

Left Atrial Appendage Closure Comparable to Anticoagulants for Ischemic Stroke and TIA Prevention in Atrial Fibrillation Patients

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Key Findings:

- The prevalence of ischemic stroke does not significantly differ between atrial fibrillation patients treated with a left atrial appendage closure (LAAC) procedure alone, LAAC with anticoagulation, and anticoagulation alone in the first five years post treatment initiation.
- Patients treated with anticoagulation alone have higher rates of transient ischemic attacks (TIAs) compared to those treated with LAAC with anticoagulation. Patients treated with LAAC alone had no statistically significant difference in rates of TIA compared to those treated with LAAC anticoagulation and those treated with anticoagulation alone.
- Patients treated with LAAC alone had a significantly higher rate of hemorrhagic stroke within five years following intervention compared to the other two treatment groups. However, an elevated bleeding risk is an indication for treating a patient with an LAAC, which may explain this increased rate.

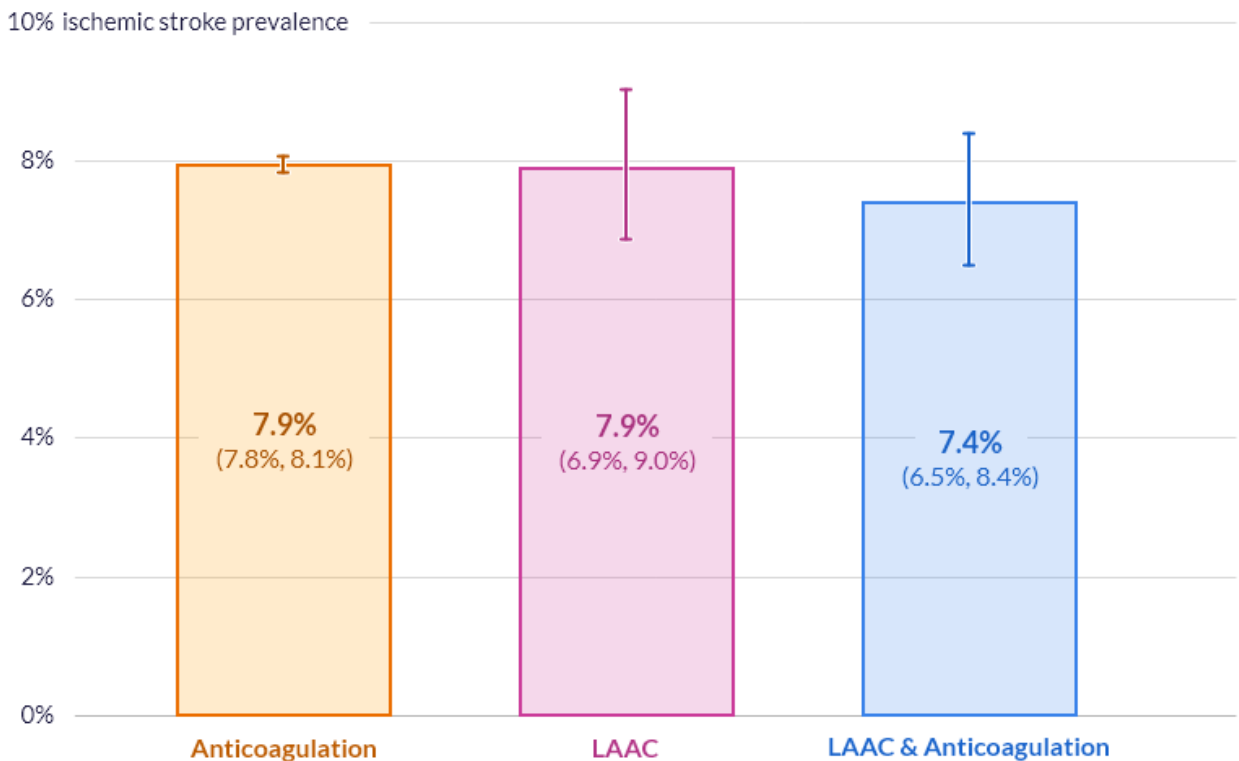
The left atrial appendage closure (LAAC) procedure presents an alternative treatment for patients with atrial fibrillation (AFib) who are at a high risk for bleeding.^{1,2} Initial studies compared LAAC to the use of warfarin, with results indicating improved outcomes for hemorrhagic stroke but a slightly increased risk of ischemic stroke for patients undergoing the LAAC procedure.¹

