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Direct oral anticoagulants for stroke prevention in patients with device-detected atrial fibrillation: assessing net clinical benefit

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Subclinical, device-detected atrial fibrillation (AF) is frequently recorded by pacemakers and other implanted cardiac rhythm devices. Patients with device-detected AF have an elevated risk of stroke, but a lower risk of stroke than similar patients with clinical AF captured with surface electrocardiogram. Two randomized clinical trials (NOAH-AFNET 6 and ARTESiA) have tested a direct oral anticoagulant (DOAC) against aspirin or placebo. A study-level meta-analysis of the two trials found that treatment with a DOAC resulted in a 32% reduction in ischaemic stroke and a 62% increase in major bleeding; the results of the two trials were consistent. The annualized rate of stroke in the control arms was ~1%. Several factors point towards overall net benefit from DOAC treatment for patients with device-detected AF. Strokes in ARTESiA were frequently fatal or disabling and bleeds were rarely lethal. The higher absolute rates of major bleeding compared with ischaemic stroke while on treatment with a DOAC in the two trials are consistent with the ratio of bleeds to strokes seen in the pivotal DOAC vs. warfarin trials in patients with clinical AF. Prior research has concluded that patients place a higher emphasis on stroke prevention than on bleeding. Further research is needed to identify the characteristics that will help identify patients with device-detected AF who will receive the greatest benefit from DOAC treatment.

Introduction

Stroke is both common and a major cause of death and disability in patients with atrial fibrillation (AF).[1] Oral anticoagulation (OAC) can prevent the majority of strokes in patients with AF.[2-4] However, the use of OAC is associated with an increased risk of major bleeding. This risk has generally been accepted, due to the severity of strokes associated with AF and patient preferences.[2,3,5] Over the last decades, the introduction of direct oral anticoagulants (DOACs), a reduction in the use of concomitant antiplatelet therapies, and improvements in background therapy for AF and stroke risk factors (e.g. hypertension, heart failure, diabetes mellitus) have reduced the rates of both stroke and major bleeding, particularly life-threatening and fatal bleeding.[6-8]

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Long-term continuous monitoring with implanted cardiac rhythm devices can identify patients with AF episodes that would otherwise not have been detected. Patients with so-called 'device-detected' AF have a lower risk of stroke than similar patients with clinical AF captured with surface electrocardiogram (ECG). Given the emergence of device-detected AF and the associated risks of stroke, it is timely to re-evaluate the risk–benefit ratio for using OAC for patients with this common clinical entity.

What is device-detected atrial fibrillation?

The introduction of pacemakers with the ability to record and catalogue atrial electrograms demonstrated that around 80% of all AF in patients with pacemakers was not clinically recognized.[9-11] This phenomenon was first described in studies of pacemaker patients, where it was initially given the more descriptive term 'atrial high-rate episodes' (AHREs).[9,10,12] After early studies showed an association with ischaemic stroke or systemic embolism, the term 'subclinical' AF came into use. As this clinical entity lies on the spectrum of AF (along with paroxysmal, persistent, and permanent AF), it is now more appropriately being described as 'device-detected' AF. Device-detected AF is typically short-lasting, detected only with long-term continuous rhythm monitoring, and has not been captured on surface ECG.[10,13,14] Whether patients with device-detected AF respond in the same way to evidence-based therapies as patients with clinical AF is an area of clinical interest. Short-lasting AF detected after months or years of monitoring represents a low overall burden of AF, which conveys an increased risk of stroke, albeit lower than would be expected in otherwise similar patients with clinical AF.[15,16] Device-detected AF is common. An estimated 720 000 devices are implanted every year in North America and Western Europe.[17] Estimates of the incidence of new device-detected AF have consistently ranged around 30% in the first few years after implantation.[10,11,18,19] This means that the worldwide number of patients who are at risk for this condition is enormous.

