Journal of the American College of Cardiology
© 2013 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 62, No. 2, 2013
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2013.01.017

Thoracoscopic Stand-Alone Left Atrial Appendectomy for Thromboembolism Prevention in Nonvalvular Atrial Fibrillation

Toshiya Ohtsuka, MD,* Mikio Ninomiya, MD,* Takahiro Nonaka, MD,* Motoyuki Hisagi, MD,* Takahiro Ota, MD,† Toru Mizutani, MD†

Tokyo, Japan

Objectives This study sought to evaluate thoracoscopic stand-alone left atrial appendectomy for thromboembolism prevention in nonvalvular atrial fibrillation (AF).

Background Closing the left atrial appendage (LAA) is an efficacious alternative to oral anticoagulation as prevention against AF-induced thromboembolism, provided that the procedure is safe and complete.

Methods Thirty patients (mean age, 74 ± 5.0 years) who had had thromboembolisms were selected. A subgroup of 21 patients (mean age, 75 years; mean CHA_2DS_2 VASc score, 4.5) urgently needed an alternative treatment to anticoagulation: warfarin was contraindicated due to hemorrhagic side effects in 13, the international normalized ratio was uncontrollable in 7, and transient ischemic attacks had developed immediately after the warfarin dose was reduced for oncological treatment in 1. The LAA was thoracoscopically excised with an endoscopic cutter.

Results Thoracoscopic appendectomy (mean operating time, 32 min, switched to mini-thoracotomy in 2 cases) led to no mortality and no major complications. Three-month post-operative 3-dimensional enhanced computed tomography, performed with patients' consent, confirmed the completeness of the appendectomy. Patients have been followed for 1 to 38 months (mean, 16 ± 9.7 months [18 ± 9.4 months for the subgroup]). One patient died of breast cancer 28 months after surgery. Despite discontinued anticoagulation, no patients have experienced recurrence of thromboembolism.

Conclusions Thoracoscopic stand-alone appendectomy is potentially safe and may allow surgeons to achieve relatively simple, complete LAA closure. Further experience may demonstrate this technique to be a viable option for thromboembolism prevention in nonvalvular AF. (J Am Coll Cardiol 2013;62:103–7) © 2013 by the American College of Cardiology Foundation

Most clots originate in the left atrial appendage (LAA) when atrial fibrillation (AF) is nonrheumatic, so that sequestration of the LAA should prevent thromboembolism. Various effective surgical and transcatheter techniques have been devised to this end (1).

Blackshear et al. (2) have pioneered thoracoscopic surgical LAA closure aimed at preventing AF-induced stroke. Their good clinical results encouraged us to develop a new thoracoscopic technique for excising the LAA entirely from its base; we have applied the method to selected patients with nonvalvular ablation-refractory AF to prevent stroke and other thromboembolism recurrence. This paper describes the early clinical outcomes of thoracoscopic stand-alone appendectomy.

Methods

Patient selection. Thoracoscopic stand-alone appendectomy was offered to nonvalvular AF patients for secondary prevention of AF-induced thromboembolism on the condition that AF was expected to be refractory to ablative treatment. If AF was expected to be responsive to ablation, the patients underwent extracardiac radiofrequency ablation thoracoscopically and were excluded from the study. AF was judged to be ablation refractory when the patient manifested significant heart remodeling in routine checkups. Cardiogenicity of the thromboembolism was verified by neurologists, who used ultrasonography and magnetic resonance

See page 119

From the *Department of Cardiovascular Surgery, Tokyo Metropolitan Tama Medical Center, Tokyo Japan; and the †Department of Neurosurgery, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received June 5, 2012; revised manuscript received November 28, 2012, accepted January 2, 2013.

Abbreviations and Acronyms

AF = atrial fibrillation
LA = left atrium
LAA = left atrial appendage
TEE = transesophageal echocardiography

imaging angiography to rule out other ischemic etiologies. The LAA had to be clotless, as confirmed by enhanced computed tomography of the left atrium (LA). The patients had to be able to give informed consent for the operation. The protocol was approved by the institutional review board of the authors' institution.

Totally endoscopic LAA. The procedure was performed by a single surgeon. Anticoagulation was discontinued the day before surgery, after which intravenous drip infusion of heparin was given. Each patient was anesthetized through a double-lumen endotracheal tube and placed in the right lateral recumbent position. Transesophageal echocardiography (TEE) was performed with the patient in the optimal position to display the LAA. The left lung was spontaneously deflated, and 4 endoscopic ports were made in the left lateral thorax: one for a 5-mm, 45-degree camera, another for an endoscopic cutter (EZ45G Endoscopic Linear Cutter, Ethicon Endo-Surgery, Cincinnati, Ohio), and the other 2 for endo-forceps. A 5-cm-long pericardiotomy was made just above the LAA and 2 cm anterior to the left phrenic nerve. The endoscopic cutter was introduced into the chest, and the base of the LAA was divided (Fig. 1, Online Video 1). A single chest tube was left in the pleural cavity.