To further examine differences in cardiovascular outcomes for AFib patients on various stroke-prevention treatments, we studied 437,409 patients newly diagnosed with AFib who had no prior history of heart valve issues. We compared the five-year rates of ischemic stroke, transient ischemic attacks (TIAs), and hemorrhagic strokes among patients treated with LAAC alone, LAAC with anticoagulation, and anticoagulation alone. The anticoagulation treatments included were warfarin and direct oral anticoagulation (DOAC) medications. Patients with a history of ischemic stroke were excluded from the ischemic stroke rates, patients with a history of TIA were excluded from the TIA rates, and patients with a history of hemorrhagic stroke were excluded from the hemorrhagic stroke rates.

We found that patients treated with anticoagulation alone, patients treated with LAAC alone, and patients treated with combination therapy had no statistically significant difference in the prevalence of ischemic stroke within five years, as seen in Figure 1.

Ischemic Stroke Prevalence Five Years After Start of Treatment

I 95% confidence interval



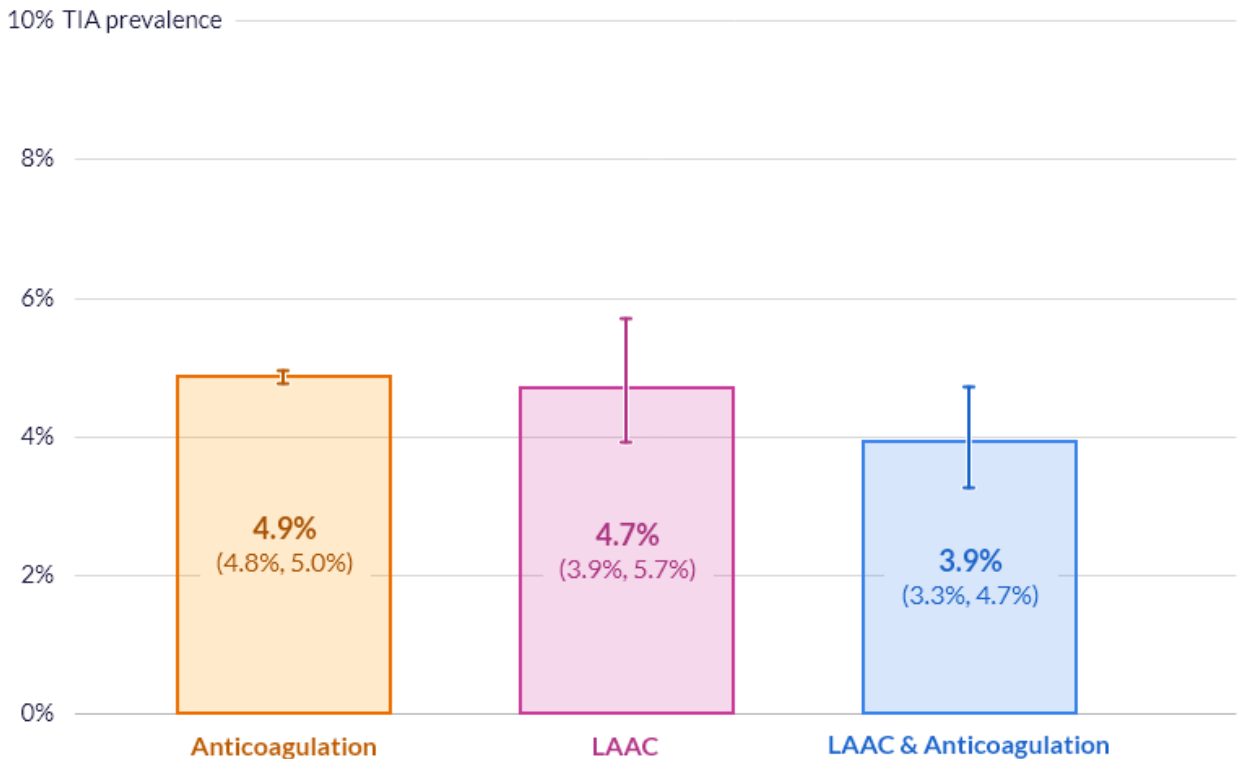
N=429,808 patients "Ischemic Stroke Prevalence Five Years After Start of Treatment," 2024. EpicResearch.org

Figure 1. The prevalence of an AFib patient experiencing an ischemic stroke within five years after treatment started.