The Relationship Between Daily Atrial Tachyarrhythmia Burden From Implantable Device Diagnostics and Stroke Risk (TRENDS), published in 2009, suggested that device-detected AF was associated with an increased risk of thromboembolism.[9] Compared with participants without AF, participants with >5 .5 h of device-detected AF in a 30-day window had nominally higher rates of stroke {2.4% vs. 1.1%, adjusted hazard ratio 2.20 [95% confidence interval (CI) 0.96–5.05, $P = 0.06$]} over a mean follow-up of 1.4 years. An important limitation of TRENDS is that this prospective observational study included some patients with clinical AF (roughly 20%). The increased stroke risk associated with device-detected AF was confirmed in The Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing Trial (ASSERT).[10] This trial exclusively enrolled patients without a known history of clinical AF who had recently undergone implantation of a pacemaker or implantable cardioverter defibrillator.[10] In ASSERT, device-detected AF recorded in the first 3 months following enrolment was associated with a subsequently increased risk of ischaemic stroke or systemic embolism [hazard ratio (HR) 2.49, 95% CI 1.28–4.85] over a mean follow-up of 2.5 years. However, among study participants with a $CHADS_2$ score of 2, the annual risk of stroke was only 1.3%, lower than would be expected in similar patients with clinical AF (*Table 1*).[20,21]

Table 1 Comparison of event rates in patients with a $CHADS_2$ score of 2 and clinical atrial fibrillation or device-detected subclinical atrial fibrillation

Annual risk of ischaemic stroke or systemic embolism			
Clinical AF		Device-detected subclinical AF	
NRAF[20]	ATRIA[21]	TRENDS[9a]	ASSERT[10]
4.0%/year	2.5%/year	1.3%/year	1.3%/year[10]

[a]In TRENDS, 36% of participants with device-detected AF had a prior history of clinically diagnosed AF. In TRENDS, the mean $CHADS_2$ score was 2. The estimates for NRAF, ATRIA, and ASSERT refer to the subgroup with a $CHADS_2$ score of 2.

Given the high prevalence of device-detected AF, clinicians questioned if these patients would derive any benefit from OAC, particularly in view of their lower absolute stroke risk compared with otherwise similar patients with clinical AF.[22] At the same time, OAC was also getting safer, driven by a widespread use of DOACs.[3,23] This set the stage for two prospective clinical trials evaluating DOAC therapy in patients with device-detected AF.[24,25]

Benefits and risks of oral anticoagulation in the treatment of clinical atrial fibrillation

A critical appraisal of the net clinical benefit for OAC treatment of device-detected AF first requires an understanding of the risks and benefits of OAC for patients with clinical AF. The net clinical benefit of antithrombotic therapy is commonly evaluated by the balance between reducing ischaemic events and increasing haemorrhage. Between 1989 and 1993, six pivotal randomized trials of warfarin for stroke prevention in patients with clinical AF were completed and published.[26-31] A meta-analysis of these trials showed that OAC with warfarin reduced all-cause stroke by 64% (95% CI 49–74%) and ischaemic stroke by 67% (95% CI 54–77%) compared with placebo or no antithrombotic treatment.[2] The pooled rates of all-cause stroke (including intracranial haemorrhage) were reduced by 3.8 per 100 patient-years with warfarin compared with no treatment. Nearly two-thirds of strokes in these trials were disabling, and there was a similar reduction in stroke with warfarin irrespective of event severity. Warfarin increased major extracranial bleeding compared with placebo or no antithrombotic therapy (three additional major bleeding events per 100 patient-years). In the meta-analysis, warfarin reduced all-cause mortality (one possible measurement of net benefit) by 26% (95% CI 3–43%) compared with control.[2]

Table 2 International Society on Thrombosis and Haemostasis definition of major bleeding in non-surgical patients[36]

1. Fatal bleeding
2. Symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome
3. Bleeding causing a fall in haemoglobin level of 2.0 g/dL (1.24 mmol/L) or more or leading to transfusion of two or more units of whole blood or red cells.

The pivotal DOAC non-inferiority trials testing dabigatran or an oral factor Xa inhibitor vs. warfarin were completed and published between 2009 and 2013.[32-35] All of these trials used the International Society on Thrombosis and Haemostasis (ISTH) criteria (or very similar criteria) to define major bleeding. The ISTH definition of major bleeding was first introduced in 2005, more than 10 years after the last warfarin trial had been completed (*Table 2*).[36] The ISTH definition of major bleeding includes both very serious events (i.e. fatal or intracranial bleeding) and bleeding events that are less critical, but still relevant (i.e. bleeding causing a drop in haemoglobin of at least 2 g/dL or leading to transfusion of two or more units of whole blood or red cells). Notably, all four pivotal DOAC vs. warfarin trials showed a markedly higher rate of major bleeding events [2.1–2.8 (DOAC) and 3.1–3.4 (warfarin) per 100 patient-years] compared with ischaemic strokes [0.9–1.3 (DOAC) and 1.1–1.4 (warfarin) per 100 patient-years] (*Table 3*).[32-35]

