



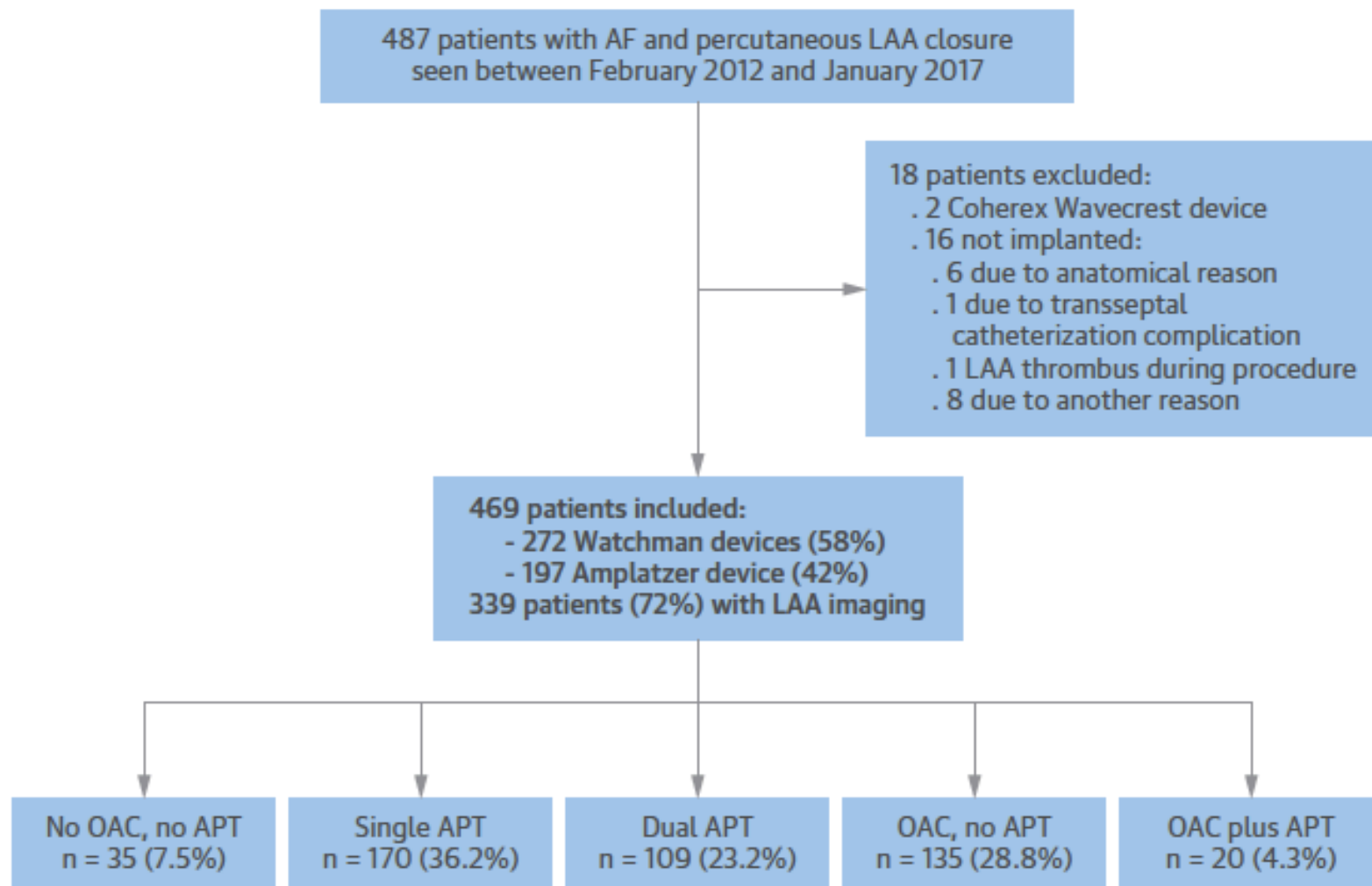
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Device-Related Thrombosis After Percutaneous Left Atrial Appendage Occlusion for Atrial Fibrillation

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FIGURE 1 Flowchart of the Study Group



The study cohort from RELEXAO (REgistry on Real-Life EXperience With Left Atrial Appendage Occlusion: [NCT03279406](https://clinicaltrials.gov/ct2/show/study/NCT03279406)) between February 1, 2007 and January 31, 2017 is shown. The proportions of the different devices for left atrial appendage (LAA) closure and patients with left atrial appendage imaging are shown, as well as the different antithrombotic regimens at hospital discharge. AF = atrial fibrillation; APT = antiplatelet therapy; OAC = oral anticoagulation.

