 mm at 135°. The average increase in orifice was 1.9 mm ($p < 0.0001$). The depth of the LAA also increased by an average of 2.5 mm after volume loading ($p < 0.0001$).

CONCLUSIONS Intraprocedural volume loading with saline increased the LAA orifice and depth dimensions during LAA closure. Operators should consider optimizing the left atrial pressure with volume loading before final device sizing. (J Am Coll Cardiol Intv 2015;8:1935–41) © 2015 by the American College of Cardiology Foundation.

Atrial fibrillation (AF) is thought to account for 15% to 20% of all ischemic strokes and, due to an increasingly aging population, is growing in prevalence. Studies predict that by the year 2050, there will be between 12 and 16 million patients with AF in the United States alone (1). AF is associated with a 4- to 5-fold increase risk of ischemic stroke, this being its most devastating complication (2). Although warfarin and the novel oral anticoagulants reduce the risk of ischemic stroke in many patients with AF, they carry significant risks of bleeding and may not be tolerated by all. Accordingly, alternative treatment strategies for reducing the bleeding complications associated

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ABBREVIATIONS AND ACRONYMS

ACP = Amplatzer Cardiac Plug

AF = atrial fibrillation

CT = computed tomography

IV = intravenous

LAA = left atrial appendage

TEE = transesophageal echocardiography

with lifelong anticoagulation have been widely sought.

Two randomized controlled trials have shown the safety and efficacy of percutaneous left atrial appendage (LAA) closure, and this procedure has emerged as an alternative for patients with AF and significant stroke risk, who are at increased risk of bleeding (3,4). Percutaneous LAA closure has obvious benefits, including removing the need for ongoing adherence to anticoagulation, eliminating monitoring, decreasing medication interactions, and reducing ongoing bleeding risk. Minimizing periprocedural complications of percutaneous LAA closure is critical in order to offer a favorable risk-benefit ratio to patients. These include access site complications, pericardial effusion and tamponade, residual leak around the device, and embolization of the implanted device. Appropriate sizing of the currently available implantable devices is paramount for both procedural success and to reduce periprocedural complications. Choosing the correctly sized device relies on accurate measurement of LAA size.

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The 2 most widely implanted LAA closure devices are the WATCHMAN (Boston Scientific, Natick, Massachusetts) and the Amplatzer Cardiac Plug (ACP)/Amulet (St. Jude Medical, Plymouth, Minnesota). Choosing the correct device size is important to achieve proper apposition of the device and its hooks against the LAA wall. An undersized device may result in embolization or residual leak, whereas aggressive oversizing may cause tamponade, or device embolization due to inadequate engagement of the hooks. Hence, accurately measuring the LAA size is integral to safe percutaneous LAA closure. Both transesophageal echocardiography (TEE) and computed tomography (CT) have been used pre-procedurally to measure the depth and orifice diameter of the LAA, and been shown to correlate reasonably well (5). Although CT is usually undertaken in a euvolemic state, pre-procedural and intra-procedural TEE involves at least 6 h of fasting. This may affect the volume status of the patient, which in turn may affect LAA size. Previous studies in animals and patients in sinus rhythm have shown the LAA to be more compliant than the left atrium (6,7), supporting a hypothesis that clinically significant increases in LAA size may occur with volume loading. A single canine study demonstrated small increases in LAA size after volume loading (8), leading to speculation that LAA measurements used for percutaneous closure may be affected by volume status and the fasting state (5).

We hypothesized that volume loading during the procedure (to overcome the fluid restriction pre-procedure) affects LAA dimensions, and thus we routinely administer intravenous (IV) normal saline before sizing measurements. Our study aims to assess the impact of an intravenous fluid bolus on LAA size, and thus determine whether there is clinical utility in optimizing fluid status before measuring maximum LAA dimensions.