The randomized NOAH-AFNET 6 and ARTESiA trials

NOAH-AFNET 6 was a double-blind trial, which enrolled 2536 patients with at least one atrial high-rate episode lasting at least 6 min.[25] The trial randomized patients to edoxaban or control. Patients in the control arm received aspirin if it was clinically indicated (e.g. due to the presence of coronary or peripheral artery disease), otherwise they received placebo. Patients were followed for a mean of 21 months for the primary efficacy outcome, a composite of ischaemic stroke, systemic embolism (including peripheral arterial embolism, pulmonary embolism, and myocardial infarction), or cardiovascular death. The primary safety outcome was a composite of all-cause mortality or major bleeding. The trial was stopped prematurely after an independent, informal assessment suggested futility for efficacy with a signal for harm with edoxaban.[39] The primary efficacy outcome occurred at an annual rate of 4.0% in patients in the control arm and 3.2% per year in the edoxaban arm (HR 0.81, 95% CI 0.60–1.08). The primary safety outcome, a composite of death or major bleeding, was increased from 4.5% per year in the control arm to 5.9% per year with edoxaban (HR 1.31, 95% CI 1.02–1.67). In the intention-to-treat analysis, ischaemic stroke occurred at a rate of 1.0% per year in the control arm and 0.8% per year with edoxaban (*Table 3*).

The double-blind, double-dummy ARTESiA trial enrolled 4012 patients with at least one episode of subclinical AF lasting at least 6 min, but not more than 24 h.[24] Patients were randomized to apixaban or aspirin. If patients developed subclinical AF > 24 h or had clinical AF detected during the course of the trial, they were taken off study medication and recommended for treatment with open-label OAC. The primary efficacy outcome was all-cause stroke or systemic embolism, and the primary safety outcome was major bleeding. As compared with aspirin, apixaban reduced the risk of the primary efficacy outcome from 1.2% per year to 0.8% per year (HR 0.63, 95% CI 0.45–0.88).[40] The trial also found a 49% reduction in disabling or fatal strokes (i.e. modified Rankin Scale score of 3–6) (HR 0.51, 95% CI 0.29–0.88); 45% of strokes in the aspirin arm met these criteria. The rates of major bleeding during treatment with apixaban and aspirin were 1.7 and 0.9 per year, respectively (HR 1.80, 95 CI 1.26–2.57) (*Table 3*). After a mean follow-up of 3.5 years, ~50% of patients were off study drug, roughly half of them due to the development of longer-lasting AF.

A study-level meta-analysis of ARTESiA and NOAH-AFNET 6 demonstrated a 32% reduction in ischaemic stroke with a DOAC and a 62% increase in major bleeding.[41] Importantly, the meta-analysis demonstrated the results of the two trials were entirely consistent, without any evidence of statistical heterogeneity.[41] While the use of edoxaban or apixaban clearly reduced stroke and increased major bleeding to a similar extent, it is important to note the absolute risk of stroke in the pooled control arm (>81% of patients receiving aspirin across both trials) was low at around 1.0% per year. This is lower than the rate of ischaemic stroke in earlier observational studies of device-detected AF[9,10] and in the aspirin arms of randomized trials of patients with clinical AF (*Table 3*).[37,38] This lower rate of stroke may be due to several factors, including the low burden of AF at baseline, treatment of patients with open-label anticoagulation when they developed subclinical AF > 24 h, or clinical AF,[15] inclusion of fewer patients with a history of stroke as compared with trials that enrolled patients with clinical AF, and more stringent treatment goals of modifiable risk factors (e.g. hypertension and diabetes mellitus) over the last decades. The stroke rate observed in the control arms of ARTESiA and NOAH is similar to a more contemporary observational study[42]; therefore, it is plausible that the risk of SCAF-related stroke could be decreasing over time.