Next, we examined the prevalence of TIAs within five years after treatment for AFib and found that patients treated with LAAC in combination with anticoagulants had a lower rate (3.9% versus 4.9%) of experiencing TIAs than those treated with anticoagulation alone, as depicted in Figure 2. Patients treated with LAAC alone had an increased rate of TIA compared to LAAC with anticoagulation, but this increase was not statistically significant.

Transient Ischemic Attack Prevalence Five Years After Start of Treatment

I 95% confidence interval



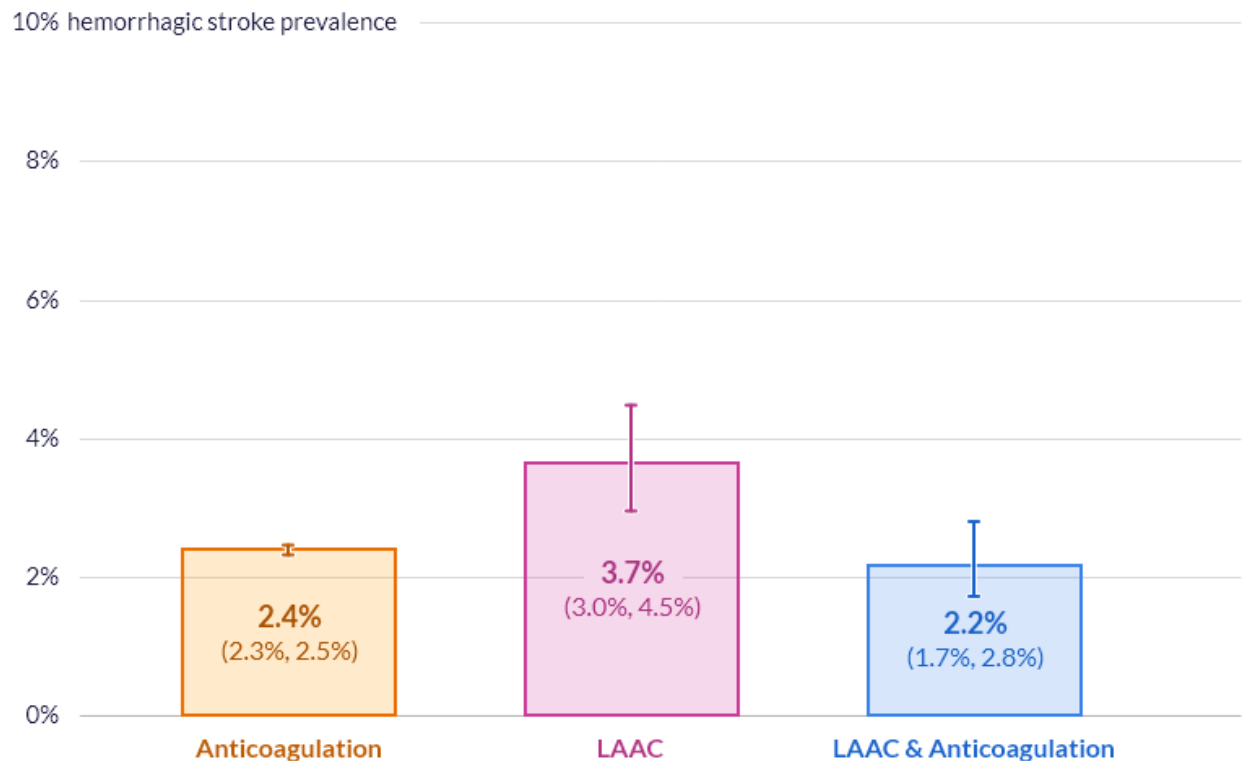
N=434,142 patients "Transient Ischemic Attack Prevalence Five Years After Start of Treatment," 2024. EpicResearch.org

Figure 2. The likelihood of an AFib patient experiencing a transient ischemic attack within five years after treatment started.