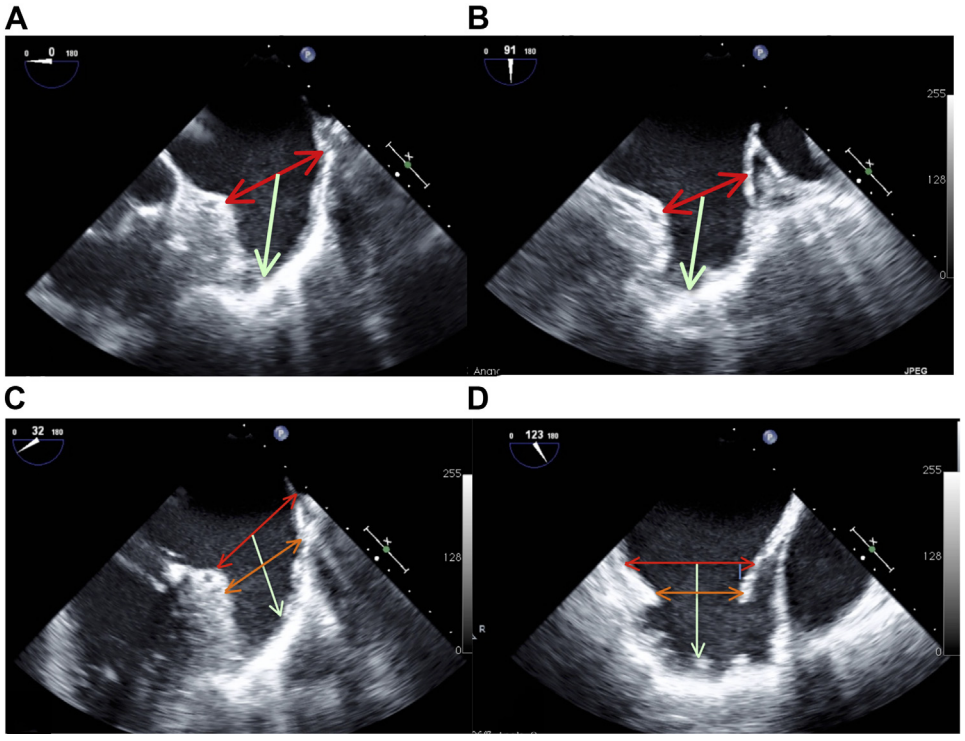
METHODS

Thirty-one consecutive patients who underwent percutaneous LAA closure (with either the ACP or WATCHMAN devices) at our center between March 2014 and May 2015 were included in this study. All patients received IV normal saline targeting a left atrial pressure of >12 mm Hg. Indications for LAA closure were nonvalvular AF with contraindications to long-term anticoagulation, with CHADS2 ≥1 and CHADS-VASc ≥2 (in accordance with the American College of Cardiology and the Canadian Cardiovascular Society AF guidelines for oral anticoagulation) (9,10). All patients underwent general anesthesia after a minimum of 6 hours of fasting.

A Philips IE33 echocardiography machine and X7-2t TEE probe (Philips, Andover, Massachusetts) were used to obtain baseline measurements of the LAA orifice diameter and depth before normal saline administration. Measurements were taken as per the manufacturer's guidelines. For ACP/Amulet, the widest landing zone was measured at ~10 mm inside the orifice for ACP and ~12 mm for Amulet. For WATCHMAN, the widest anatomic orifice (from the circumflex artery inferiorly to a point 1 to 2 cm inside the tip of the pulmonary vein ridge superiorly) and the LAA depth were recorded (**Figure 1**). For the purpose of this study, we measured the LAA orifice and depth at 90° and 135°, because these usually produce the largest dimensions; and utilized the WATCHMAN orifice definition to measure the orifice diameter (**Figures 1 and 2**). Measurements were taken when LAA width was greatest, which usually occurs at end-systole.

Following baseline measurements, a 500- to 1,000-ml IV bolus of normal saline was infused. One liter was given unless the patient had known left ventricular dysfunction or there were pre-operative concerns of volume overload, in which case 500 ml was given instead. We proceeded with transseptal puncture during the saline infusion, and the left atrial pressure was measured after transseptal access was achieved. After the infusion was completed, and the left atrial pressure was >12 mm Hg, we then repeated the LAA