Comparing the severity of stroke and major bleeding

The severity of stroke and bleeding events may depend on perceptions and individual preferences of both patients and clinicians.[5] In general, a stroke occurring in a patient with clinical AF treated with or without OAC often causes significant disability or may even result in death. For example, the percentage of strokes that were fatal or disabling (commonly defined as a modified Rankin Scale score of 3–6) ranged from 42% to 56% on a

Table 3 Selected outcomes of patients enrolled in trials of antithrombotic therapy in patients with atrial fibrillation—expressed as event rate per 100 patient-years

Clinical AF + risk factors

	RE-LY[32a]		ROCKET AF[34b]	
	Dabigatran 150 mg bid	Warfarin (target INR 2.0-3.0)	Rivaroxaban 20 (15) mg daily[c]	Warfarin (target INR 2.0-3.0)
Ischaemic stroke	0.9	1.2	1.3	1.4
Major bleeding	3.1	3.4	3.6	3.4
Intracranial haemorrhage	0.3	0.7	0.5	0.7
Death	3.6	4.1	4.5	4.9
	ARISTOTLE[33]		ENGAGE AF-TIMI 48[35]	
	Apixaban 5 (2.5) mg bid[c]	Warfarin (target INR 2.0-3.0)	Edoxaban 60 (30) mg daily[c]	Warfarin (target INR 2.0-3.0)
Ischaemic stroke	1.0	1.1	1.3	1.3
Major bleeding	2.1	3.1	2.8	3.4
Intracranial haemorrhage	0.3	0.8	0.4	0.9
Death	3.5	3.9	4.0	4.4

Clinical AF + risk factors, deemed unsuitable for OAC with a vitamin K antagonist

	ACTIVE A[37a]		AVERROES[38]	
	Clopidogrel 75 mg daily + aspirin 75-100 mg daily	Aspirin 75-100 mg daily	Apixaban 5 mg bid	Aspirin 81-324 mg daily
Ischaemic stroke	1.9	2.8	1.1	3.0
Major bleeding	2.0	1.3	1.4	0.9
Intracranial haemorrhage	0.4	0.2	0.4	0.4
Death	6.4	6.6	3.5	4.4

Device-detected AF + risk factors

	NOAH-AFNET 6[39a]		ARTESiA[40]	
	Edoxaban 60 (30) mg daily[c]	Aspirin 100 mg daily/placebo	Apixaban 5 (2.5) mg bid[c]	Aspirin 81 mg daily
Ischaemic stroke	0.8	1.0	0.6	1.0
Major bleeding[a]	2.3	1.2	1.7	0.9
Intracranial haemorrhage[a]	Not reported		0.2	0.3
Death	4.7	4.3	5.1	4.8

Event rates for ischaemic stroke and death are reported for intention-to-treat (ITT) populations. Corresponding rates for bleeding events are reported for the on-treatment populations, unless indicated otherwise. Data are not shown for dabigatran 110 mg twice daily (RE-LY) and edoxaban 30 (15) mg daily (ENGAGE AF-TIMI 48), because these dosing regimens are only approved in selected regions.

[a]Data are shown for the ITT population.

[b]Data are shown for the on-treatment (as treated) population.

[c]The doses of apixaban, rivaroxaban, and edoxaban were adjusted based on predefined criteria.

DOAC and from 43% to 64% on warfarin in the pivotal DOAC vs. warfarin trials.[32-35] In contrast, most major bleeding events resolve without significant long-term sequelae.[43,44] The most frequent site of major bleeding in patients who are taking a DOAC is the gastrointestinal tract. An analysis of the ENGAGE AF-TIMI 48 trial showed that gastrointestinal bleeding occurred at a rate of 1.5 and 1.3 per 100 patient-years in patients with AF randomized to edoxaban and warfarin, respectively.[35,45] Roughly one in nine gastrointestinal bleeds were life-threatening, and only 2% were fatal.[45] Intracranial bleeding, in contrast, remains the most feared complication of antithrombotic therapy. There is a class effect of DOAC therapy that shows a consistent reduction of intracranial haemorrhage with thrombin or factor Xa inhibition vs. warfarin. In the pivotal DOAC vs. warfarin trials, the rate of intracranial haemorrhage was low in patients receiving a DOAC, ranging from 0.2 to 0.5 per 100 patient-years. Nonetheless, approximately one-third of these events resulted in death.[32-35]

