AFib Patients on Direct Oral Anticoagulant Medications Have Lower Rates of Stroke and Embolism Than Those on Warfarin

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Key Findings:

- Patients with atrial fibrillation (AFib) who are prescribed direct oral anticoagulants (DOACs) have lower rates of ischemic stroke, hemorrhagic stroke, arterial embolism, and pulmonary embolism compared to those treated with warfarin.

We recently published findings that the rates of ischemic stroke, transient ischemic attack (TIA), and hemorrhagic stroke among atrial fibrillation (AFib) patients are similar for those treated with a left atrial appendage closure (LAAC) procedure alone, an LAAC with anticoagulation, or anticoagulation alone.[1] However, we did not differentiate between different types of anticoagulant medications and wanted to better understand whether specific anticoagulant treatments are associated with stroke, TIA, embolism, or major bleeding events.

We studied 323,256 patients with AFib who were treated with warfarin, rivaroxaban, apixaban, or dabigatran. Patients with a history of an LAAC procedure, heart valve problems, congestive heart failure, heart attack, ischemic stroke, TIA, hemorrhagic stroke, major bleeding, arterial embolism, pulmonary embolism, or end stage renal disease were excluded from the analysis.

We found that patients treated with rivaroxaban or apixaban had a lower rate of ischemic stroke and TIA within five years of treatment than patients treated with warfarin or dabigatran. Hemorrhagic stroke was the least common of the outcomes studied. However, patients treated with warfarin had a higher rate of hemorrhagic stroke in the five years after starting treatment than patients on any of the other anticoagulants studied.

Five-Year Stroke Rate After Start of Treatment for AFib

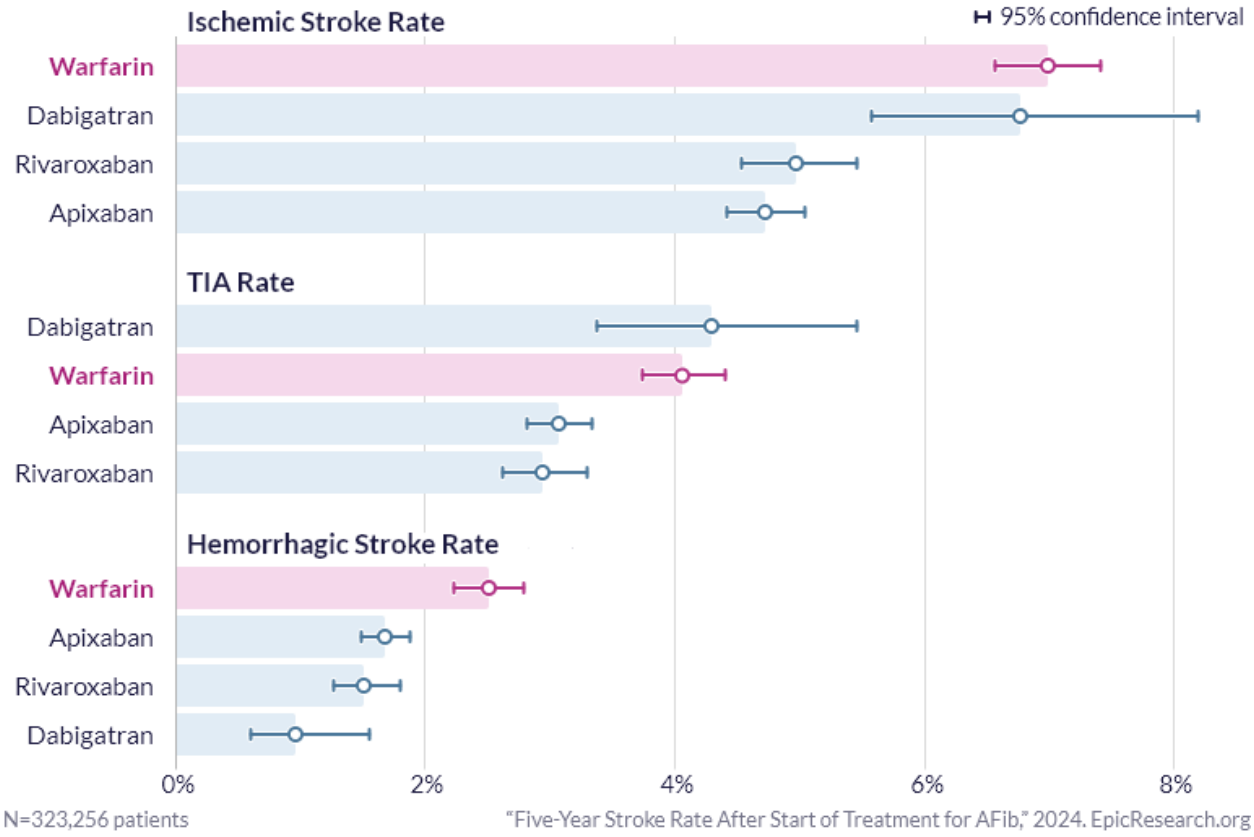

Figure 1. The rate of AFib patients experiencing a stroke or TIA within five years after treatment start.