Follow-up. Patients underwent regular checkups, including imaging examinations if necessary, to investigate thromboembolic symptoms. Three-dimensional enhanced computed tomography of the LA was performed with patients' consent 3 months after surgery.

Results

Most of the 14 male and 16 female subjects (mean age, 74 ± 5.0 years; median age, 75 years; range, 61 to 84 years) (Table 1) had had AF for >10 years. In all patients, heart remodeling was significant; the LA diameter was dilated to 52 mm on average (range, 46 to 61 mm), and the amplitude of fibrillatory waves was <1 mm on the V_1 electrocardiograph electrode. All 30 patients had had a previous thromboembolism; 29 had had strokes and/or transient ischemic attacks (TIAs), and 1 patient had had superior mesenteric artery occlusion. Seven patients (23%) had had multiple episodes of thromboembolism. Thus, all patients had received warfarin for anticoagulation.

A subgroup of 21 patients (Patient #10 through #30; 10 men, 11 women; mean age, 75 ± 5.5 years; median age, 76 years; range, 61 to 83 years) urgently required alternative treatment to warfarin. Twenty of these had a high risk of imminent thromboembolism recurrence because of problems with the administration of warfarin: 13 had been commonly underdosed or often kept off warfarin due to hemorrhagic side effects (cerebral bleeding in 3 patients, persistent gastrointestinal bleeding in 9 patients [including occasional massive hemorrhoid bleeding in 1 patient], and unidentified severe anemia in 1 patient). Six patients had been continually underdosed because of difficulties controlling the international normalized ratio within the therapeutic range recommended for elderly populations (3). In 1 patient who had been given warfarin for the first time for a superior mesenteric artery embolism, the international normalized ratio had fluctuated uncontrollably, probably due to digestive dysfunction caused by extensive bowel resection. In another patient (a 66-year-old man with a diagnosis of early gastric cancer), the international normalized ratio was brought down to 1.25 2 days before gastroscopic mucosal resection, but the treatment had to be postponed because transient ischemic attacks soon developed and he went back on full anticoagulation. Except in 3 patients, 1 with a history of coronary artery bypass grafting, 1 with a midcerebral artery revascularization, and 1 with arteriosclerosis obliterans in the lower extremity, aspirin had been avoided, perhaps because of a report by the Japan Atrial Fibrillation Stroke Trial (4) indicating that low-dose aspirin does not

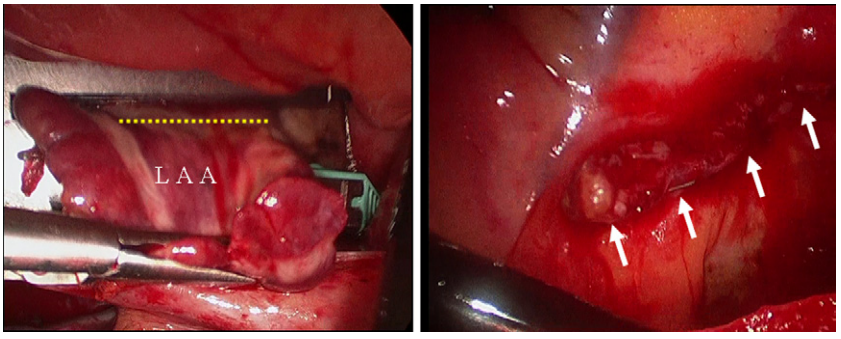

Figure 1 Thoracoscopic Views of Left Atrial Appendectomy

(Left) The **broken line** represents a long axis of the oval-shaped appendage's base sandwiched between endoscopic cutter's legs. **(Right) Arrows** indicate a stapled seam. See accompanying Online Video 1. LAA = left atrial appendage.