Determining the relative weight of stroke and bleeding events is challenging. One method is to determine the risk of subsequent death following an outcome event, using an ischaemic stroke as the reference category (i.e. a weight of 1.0). Using this methodology, the ACTIVE Investigators calculated a relative weight of 0.67 for a major extracranial bleeding event and 3.08 for a haemorrhagic stroke.[46] A widely cited Markov decision model assigned a quality of life value of 0.84 (with 1.0 being well) for an extracranial bleed, 0.76 for a stroke with mild-long-term disability, and 0.11 for a stroke with severe long-term disability.[43] Other groups have proposed different methods to estimate the net benefit of OAC using variable thresholds for relative event severity based on biomarker-based risk prediction (e.g. stroke equally harmful as major bleeding or stroke twice as harmful as major bleeding).[47] However, even modern risk stratification schemes for both thrombotic and bleeding events remain imperfect. In addition, there may be significant inter-individual variation in the accepted thresholds for stroke prevention at the cost of additional bleeding events. A study conducted in the warfarin era suggested that patients at high risk for AF placed more value on stroke prevention than avoidance of bleeding compared with physicians treating patients with AF.[5]

Current guideline recommendations for the initiation of OAC in patients with clinical AF are solely based on the estimated risk of stroke without such treatment.[48-50] Several scores to estimate bleeding risk have been proposed, but are usually not considered when deciding for or against the initiation of treatment. For example, the 2020 European Society of Cardiology (ESC) guidelines for the diagnosis and management of AF state that 'estimated bleeding risk, in the absence of absolute contraindications to OAC, should not in itself guide treatment decisions to use OAC for stroke prevention' (Class III recommendation).[48] Similarly, the 2023 American College of Cardiology (ACC)/American Heart Association (AHA)/American College of Clinical Pharmacy (ACCP)/Heart Rhythm Society (HRS) guidelines state that 'bleeding risk scores should not be used in isolation to determine eligibility for OAC, but instead to identify and modify bleeding risk factors and to inform medical decision-making'.[49]

The meta-analysis of the NOAH-AFNET 6 and ARTESiA trials showed a consistent 32% reduction in ischaemic stroke, a 35% reduction in all-cause stroke or systemic embolism, and a 62% increase in major bleeding with oral factor Xa inhibition compared with aspirin or placebo in patients with device-detected AF.[41] However, the annualized rate of ischaemic stroke in the control arms of these trials was relatively low at 1.0% (NOAH-AFNET 6) and 1.0% (ARTESiA) (*Table 3*).[39,40] These annualized rates are markedly lower than those observed in patients randomized to aspirin in the ACTIVE A (2.8%) and AVERROES (3.0%) trials in patients with clinical AF (*Table 3*).[32,38] However, it is unclear whether NOAH-AFNET 6 and ARTESiA enrolled lower-risk populations, as observational studies have suggested higher event rates in patients with device-detected AF not treated with OAC.[10,51] The corresponding rates of ISTH major bleeding were 1.2 and 0.9 per 100 patient-years in patients randomized to aspirin/placebo and 2.3 and 1.7 per 100 patient-years in patients randomized to receive a factor Xa inhibitor, respectively. In ARTESiA, the rate of intracranial haemorrhage was numerically lower in patients randomized to apixaban compared with those receiving aspirin.[40] This finding is consistent with numerically lower rates of intracranial haemorrhage with apixaban vs. aspirin in the AVERROES trial that enrolled patients with clinical AF who were deemed unsuitable for OAC with a vitamin K antagonist.[46]

In summary, all trials of DOAC in both clinical and, more recently, in device-detected AF demonstrate higher absolute rates of ISTH major bleeding than of ischaemic stroke in patients randomized to receive a DOAC. In the absence of precise risk estimation schemes, the decision to treat an individual patient with device-detected AF with a DOAC for stroke prevention will often be based on the notion that an ischaemic stroke typically carries a higher risk of death or permanent disability than most bleeding events. Secondary analyses of the NOAH-AFNET 6 and ARTESiA trials will aim at identifying subgroups of patients with device-detected AF most likely to derive the largest net clinical benefit from treatment with an oral factor Xa inhibitor. Until these results become available, treatment decisions in device-detected AF may thus largely remain individual.

Oral anticoagulation for stroke prevention in device-detected AF: shared decision-making

The 2020 ESC guidelines provide a class I recommendation to optimize shared decision-making for AF patients by discussing risks and benefits and the burdens of potential treatments.[48]

For OAC, this relates specifically to balancing stroke prevention with increased bleeding. A widely cited Markov model study concluded that warfarin was advantageous above a baseline stroke rate of 1.7% per year and that this threshold could be lowered to 0.9% when using the DOACs.[43] Accordingly, the 2020 ESC AF guidelines set the stroke risk threshold for initiation of OAC in patients with AF at 1%/year.[48] The 2023 American AF guidelines are more conservative, offering a Class I, Level A, recommendation for OAC for AF patients with an estimated >2% annual stroke risk and a Class 2a,