TABLE 1 Baseline Characteristics of Patients Treated With LAA Occlusion

	All Patients (N = 487)	Nitinol Cage (n = 272)	Nitinol Plug (n = 197)	p Value (Nitinol Cage vs. Nitinol Plug)
Age, yrs	74.9 ± 8.9	74.6 ± 9.2	75.6 ± 8.5	0.25
Men	299 (61.4)	169 (62.1)	112 (61.9)	0.99
Medical history				
Hypertension	328 (84.1)	217 (84.1)	102 (85.7)	0.69
Diabetes mellitus	119 (30.6)	76 (29.6)	39 (32.8)	0.53
Ischemic stroke	179 (41.1)	102 (38.6)	69 (44.2)	0.26
Vascular disease	141 (43.4)	85 (44.0)	50 (42.0)	0.73
Permanent AF	244 (51.2)	132 (49.6)	102 (52.0)	0.61
LV ejection fraction, %	55.9 ± 10.0	56.4 ± 9.3	55.4 ± 10.4	0.32
LAA maximum diameter, mm (n = 353)	21.9 ± 4.4	21.4 ± 4.1	22.6 ± 4.9	0.01
CHA ₂ DS ₂ -VASc score	4.5 ± 1.4	4.4 ± 1.5	4.7 ± 1.2	0.008
HAS-BLED score	3.7 ± 1.0	3.7 ± 1.0	3.8 ± 1.0	0.08
Indication				
Previous bleeding	426 (90.1)	237 (89.4)	174 (91.1)	0.55
Contraindication to OAC	345 (72.8)	199 (74.8)	136 (71.2)	0.40
Recurrent ischemic stroke	25 (5.3)	18 (6.8)	5 (2.6)	0.05

LAA closure device				
Nitinol cage	272 (55.9)	–	–	–
Nitinol plug	197 (40.5)	–	–	–
WaveCrest	2 (0.4)	–	–	–
Implantation failure	16 (3.3)	–	–	–
Antithrombotic therapy at discharge				
No OAC, no APT	37 (7.7)	9 (3.3)	26 (13.2)	<0.0001
Single APT	171 (35.8)	82 (30.1)	88 (44.7)	0.002
Dual APT	110 (23.0)	63 (23.2)	46 (23.4)	0.96
OAC, no APT	138 (28.9)	101 (37.1)	34 (17.3)	<0.0001
OAC plus APT	22 (4.6)	17 (6.3)	3 (1.5)	0.009
LAA imaging during follow-up*	340 (72.1)	238 (87.5)	101 (51.3)	<0.0001

Values are mean \pm SD or n (%). Percentages calculated from available data. *In patients with implanted device.

AF = atrial fibrillation; APT = antiplatelet therapy; CHA₂DS₂-VASc = congestive heart failure, hypertension, age \geq 75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65 to 74 years, and female sex; HAS-BLED = hypertension, abnormal renal and liver function, stroke, bleeding, labile international normalized ratio, elderly (age <65 years), drug or alcohol use; LAA = left atrial appendage; LV = left ventricular; OAC = oral anticoagulation.

TABLE 2 Major Adverse Events (n = 98) in Patients Treated With LAA Occlusion Using the Nitinol Plug or Nitinol Cage Devices

	Overall (N = 469)	Nitinol Cage (n = 272)	Nitinol Plug (n = 197)	p Value (Nitinol Cage vs. Nitinol Plug)
Death	33 (6.9)	18 (6.7)	15 (7.1)	0.85
Ischemic stroke	19 (4.0)	10 (3.7)	9 (4.3)	0.86
TIA	2 (0.4)	2 (0.7)	0 (0)	—
Major hemorrhage	18 (3.8)	10 (3.7)	8 (3.8)	0.76
Thrombus on the device				
In the whole study group	26 (5.4)	13 (4.8)	13 (6.2)	0.36
In patients with LAA imaging	26 (7.2)	13 (5.5)	13 (11.0)	0.02

Values are n (yearly rate %).