Table 1 Patients Characteristics and Outcomes

Patient #	Age, yrs	Sex	AF Duration, yrs	LA Size, mm	Anticoagulation History		TE/mRS Score	$CHADS_2$ (CHA_2DS_2-VASc) Score	Interval Between TE and Appendectomy (I <1 month, II <1 month to <2 months, III <2 months to <3 months)	Follow-Up	
					Hemorrhagic Side Effect	Warfarin Before TE				Duration, months	Recurrence
1	74	M	Unknown	60	None	NE	Stroke/0	2 (4)	2 yrs	24	None
2	73	F	>10	51	None	UD	Stroke/0	3 (5)	7 yrs	22	None
3	69	M	>10	48	None	NE	TIA/0	3 (4)	9 mo	19	None
4	71	F	>10	52	None	NE	Stroke/0	3 (5)	6 yrs	14	None
5	72	F	>10	54	None	UD	TIA/0	2 (4)	1 yr	10	None
6	74	M	Unknown	51	None	NE	Stroke/1	3 (5)	1 yr	7	None
7	77	F	Unknown	50	None	NE	Stroke/0	4 (5)	3 yrs	4	None
8	68	M	>10	54	None	UD	TIA/0	2 (4)	10 months	1	None
9	74	F	Unknown	50	None	NE	Stroke/0	3 (5)	1 yr	1	None
10	81	M	>10	61	Hemorrhoid	TH	TIA/0	4 (5)	II	38	None
11	76	F	Unknown	58	Cerebral	TH	Stroke/2	5 (7)	II	32	None
12	73	M	>10	51	GI	TH	Stroke/1	3 (4)	I	28	None
13	75	F	>10	52	GI	UD	Stroke, TIA/1	3 (5)	II	26	None
14	77	F	>10	49	Unidentified anemia	UD	Stroke/1	4 (5)	III	23	None
15	71	M	>10	60	GI	UD	Stroke/2	3 (4)	II	21	None
16	82	F	Unknown	50	Cerebral	TH	Stroke, TIA/3	4 (5)	III	21	None
17	69	M	>10	54	GI	UD	Stroke/0	2 (3)	I	19	None
18	73	F	>10	50	GI	UD	Stroke/1	3 (5)	II	15	None
19	79	F	>10	48	Cerebral	TH	TIA/0	4 (5)	II	14	None
20	70	M	>10	53	GI	UD	Stroke/1	4 (5)	I	13	None
21	72	F	>10	49	GI	UD	TIA/0	3 (5)	I	11	None
22	77	M	>10	48	GI	UD	Stroke/0	4 (4)	I	5	None
23*	78	F	>10	51	None	UD	Stroke/0	4 (5)	I	28	None
24	83	F	>10	52	None	UD	Stroke/1	4 (5)	II	19	None
25	79	M	>10	52	None	UD	Stroke/1	4 (4)	II	16	None
26	73	M	>10	54	None	UD	Stroke/0	3 (4)	I	12	None
27	76	F	>10	50	None	UD	Stroke, TIA/1	4 (5)	I	3	None
28	81	F	>10	58	None	UD	TIA/0	4 (5)	I	1	None
29†	61	M	Unknown	46	None	NE	SMAO/NA	2 (2)	III	24	None
30‡	66	M	>10	47	None	UD	TIA/0	2 (3)	II	16	None

Subgroup is from #10 to #30. *Died of breast cancer. †Warfarin was given after SMAO but the international normalized ratio was uncontrollable after extensive bowel resection. ‡TIAs occurred as the international normalized ratio was reduced to 1.25 for oncological treatment.

AF = atrial fibrillation; LA = left atrium; GI = gastrointestinal; TE = thromboembolism; mRS = modified Rankin scale; NE = no experience; UD = underdose; TH = temporary halt; TIA = transient ischemic attack; SMAO = superior mesenteric artery occlusion; NA = not available.

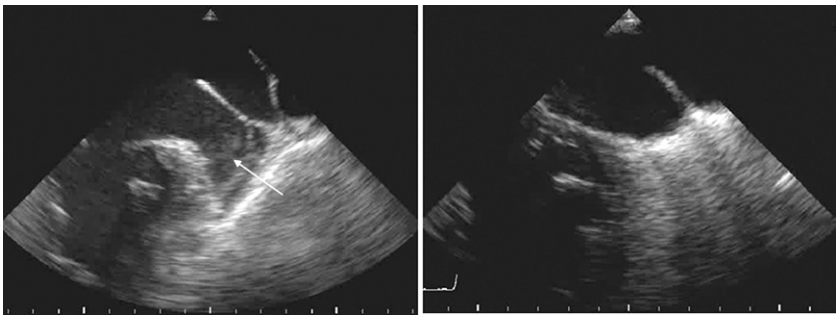

Figure 2 Intraoperative Transesophageal Echocardiograms Before and After Appendectomy

Intraoperative transesophageal echocardiograms before **(left)** and after **(right)** appendectomy. **Arrow** indicates a spontaneous echo contrast in the appendage.

seem to be either effective or safe. Post-stroke modified Rankin Scale scores were 0 for 9 of the patients, 1 for 8, 2 for 2, and 3 for 1. The mean $CHADS_2$ and CHA_2DS_2 VASc scores were 3.5 (range, 2 to 5) and 4.5 (range, 2 to 7), respectively. Surgery was performed within 1 month of thromboembolism in 9 of the subgroup patients, 1 to 2 months after thromboembolism in 9 patients, and 2 to 3 months after in 3 patients.