Because a primary indication for anticoagulant use is the prevention of blood clots, we analyzed the rate of pulmonary and arterial embolism five years after the start of anticoagulation treatment. Pulmonary embolism occurred in less than 3% of the population, and arterial embolism was even less prevalent, diagnosed in less than 2% of the population. However, patients prescribed warfarin had the highest rate of both outcomes compared to the other anticoagulants studied.

Five-Year Embolism Rate After Start of Treatment for AFib

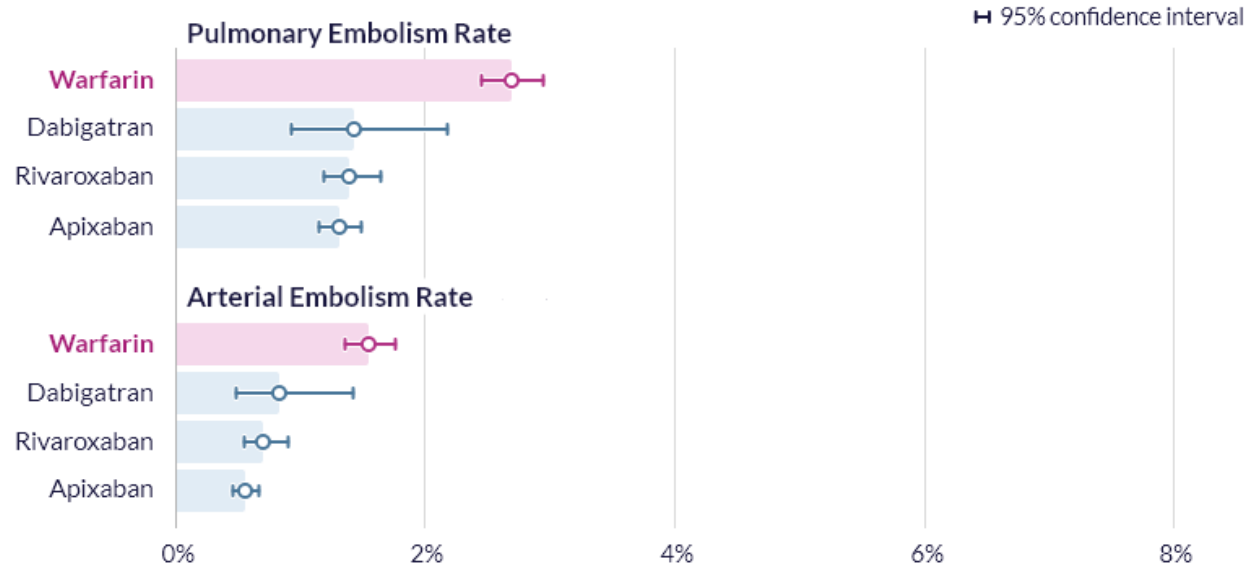

Figure 2. The rate of AFib patients experiencing an embolism within five years after treatment start.

We also examined the rate of a major bleeding event among AFib patients within five years of starting anticoagulant treatment. We found that this event occurred in less than 2% of patients, with patients treated with dabigatran experiencing the lowest rate of major bleeding events.

Five-Year Major Bleeding Rate After Start of Treatment for AFib

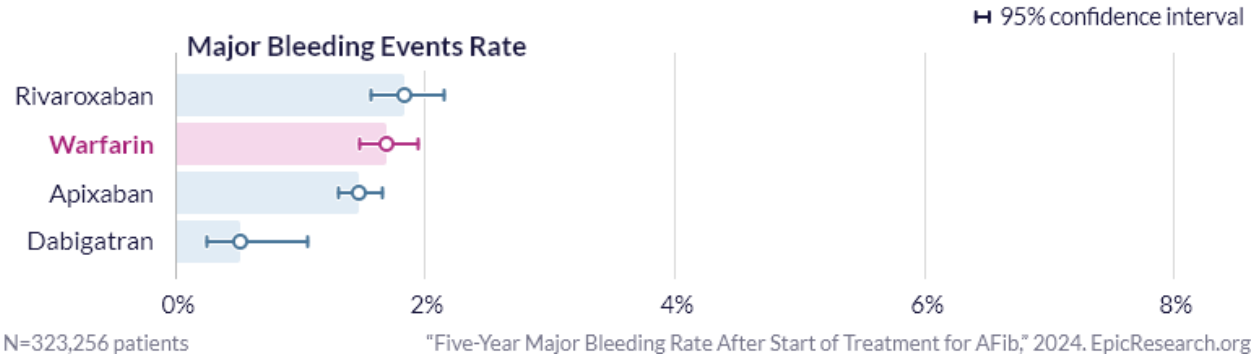

Figure 3. The rate of AFib patients experiencing a major bleeding event within five years after treatment start.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 270 million patient records from 1,500 hospitals and more than 35,500 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. Little D, Tapper J, Barkley E, Bartelt K, Piff A. Left Atrial Appendage Closure Comparable to Anticoagulants for Ischemic Stroke and TIA Prevention in Atrial Fibrillation Patients. Epic Research. https://epicresearch.org/articles/left-atrial-appendage-closure-comparable-to-anticoagulants-for-ischemic-stroke-and-tia-prevention-in-atrial-fibrillation-patients. Accessed on July 15, 2024.