Last, we examined the prevalence of hemorrhagic stroke within five years after starting AFib treatment. Patients treated with LAAC alone had significantly higher rates, with 3.7% experiencing a hemorrhagic stroke within five years, compared to 2.2% of patients treated with both LAAC and anticoagulants and 2.4% of patients treated with only anticoagulants. However, the higher rate of hemorrhagic stroke among patients treated with LAAC alone may be attributable to these patients' higher risk of bleeding, which is a key risk factor for hemorrhagic stroke and may have warranted the LAAC without anticoagulation in the first place.

Hemorrhagic Stroke Prevalence Five Years After Start of Treatment

I 95% confidence interval



N=437,409 patients

"Hemorrhagic Stroke Prevalence Five Years After Start of Treatment," 2024. EpicResearch.org

Figure 3. The likelihood of an AFib patient experiencing a hemorrhagic stroke within five years after treatment started.

Patients treated with LAAC and anticoagulants had the lowest rates of all three conditions studied, while patients treated with anticoagulants alone or LAAC alone showed similar rates of ischemic strokes and TIAs. These findings support earlier studies that showed LAAC procedures and anticoagulant treatment have similar rates of stroke prevention in AFib patients.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 249 million patient records from 1,400 hospitals and more than 32,900 clinics from all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Holmes DR Jr, Doshi SK, Kar S, et al. Left atrial appendage closure as an alternative to warfarin for stroke prevention in atrial fibrillation. J Am Coll Cardiol. 2015;65(24):2614-2623. doi:10.1016/j.jacc.2015.04.025
2. Kumar K. Atrial fibrillation: Overview and management of new-onset atrial fibrillation. UpToDate. Published October 31, 2023. https://www.uptodate.com/contents/atrial-fibrillation-overview-and-management-of-new-onset-atrial-fibrillation?search=atrial%20fibrillation&source=search_result&selectedTitle=1%7E150&usage_type=default&display_rank=1. Accessed March 14, 2024.

Data Definitions

The rates presented were based on an unadjusted Kaplan-Meier survival analysis. A lack of statistical significance between the groups was also seen when analyzed with an adjusted CoxPH regression and an unconditional logistic regression on two-year stroke or TIA risk.

Term	Definition
Study period	1/1/2010 to 2/26/2024
	Patients with an initial diagnosis of atrial fibrillation and no history of heart valve problems, congestive heart failure, heart attack, or stroke prior. At least one encounter one year or more prior to the AFib diagnosis.
Study population	Patients had no gaps longer than three years between clinical visits.
	A procedure with one of the following: • ICD-9 code 37.36 or 37.90 • ICD-10-PC: 02L74ZK, 02B74ZK, 02L73CK, 02573ZK, 02574ZK, 02L73ZK, 02L73DK, 02L74CK, 02L70CK, 02L74DK, 02L70DK, 02L70ZK, 02B70ZK, 02B73ZK, or 02570ZK • CPT code 33340 or 0281T • An unmapped procedure with an order name containing: ○ “watchman” without “referral” or “consult” ○ “amplatzer” and any of “laa,” “append,” or “amulet” ○ “lariat” without “vaculariat” ○ “atriclip” ○ “wavecrest” ○ Starts with “laa” or contains both “append” and “atrial” AND contains “lao,” “occlu,” “exclusion,” “implant,” or “closure” AND does not start with “CT”
LAAC procedure	• A diagnosis mapped to SNOMED CT 1259226009
Anticoagulation medications	A prescription for warfarin or a DOAC
	A prescription with at least one of the following: • Simple generic name of WARFARIN SODIUM • RxNorm code 11289, 82118, 114194, 202421, 405155, 855289, 855291, 855297, 855299, 855303, 855305, 855309, 855313, 855315, 855319, 855321, 855325, 855327, 855333, 855335, 855339, 855341, 855345, 855347, 855349, 855287, 855295, 855301, 855307, 855311, 855317, 855323, 855331, 855337, 855343, 855350, 855288, 855296, 855302, 855308, 855312, 855318, 855324, 855332, 855338, 855344, 855290, 855298, 855304, 855310, 855314, 855320, 855326, 855334, 855340, 855346, 855292, 855300, 855306, 855316, 855322, 855328, 855336, 855342, 855348, 1161789, 1161790,
Warfarin	