FIGURE 1 Measuring the Orifice and Depth of the LAA for Percutaneous Closure



(A and B) A WATCHMAN device requires measuring from a point adjacent to the circumflex artery to the widest point 1 to 2 cm down from the tip of the pulmonary vein ridge at 0°, 45°, 90°, and 135°. **(C and D)** Similar measurements are required for the ACP/Amulet devices although the orifice is defined as the tip of the pulmonary vein ridge, and an extra measurement, 10 to 12 mm down from the orifice, is also required. ACP = Amplatzer Cardiac Plug; LAA = left atrial appendage; **(A and B): Red** = WATCHMAN ostium measurement zone; **green** = WATCHMAN depth measurement; **(C and D): Red** = echocardiographic orifice; **orange** = ACP landing zone; **green** =ACP depth measurement.

measurements on TEE. Saline infusion occurred during typical procedural steps and did not delay procedural completion. Given that mechanical ventilation may reduce pre-load, we ensured that the left atrial pressure was >12 mm Hg in addition to volume loading alone, before repeating TEE measurements.

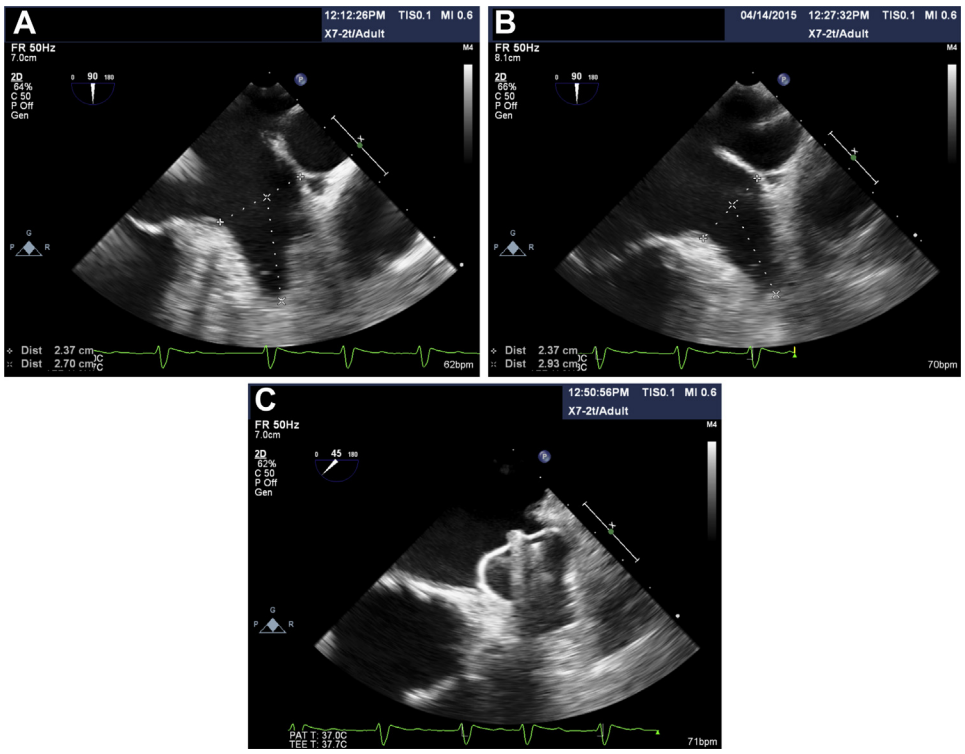
Device size selection was based on the widest orifice/landing zone dimensions measured post-fluid bolus, incorporating an upsize by 3 to 5 mm for ACP and 9% to 25% for WATCHMAN. Patients then underwent LAA closure with either a WATCHMAN or ACP/Amulet, according to our previously described protocol (11). In an effort to reduce bias and improve accuracy, all LAA TEE images were reread utilizing a commercially available offline workstation (Xcelera, Philips, Andover, Massachusetts) by 1 of 3 echocardiographers (R.S., M.T., J.J.) blinded to the stage of the procedure. Only these blinded measurements were used in this study.

STATISTICAL ANALYSIS. Descriptive statistics were used to describe the baseline characteristics of patients. Continuous variables were summarized as mean ± SD or median and interquartile range. Categorical variables were summarized as frequency and percentage. Continuous variables were compared using the paired Student *t* test. Statistical tests were 2-sided, and a p value <0.05 was considered significant. Statistical analyses were performed with the SPSS software (IBM SPSS version 20, Armonk, New York).