Data Definitions

Term	Definition
Study period	1/1/2000 to 4/3/2024
Study population	• Patients started on **DOACs** or **warfarin** within 90 days of atrial fibrillation diagnosis • Patients diagnosed with **atrial fibrillation** during **study period** • At least one face-to-face encounter in the 0-24 months prior to their **atrial fibrillation** diagnosis. • We excluded patients with documentation of an **exclusion condition** or any of the **outcomes** prior to their **atrial fibrillation** diagnosis
Censoring	At the earliest of: • Outcome • Last face-to-face encounter • Documented death • **DOAC** or **warfarin** start or stop • **LAAC procedure**
Atrial fibrillation	A diagnosis with ICD-10 code I48.0*, I48.1*, I48.2*, or I48.91, ICD-9-CM code 427.31, or SNOMED CT code 49436004
DOACs	Simple generic names of APIXABAN or RxNorm code 1364430, RIVAROXABAN or RxNorm code 1114195, DABIGATRAN ETEXILATE MESYLATE or RxNorm code 1037042, or EDOXABAN TOSYLATE or RxNorm code 1599538
Warfarin	Simple generic name of "warfarin sodium" or 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, 1161791, 1171654, 1171655, 1171656, 1167808, or 1167809
LAAC procedure	A diagnosis with SNOMED CT code 1259226009, a procedure with ICD-9-CM 37.36 or 37.90, ICD-10-PCS code 02L74ZK, 02B74ZK, 02L73CK, 02573ZK, 02574ZK, 02L73ZK, 02L73DK, 02L74CK, 02L70CK, 02L74DK, 02L70DK, 02L70ZK, 02B70ZK, 02B73ZK, or 02570ZK, or CPT code 33340 or 0281T
Exclusion condition	Heart valve problem: ICD-10-CM code I34*-I39* Stroke: ICD-10-CM code Z86.73, I69.3*, or I60*-I63* Congestive heart failure: ICD-10-CM code I50* Heart attack: ICD-10-CM code Z86.73, Z86.7*, or I21* End stage renal disease: SNOMED CT code 265764009 or ICD-10-CM code N18*
Outcomes	Arterial embolism: ICD-10-CM code I74* Pulmonary embolism: ICD-10-CM code I26*

	Ischemic stroke: ICD-10-CM code I63* TIA: ICD-10-CM code G45.9 Major bleeding: ICD-10-CM code K25.0, K25.2, K25.4, K25.6, K26.0, K26.2, K26.4, K26.6, K27.0, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4, K28.6, K29.01, K29.21, K29.31, K29.41, K29.51, K29.61, K29.71, K29.81, K29.91, or S06.4*-S06.6* Hemorrhagic stroke: ICD-10-CM code I60*-I62* Ischemic heart disease: ICD-10-CM code I20*-I25*
Model Specifications	We analyzed outcomes with an unadjusted Kaplan-Meier survival model for each treatment population.

Table 1: Five-Year Stroke Rate After Start of Treatment for AFib

Event	Med	Rate	CI Low Width	CI High Width
	Warfarin	7.0%	0.4%	0.4%
	Dabigatran	6.8%	1.2%	1.4%
	Rivaroxaban	5.0%	0.4%	0.5%
Ischemic	**Apixaban**	4.7%	0.3%	0.3%
	Dabigatran	4.3%	0.9%	1.2%
	Warfarin	4.1%	0.3%	0.3%
	Apixaban	3.1%	0.2%	0.3%
TIA	**Rivaroxaban**	2.9%	0.3%	0.4%
	Warfarin	2.5%	0.3%	0.3%
	Apixaban	1.7%	0.2%	0.2%
	Rivaroxaban	1.5%	0.2%	0.3%
Hemorrhagic	**Dabigatran**	1.0%	0.4%	0.6%

Table 2: Five-Year Embolism Rate After Start of Treatment for AFib

Event	Med	Rate	CI Low Width	CI High Width
	Warfarin	2.7%	0.2%	0.3%
	Dabigatran	1.4%	0.5%	0.8%
	Rivaroxaban	1.4%	0.2%	0.2%
Pulmonary Embolism	Apixaban	1.3%	0.2%	0.2%
	Warfarin	1.5%	0.2%	0.2%
	Dabigatran	0.8%	0.3%	0.6%
	Rivaroxaban	0.7%	0.2%	0.2%
Atrial Embolism	Apixaban	0.6%	0.1%	0.1%

Table 3: Five-Year Major Bleeding Rate After Start of Treatment for AFib

Event	Med	Rate	CI Low Width	CI High Width
	Rivaroxaban	1.8%	0.3%	0.3%
Major Bleed	Warfarin	1.7%	0.2%	0.2%

	Apixaban	1.5%	0.2%	0.2%
	Dabigatran	0.5%	0.3%	0.5%