Surgery took 32 min on average (range, 18 to 91 min). Surgery was switched to mini-thoracotomy due to pericardial or pleural adhesions in 2 patients (6.7%). Blood loss was negligible, so no homologous blood products were used. Intraoperative TEE clearly demonstrated in 26 patients (87%) a spontaneous echo contrast in the LAA that vanished soon after appendectomy (Fig. 2). The mean post-operative hospital stay was 3.1 days (range, 2 to 6 days). The chest tube was removed 24 h after surgery from all but 1 patient, who experienced minor air leakage due to pleural adhesiolysis; drainage was prolonged for 2 days. A minor wound complication occurred in 1 patient on hemodialysis, but no operative death or major complications (e.g., stroke, cardiac events, pulmonary morbidity, left phrenic palsy) occurred.

Aspirin was continued in the 3 preoperatively medicated subgroup patients, but warfarin was discontinued in every patient after appendectomy. Three-dimensional enhanced computed tomography images of 19 patients (63%) obtained 3 months after surgery confirmed the absence of LAA stumps and clots in the LA cavity (Fig. 3). Follow-up of the total group of 30 patients ranged from 1 to 38 months, with a median of 16 months and a mean of 16 ± 9.7 months; the corresponding figures for the subgroup were 1 to 38 months, 19 months, and 18 ± 9.4 months, respectively. All patients avoided re-anticoagulation and recurrent thromboembolism. The only death was a woman in the subgroup who died 28 months later of breast cancer.

Discussion

Long-term oral anticoagulation is contraindicated in 14% to 40% patients with AF who are at risk of stroke (5), and use of newly available oral anticoagulants (e.g., dabigatran) is still risky for elderly patients (6). Optional prophylactic treatments must, therefore, be devised for vulnerable AF patients.

When permanent closure of the LAA was demonstrated to be an effective adjunct for stroke prevention in open-heart surgery (7), both surgeons and catheter interventionists focused on minimally invasive approaches to achieve this simple procedure. However, the LAA closure is not easy for 2 reasons. First, the LAA is fragile. Blackshear et al. (2) had 1 case of catastrophic bleeding among 15 cases of thoracoscopic LAA ligation, and cardiac tamponade is an occasional complication in transcutaneous LAA closure (8). Second, complete closure of the LAA is technically demanding. A retrospective TEE study by Kanderian et al. (9) found that even via the open approach, only 60% of surgical

Figure 3 3-Dimensional Image of the Left Atrium Constructed by 3-Month Post-Operative-Enhanced Computed Tomography

A stapled seam is encircled with a **broken line**; no stump is left.

LAA closures were completed without stumps and gaps. The percutaneous Watchman device has also been reported to result in peridevice flow in 32% of implanted patients (10). Incompletely closed LAAs may lead to continued clot formations and stroke recurrence (11). One TEE study (12) showed that 50% of incompletely ligated LAAs still produced thrombi and that 22% of them produced thromboembolic events.

We devised the present technique with the aim of materializing safe, complete, and minimally invasive LAA closure. Anatomic understanding of the LAA is essential; the LAA's ostium is as thick as the LA wall, but its body is thin and fragile, and the ostial plane is elliptical. We speculate that this morphology might make the simple extracardiac ligation of enlarged LAA bases with a suture or the newly developing LARIAT device technically difficult (13). In our technique, a long axis of the oval LAA ostium (Fig. 1) is recognized, and the axis is extended until it penetrates the chest wall. The intercostal site to be penetrated by this extended line, usually the seventh or eighth intercostal space on the posterior axillary line, becomes the port site for the endoscopic cutter. The LAA Occlusion Study reported that 28% of stapled LAAs left stumps (14). The failure is possibly due to suboptimal stapler angles through sternotomy in addition to the lack of the intraoperative TEE guidance.