RESULTS

All 31 patients had underlying nonvalvular AF with contraindications to anticoagulation. The average age of the patients was 77 ± 7 years, and the mean CHADS2 score was 3.0 ± 1.4. Baseline characteristics are described in Table 1. All patients achieved mean left atrial pressure >12 mm Hg (28 of 31, or 90.3%, had a left atrial pressure of at least 15 mm Hg) after volume loading. Left atrial pressures were not obtained before volume loading, because all baseline TEE

FIGURE 2 LAA Measurements Made Before Closure With a WATCHMAN Device



(A) Measurements made before the fluid bolus. **(B)** Measurements post-fluid bolus. **(C)** Final image after WATCHMAN deployment showing occlusion of the LAA. LAA = left atrial appendage.

measurements were taken before transseptal puncture to minimize procedural time. All patients had 90° pre- and post-bolus images available for blinded analysis. Four patients had post-bolus 135° images that were either obscured by the delivery catheter or not stored, leaving 31 90° measurements and 27 135° measurements for analysis.

The average orifice size of the LAA at baseline was 20.5 ± 4.5 mm at 90°, and 22.5 ± 4.4 mm at 135°. Following volume loading, the average orifice size of the LAA increased to 22.5 ± 4.0 mm at 90°, and 23.5 ± 4.7 mm at 135° (Figure 3A). The average depth of the LAA at baseline was 24.5 ± 5.4 mm at 90°, and 22.7 ± 5.6 mm at 135°. After volume loading, the average depth of the LAA was 26.1 ± 5.0 mm at 90°, and 25.0 ± 5.3 mm at 135° (Figure 3B). The average increase in orifice was 1.9 mm ($p < 0.0001$), and increase in depth was 2.4 mm ($p < 0.0001$) (Table 2). Twenty-nine of the 31 patients had an increase in width measurements after volume loading. Analysis by sex and by age quartiles did not detect any significant interactions.

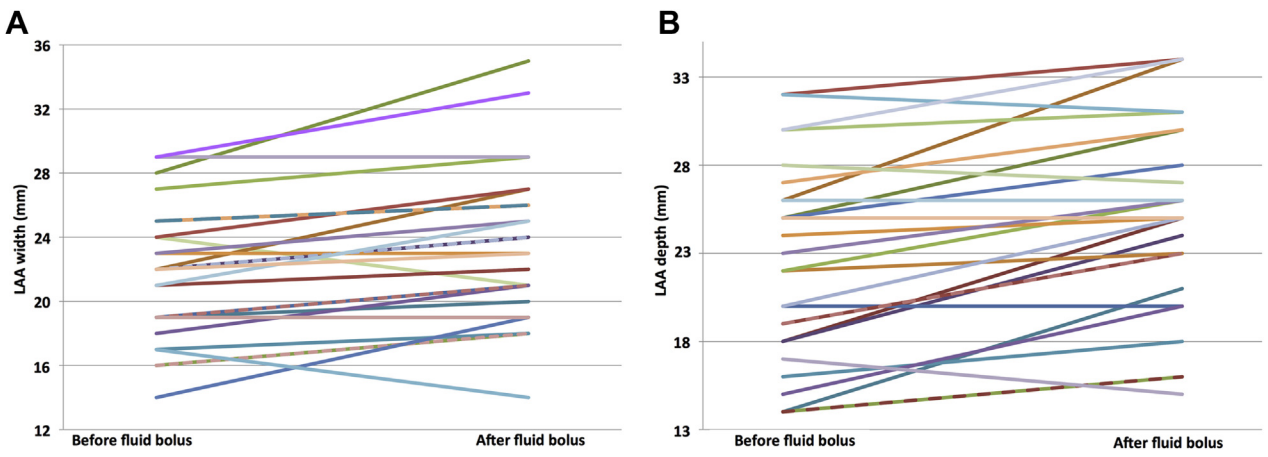
All patients proceeded to successful LAA closure with no periprocedural stroke or major bleeding. No pericardial effusions or congestive heart failure occurred. Four of the 31 patients were noted to have small peridevice leaks (<3 mm) on their procedural TEE. Thirty of the 31 patients were discharged the day after the procedure. One device embolization occurred with a 24-mm ACP device. This was discovered when routine transthoracic echocardiography the morning after the procedure suggested an unusual location of the device in the left atrium. This device was successfully retrieved percutaneously with no complication. This patient was delirious and

TABLE 1 Baseline and Procedural Characteristics

Age, yrs	76.7 ± 6.7
Male	55%
CHADS2 score	3.0 ± 1.4
Final LA pressure after volume, mm Hg	17.6 ± 3.5
IV normal saline given, ml	855 ± 227

Values are mean ± SD or %.
IV = intravenous; LA = left atrial.