Table 4 Required elements for shared decision-making regarding oral anticoagulation for stroke prevention in patients with device-detected atrial fibrillation

Element	Available data	Needed research
Relative reduction in stroke	32% reduction in ischaemic stroke[41]	Subgroup analyses investigating relative treatment effects
Relative increase in bleeding	62% increase in major bleeding[41]	Subgroup analyses investigating relative treatment effects
Baseline absolute stroke risk on aspirin	1.0%/year[40]	Subgroup analyses investigating baseline risk
Anticipated event severity	45% of strokes on aspirin are fatal or disabling[40]	Economic and net benefit analyses
Patient values and preferences	Patients require less stroke risk reduction to accept OAC and are more accepting of bleeding risk than clinicians[5]	Patient-centred research using device-detected AF data and scenarios

Level A, recommendation for OAC for patients with an estimated annual stroke risk of 1–2%.[49] The threshold of a 1% annual baseline risk of stroke can serve as a starting point for decision-making in patients with device-detected AF. In clinical practice, patients participate in the decision of whether to take OAC through shared decision-making (*Table 4*). Such decisions need to take into account estimation of both absolute and relative risks in addition to the anticipated severity of both stroke and bleeding events. Patients with similar clinical characteristics may arrive at different decisions according to their own preferences. Future research will help refine these parameters needed for informed decision-making.

Future work

The most pressing need in stroke prevention for patients with device-detected AF is improvement of risk stratification. There are several subgroups of patients with device-detected AF for whom the absolute or relative benefits of OAC may be different. Among the parameters of highest interest is the CHA_2DS_2-VASc score[52]; this score is the primary tool used to discriminate risk in patients with clinical AF, although it only does so modestly.[53] The second characteristic in which there is great interest is episode duration. The recent NOAH-AFNET 6 and ARTESiA trials fuel the discussion about the duration of device-detected AF that confers a high enough risk of stroke, warranting OAC treatment. The risk of stroke is known to increase with the burden of clinical AF,[54–56] and similar trends have been observed in the device-detected AF literature.[57,58] In the TRENDS study, patients with AF episodes with a median duration of ≥5.5 h had an increased stroke risk,[9] while in a *post hoc* analysis from the ASSERT trial, only patients with AF episodes >24 h were at increased risk of stroke.[15] Importantly, about 20% of the patients in the TRENDS study had already documented overt AF at inclusion. In the NOAH-AFNET 6 trial, which did not find a significant stroke risk reduction with edoxaban, but also was underpowered, the median duration of device-detected AF prior to enrolment was 2.8 h.[39] In the ARTESiA trial, which showed a statistically significant stroke risk reduction with apixaban, the median duration of the longest episode of device-detected AF in the 6 months prior to enrolment was 1.5 h.[40] The intersection of arrhythmia burden and CHA_2DS_2-VASc has also been proposed in observational series as providing better discriminative power than either parameter alone.[58–60] Atrial remodelling confers a hypercoagulable state; atrial size and structure could play a role in stroke prediction for patients with device-detected AF.[61] The development of specific risk scores for device-detected AF and testing other established clinical risk scores, including those which incorporate biomarkers (e.g. natriuretic peptides), is another area of need. It is also unknown whether the risk varies with the type of implanted device or the indication for implantation.

Conclusions

Device-detected AF is a common finding, occurring in roughly one in three older individuals with an implanted rhythm device. Device-detected AF is associated with an increased risk of stroke, although this risk is lower than for otherwise similar patients with clinical AF detected by surface ECG. Oral anticoagulation with apixaban or edoxaban decreases the risk of stroke in patients with device-detected AF compared with aspirin/placebo, at a cost of increased bleeding. Strokes associated with device-detected AF are often fatal or disabling, whereas bleeds typically resolve without major sequelae. The higher absolute rates of major bleeding compared with ischaemic stroke while on treatment with a DOAC in the recent NOAH-AFNET 6 and ARTESiA trials are consistent with the ratio of bleeds to strokes seen in the pivotal DOAC vs. warfarin trials in patients with clinical AF. Many patients and clinicians may therefore choose OAC for stroke prevention in device-detected AF, although some others may not. Further research into patient characteristics that predict stroke and bleeding will help refine risk prediction for this population and determine subgroups of patients most likely to derive the largest net clinical benefit from DOAC therapy.

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