Early discontinuation of anticoagulation could be an important benefit of thoracoscopic appendectomy, particularly to patients like those in our subgroup. Nevertheless, surgeons should know that thoracoscopy is challenging in patients who have excessively thick chests, who cannot tolerate 30-min hemipulmonary ventilation, or who have diffuse, dense adhesions in the pericardial or pleural spaces. Also, surgeons must keep in mind potential problems due to instrumental malfunction and difficult troubleshooting in thoracoscopic surgery; stapler malalignment may occur, and its mishandling would cause uncontrollable bleeding. A novel clip device may help reduce those potential risks (15).

Study limitations. This study has 2 main limitations. First, the case volume is still small, and no randomized, controlled comparisons with other therapeutic options were made. Second, the mean follow-up period was relatively short.

Conclusions

Thoracoscopic stand-alone appendectomy is potentially safe and may permit surgeons to remove the LAA relatively simply and completely.

This procedure would benefit patients who are at great risk of thromboembolisms and in whom anticoagulation is no longer tolerable. Although the experience to date is insufficient to address potential safety concerns associated with applying the technique in a limited-access environment, further experience may demonstrate this to be a viable option for thromboembolism protection in patients with nonvalvular AF.

Acknowledgment

The authors thank Dr. Randall K. Wolf for his support and inspirational advice.

Reprint requests and correspondence: Dr. Toshiya Ohtsuka, Department of Cardiovascular Surgery, Tokyo Metropolitan Tama Medical Center, 2-8-29 Musashi-dai, Fuchu-shi, Tokyo 183-8524, Japan. E-mail: toshiya_ootsuka@tmhp.jp.

REFERENCES

1. Onalan O, Crystal E. Left atrial appendage exclusion for stroke prevention in patients with nonrheumatic atrial fibrillation. Stroke 2007;38 Suppl:624–30.
2. Blackshear JL, Johnson WD, Odell JA, et al. Thoracoscopic extracardiac obliteration of the left atrial appendage for stroke risk reduction in atrial fibrillation. J Am Coll Cardiol 2003;42:1249–52.
3. Yamaguchi T. Optimal intensity of warfarin therapy for secondary prevention of stroke in patients with nonvalvular atrial fibrillation: a multicenter, prospective, randomized trial. Japanese Nonvalvular Atrial Fibrillation–Embolism Secondary Prevention Cooperative Study Group. Stroke 2000;31:817–21.
4. Sato H, Ishikawa K, Kitabatake A, et al. Low-dose aspirin for prevention of stroke in low-risk patients with atrial fibrillation: Japan Atrial Fibrillation Stroke Trial. Stroke 2006;37:447–51.
5. Onalan O, Lashevsky I, Hamad A, Crystal E. Nonpharmacologic stroke prevention in atrial fibrillation. Expert Rev Cardiovasc Ther 2005;3:619–33.
6. Harper P, Young L, Merriman E. Bleeding risk with dabigatran in the frail elderly. N Engl J Med 2012;366:864–6.
7. Cox JL, Ad N, Palazzo T. Impact of the maze procedure on the stroke rate in patients with atrial fibrillation. J Thorac Cardiovasc Surg 1999;118:833–40.
8. Reddy VY, Holmes D, Doshi SK, Neuzil P, Kar S. Safety of percutaneous left atrial appendage closure: results from the Watchman Left Atrial Appendage System for Embolic Protection in Patients with AF (PROTECT AF) clinical trial and the Continued Access Registry. Circulation 2011;123:417–24.
9. Kanderian AS, Gillinov AM, Pettersson GB, Blackstone E, Klein AL. Success of surgical left atrial appendage closure: assessment by transesophageal echocardiography. J Am Coll Cardiol 2008;52:924–9.
10. 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: a PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) substudy. J Am Coll Cardiol 2012;59:923–9.
11. Koz C, Baysan O, Yokusoglu M, Uzun M, Genc C. Left atrial appendage can still cause clinical events after ligation. Eur J Echocardiogr 2008;9:194–5.
12. Katz ES, Tsiamtsiouris T, Applebaum RM, et al. Surgical left atrial appendage ligation is frequently incomplete: a transesophageal echocardiographic study. J Am Coll Cardiol 2000;36:468–71.
13. Bartus K, Han FT, Bednarek J, et al. Percutaneous left atrial appendage suture ligation using the LARIAT device in patients with atrial fibrillation: initial clinical experience. J Am Coll Cardiol 2013;62:108–18.
14. 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.
15. Salzberg SP, Plass A, Emmert MY, et al. Left atrial appendage clip occlusion: early clinical results. J Thorac Cardiovasc Surg 2010;139:1269–74.

Key Words: left atrial appendage excision ■ nonvalvular atrial fibrillation ■ secondary prevention stroke ■ thromboembolism.

APPENDIX

For a supplementary video and its legend, please see the online version of this article.