FIGURE 3 Graph Showing Change in LAA Orifice Width and Depth



(A) Graph showing change in LAA orifice width (measured at 135°) after infusion of normal saline bolus. n = 27 (data were not recorded for 4 patients at 135°). Each **line** represents 1 patient (**long-dashed line** represents 3 patients; **short-dashed lines** represent 2 patients). **(B)** Graph showing change in LAA depth (measured at 135°) after infusion of normal saline bolus. n = 27 (data were not recorded for 4 patients at 135°). Each **line** represents 1 patient, **dashed lines** represent 2 patients. LAA = left atrial appendage.

combative during the evening after the procedure and required 4-point restraints. The aggressive physical movements in the setting of slight device malapposition were felt to be contributing factors leading to embolization, as opposed to inaccurate device sizing.

DISCUSSION

In this study, we found that LAA width and depth consistently increased by an average of ~2 mm after volume loading during general anesthesia. These results support the hypothesis that LAA size can vary with volume loading. This size difference, although relatively small, still represents an ~10% increase in the LAA dimensions following fluid bolus. This is clinically relevant when considering the appropriate device size for a given patient, because this 10% size increase typically corresponds to upsizing of the currently available devices by an entire size. For example, the WATCHMAN device comes in 5 sizes (21, 24, 27, 30, and 33 mm) and a device 10% to 20% larger than the measured orifice width is typical chosen. A 2-mm increase in the measured orifice width is likely to result in selecting a device that is 1 size larger than if measurements without volume loading were used. Theoretically, this more accurate sizing will result in better device stability and potentially lower residual LAA leak. Although the clinical significance of residual leak has not yet been established, many believe that large residual LAA leaks can contribute to higher stroke risk, as was seen with surgical LAA closure (12,13).

Although the fasting state may represent the natural state for many patients in the early hours of the day, the optimal values when choosing a closure device are the largest possible LAA dimensions. Establishing the physiological maximum width of the LAA enables the operator to select the largest device that can be accommodated by the LAA, which is likely to have the least risk of leak, embolization, and perforation. Overzealous oversizing should be avoided because this increases the risk of perforation, and may also lead to device embolization if the hooks fail to engage the LAA wall properly. Therefore, selecting a device that remains 8% to 20% compressed when the LAA is at its maximal size is of paramount importance. Our strategy of volume loading of 500 to

TABLE 2 LAA Width and Depth Measurements Before and After Volume Loading

	Before Fluid Bolus	After Fluid Bolus	p Value
90° width, mm	20.5 ± 4.5	22.5 ± 4.0	<0.001
90° depth, mm	24.5 ± 5.4	26.1 ± 5.0	<0.01
135° width, mm	22.5 ± 4.4	23.5 ± 4.7	<0.001
135° depth, mm	22.7 ± 5.6	25.0 ± 5.3	<0.001

Values are mean ± SD.
LAA = left atrial appendage.

1,000 ml during the procedure and aiming for a left atrial pressure >12 mm Hg is simple to adhere to and tolerated by all patients. This strategy maximizes the measurements for device selection.

Our findings suggest that a similar volume loading strategy may be useful for the baseline pre-procedural TEE (days to weeks before the procedure) in order to optimize LAA measurements. Because most echocardiographic laboratories require patients to fast for TEE, the measured dimensions may be similarly affected, and consideration should be given to volume loading before measuring LAA dimensions. The difference in volume status may also explain the small differences between CT angiography and TEE measurements seen in previous studies (5), because most patients are not required to restrict fluids before CT.