LAA = left atrial appendage; TIA = transient ischemic attack.

TABLE 3 Device-Related Thrombus Characteristics*

	Thrombus (n = 26)	No Thrombus (n = 313)	p Value
Age, yrs	76.1 ± 8.9	74.2 ± 9.0	0.31
Men	16 (61.5)	185 (59.1)	0.81
Medical history			
Hypertension	19 (79.2)	259 (86.3)	0.33
Diabetes mellitus	6 (25.0)	88 (29.4)	0.65
Ischemic stroke	14 (58.3)	129 (41.9)	0.12
Permanent AF	11 (42.3)	155 (49.7)	0.47
Previous bleeding	23 (92.0)	276 (90.2)	0.77
CHA ₂ DS ₂ -VASc score	4.7 ± 1.7	4.5 ± 1.4	0.49
HAS-BLED score	3.5 ± 1.3	3.7 ± 1.0	0.26
LV ejection fraction, %	53.1 ± 12.2	56.7 ± 9.4	0.15
LAA maximum diameter, mm (n=353)	22.2 ± 4.9	21.4 ± 4.3	0.48
Nitinol plug device	13 (12.9)	88 (87.1)	0.02
Nitinol cage device	13 (5.5)	225 (94.5)	0.02
Antithrombotic therapy at discharge			
No OAC, no APT	4 (15.4)	14 (4.5)	0.02
Single APT	11 (42.3)	91 (29.1)	0.15
Dual APT	1 (3.8)	81 (25.9)	0.01
OAC, no APT	10 (38.5)	108 (34.5)	0.68
OAC plus APT	0 (0.0)	19 (6.1)	0.23
Leaks			
Peridevice leakage	1 (3.8)	50 (16.0)	0.10
Peridevice leakage >5 mm	0 (0.0)	17 (5.4)	0.22

Values are mean ± SD or n (%). *Analysis restricted to patients with LAA imaging during follow-up. Abbreviations as in [Table 1](#).

TABLE 4 Multivariable Analysis (Cox Regression Model) for Predictors of Thrombus Formation on the Device and Predictors of Stroke and TIA*