	1161791, 1171654, 1171655, 1171656, 1167808, or 1167809
DOACs	A prescription for a direct oral anticoagulant (DOAC) with at least one of the following: • Pharmaceutical class of “THROMBIN INHIBITORS, SELECTIVE, DIRECT, REVERSIBLE” • Pharmaceutical subclass of “Direct Factor Xa Inhibitors” or “Indirect Factor Xa Inhibitors” • Simple generic names of APIXABAN, RIVAROXABAN, DABIGATRAN ETEXILATE MESYLATE (oral route only), EDOXABAN TOSYLATE, or <u>BETRIXABAN MALEATE</u> • RxNorm code of 1114195, 1037042, or 1599538
Atrial fibrillation	A diagnosis with one of the following: • ICD-10-CM code I48.0*, I48.1*, I48.2*, or I48.91 • ICD-9-CM code 427.31 • SNOMED CT code 49436004
Heart valve problems	A diagnosis with ICD-10-CM code I34*-I39*
Congestive heart failure	A diagnosis with ICD-10-CM code I50*
History of heart attack	A diagnosis with ICD-10-CM code Z86.7* (except Z86.73) or I21*
History of stroke	A diagnosis with ICD-10-CM code I69.3* or Z86.73
Outcomes	Ischemic stroke: A diagnosis with ICD-10-CM code I63* Hemorrhagic stroke: A diagnosis with ICD-10-CM code I60*, I61*, or I62* TIA: A diagnosis with ICD-10-CM code G45.9
Confounders	BMI classification based on the patient’s body mass index documented nearest to their initial atrial fibrillation diagnosis. • Underweight: <18.5 • Healthy: 18.5-25 • Overweight: 25-30 • Obese: >30 Age Hypertension – A diagnosis with ICD-10-CM code I10* prior to the initial atrial fibrillation diagnosis Diabetes – A diagnosis with ICD-10-CM code E10*-E11* prior to the initial AFib diagnosis Hyperlipidemia – A diagnosis with ICD-10-CM code E78.2*-E78.5* prior to the initial atrial fibrillation diagnosis

Table 1. Ischemic Stroke Prevalence Five Years After Start of Treatment

Rate with Anticoag Alone	Anticoag Alone Upper CI	Anticoag Alone Lower CI	Rate with LAAC Alone	LAAC Alone Upper CI	LAAC Alone Lower CI	Rate with LAAC & Anticoag	LAAC & Anticoag Upper CI	LAAC & Anticoag Lower CI
7.9%	8.1%	7.8%	7.9%	9.0%	6.9%	7.4%	8.4%	6.5%

Table 2. Transient Ischemic Attack Prevalence Five Years After Start of Treatment

Rate with Anticoag Alone	Anticoag Alone Upper CI	Anticoag Alone Lower CI	Rate with LAAC Alone	LAAC Alone Upper CI	LAAC Alone Lower CI	Rate with LAAC & Anticoag	LAAC & Anticoag Upper CI	LAAC & Anticoag Lower CI
4.9%	5.0%	4.8%	4.7%	5.7%	3.9%	3.9%	4.7%	3.3%

Table 3. Hemorrhagic Stroke Prevalence Five Years After Start of Treatment

Rate with Anticoag Alone	Anticoag Alone Upper CI	Anticoag Alone Lower CI	Rate with LAAC Alone	LAAC Alone Upper CI	LAAC Alone Lower CI	Rate with LAAC & Anticoag	LAAC & Anticoag Upper CI	LAAC & Anticoag Lower CI
2.4%	2.5%	2.3%	3.7%	4.5%	3.0%	2.2%	2.8%	1.7%