STUDY LIMITATIONS. These findings should be viewed in the context of the study's limitations. Our sample size was relatively small, and although a significant difference was found, caution is required when studying such small groups. Accurate echocardiographic measurement of the LAA is challenging, and obtaining identical views before and after volume loading is not always possible. Although the differences seen were small, they were consistent across the group of patients studied, and are supported by previous studies (6–8). In an effort to reduce possible bias, TEE measurements were made by echocardiographers experienced in assessing LAA size for percutaneous closure, who were blinded to the fluid status of the patient. Because we were unable to measure pre-bolus left atrial pressure, it is possible that a few patients may have started with an adequate volume status, potentially explaining the smaller LAA size change seen in some patients. From a practical perspective, because all patients fasted before the procedure and were likely to receive IV fluid after induction of anesthesia, delaying LAA measurements until after fluid administration and achievement of adequate LA pressure seems prudent. Of note, significant contrast administration during the procedure has the potential to increase LAA dimensions and could have confounded our repeat LAA measurements; however, these measurements were typically performed before contrast administration. Finally, we were not able to assess the effect of volume loading on clinical outcomes, as there was no comparative group who did not undergo volume loading.

CONCLUSIONS

Given the importance of pre-implantation LAA measurements for accurate device sizing and the increase in LAA dimensions observed with volume loading in this study, operators should consider ensuring that patients are adequately volume loaded before making final measurements and device sizing choices during percutaneous LAA closure. The clinical outcomes of this simple intervention should be further explored in larger prospective studies focusing on procedural safety and efficacy.

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PERSPECTIVES

WHAT IS KNOWN? The safety and efficacy of percutaneous LAA closure relies on accurate device sizing, which necessitates accurate measurement of LAA dimensions. LAA size may change with volume status, and as patients are fasting for these procedures, intraprocedural measurements may not be representative of true LAA size.

WHAT IS NEW? This study provides evidence that volume loading during percutaneous LAA closure increases the orifice width and depth of the LAA by ~2 mm, which can significantly impact device size selection.

WHAT IS NEXT? Further studies evaluating procedural outcomes in patients undergoing LAA closure with and without periprocedural volume loading and optimizing left atrial pressure, will help clarify the clinical impact of volume loading.

REFERENCES

1. Miyasaka Y, Barnes ME, Gersh BJ. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. Circulation 2006;114:119–25.

2. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke 1991;22:983–8.

3. Holmes DR, Reddy VY, Turi ZG, et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet 2009;374:534–42.

4. Holmes DR Jr., Kar S, Price MJ, et al. Prospective randomized evaluation of the Watchman Left

Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. J Am Coll Cardiol 2014;64:1–12.

5. López-Mínguez JR, González-Fernández R, Fernández-Vegas C, et al. Comparison of imaging techniques to assess appendage anatomy and measurements for left atrial appendage closure device selection. J Invasive Cardiol 2014;26:462–7.

6. Davis CA, Rembert JC, Greenfield JC. Compliance of left atrium with and without left atrium appendage. Am J Physiol 1990;259:H1006–8.

7. Tabata T, Oki T, Yamada H, et al. Roles of left atrial appendage in left atrial reservoir function as evaluated by left atrial appendage clamping during cardiac surgery. Am J Cardiol 1998;81:327–32.

8. Hondo T, Okamoto M, Yamane T, et al. The role of the left atrial appendage. A volume loading study in open-chest dogs. Jpn Heart J 1995;36:225–34.

9. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014;64:e1–76.

10. Skanes AC, Healey JS, Cairns JA, et al. Focused 2012 update of the Canadian Cardiovascular Society Atrial Fibrillation guidelines: recommendations for stroke prevention and rate/rhythm control. Can J Cardiol 2012;28:125–36.

11. Saw J, Lempereur M. Percutaneous left atrial appendage closure: procedural techniques and outcomes. J Am Coll Cardiol Intv 2014;7:1205–20.

12. Viles-Gonzalez JF, Kar S, Douglas P, et al. The clinical impact of incomplete left atrial appendage closure with the Watchman device in patients with atrial fibrillation. J Am Coll Cardiol 2012;59:923–9.

13. Healey JS, Crystal E, Lamy A, et al. Left Atrial Appendage Occlusion Study (LAAOS): results of a randomized controlled pilot study of left atrial appendage occlusion during coronary bypass surgery in patients at risk for stroke. Am Heart J 2005;150:288–93.

KEY WORDS left atrial appendage, left atrial appendage closure, transesophageal echocardiography, WATCHMAN