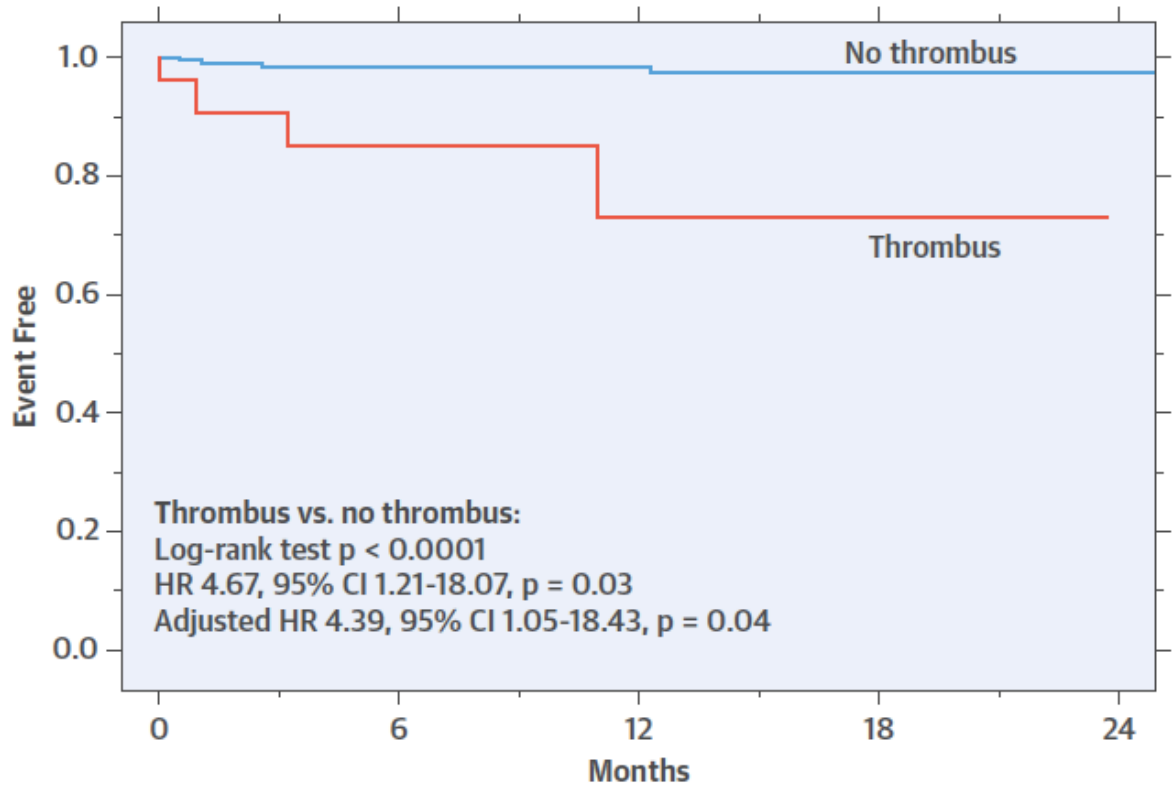
	HR (95% CI)	p Value
Thrombus formation on the device		
Age (per 1-yr increase)	1.07 (1.01-1.14)	0.02
Previous ischemic stroke	3.68 (1.17-11.62)	0.03
CHA ₂ DS ₂ -VASc score	0.69 (0.44-1.06)	0.09
APT at discharge	0.35 (0.12-1.04)	0.06
Dual APT at discharge	0.10 (0.01-0.76)	0.03
OAC at discharge	0.26 (0.09-0.77)	0.02
Strokes or TIAs		
Vascular disease	5.03 (1.39-18.23)	0.01
Thrombus on the device	4.39 (1.05-18.43)	0.04
CHA ₂ DS ₂ -VASc score	0.71 (0.47-1.06)	0.09
APT at discharge	1.35 (0.20-9.06)	0.75
Dual APT at discharge	0.64 (0.15-2.69)	0.54
OAC at discharge	0.39 (0.06-2.61)	0.33

*Analysis restricted to patients with LAA imaging during follow-up. For prediction of thrombus formation on the device, time zero is time at discharge after LAA closure. For prediction of stroke or TIA, time zero is time at first post-procedure LAA imaging.

CI = confidence interval; HR = hazard ratio; other abbreviations as in [Table 1](#).

CENTRAL ILLUSTRATION Kaplan-Meier Cumulative Event-Free Curves of Ischemic Strokes and Transient Ischemic Attacks With and Without Thrombus on the Device

Ischemic Stroke / Transient Ischemic Attack



N at risk		Months				
	0	6	12	18	24	
No thrombus	300	100	72	62	39	
Thrombus	25	12	6	2	0	

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The curves are representative of being event-free for ischemic strokes and transient ischemic attacks, with and without thrombus on the device, after left atrial appendage occlusion. Time zero is time at first post-procedure left atrial appendage imaging. The curves demonstrate a higher risk for ischemic strokes or transient ischemic attacks in the patients with a diagnosis of device-associated thrombus after left atrial appendage occlusion. The mean follow-up time was 13 ± 13 months. CI = confidence interval; HR = hazard ratio.

COMPETENCY IN MEDICAL KNOWLEDGE: Transcatheter LAA occlusion has emerged as an alternative strategy for stroke prevention in patients with AF who are poor candidates for long-term OAC. Thrombus formation on the device is not uncommon in patients with AF treated by LAA closure.

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Thrombus formation on the device after LAA closure is strongly associated with a higher risk of ischemic stroke during follow-up. Therefore, active screening for early detection and treatment of device-associated thrombus should be performed during post-implantation surveillance.

TRANSLATIONAL OUTLOOK: Further studies are still needed to characterize the patients who are optimal candidates for LAA for stroke prevention and the best antithrombotic regimen that considers individual risks of device-related thrombus after LAA closure.