AFA
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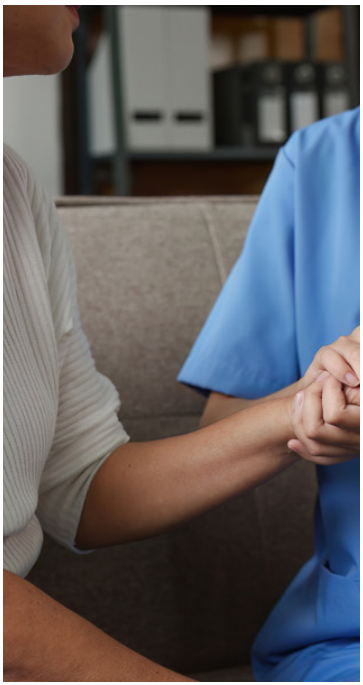
Preventing an AF-related stroke


Working to provide information, support and access to established, new or innovative treatments for Atrial Fibrillation (AF)

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Glossary

Anticoagulation Medications used to thin the blood and prevent blood clots from forming

Antiplatelets Medications which help prevent platelets from sticking together

Atrial fibrillation (AF) Irregular heart rhythm

CHA2DS2-VASc score A quick method to calculate individual risk of an AF-related stroke and the need for anticoagulation

Embolism A blocked artery caused by a foreign body, such as a blood clot

Fibrin A protein that is formed when blood clots which is vital in holding the clot together

International normalised ratio (INR) The test used to measure the blood's clotting capability

Ischaemia A serious problem where a part of your body, like your heart or brain, is not getting enough blood

Ischaemic stroke Caused by a blocked vessel in the brain preventing blood flow to that part of the brain. Ischaemic strokes are the most common type of stroke

Direct Oral Anticoagulants (DOACs) Drugs that block a single blood clotting factor to treat or prevent blood clots.

Left Atrial Appendage Occlusion (LAAO) A minimally invasive surgical procedure which is thought to reduce the risk of stroke in people with AF

Contents

Oral Refers to the way you take medicine, by mouth

Platelets Small fragments which stick to fibrin to make the blood clot

Reversal agent (Often referred to as an 'antidote') Works to reverse the effects of a medicine

Stroke Damage to the brain caused by a blood clot or bleed into the brain

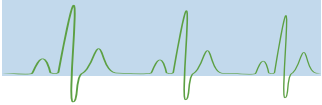
Vitamin K A fat soluble vitamin essential for the formation of several proteins involved in the regulation of blood clotting. Vitamin K is consumed by the body from food intake, particularly green leaved vegetables

Vitamin K antagonists (VKAs) Anticoagulant therapies that affect how the liver uses vitamin K to form proteins which regulate blood clotting. Warfarin in the most commonly used VKA

Transcatheter Closure of the Left Atrial Appendage or Left Atrial Appendage Occlusion (LAAO)

What happens after the procedure?

What are the benefits of the LAA closure?



Why do I need to take anticoagulation therapy?

If you have been diagnosed with Atrial Fibrillation (AF), there are changes in the upper chambers of the heart (atria) which means they no longer contract properly. Blood within the atria can slow down and stagnate, making the chances of a blood clot forming more likely. Some of these changes can be seen on a heart scan (an echocardiogram) or through other investigations, but others are not easily detected.

For everyone with AF, these changes mean the blood is more likely to form small clots in the heart. If these clots move out of the heart and into the general circulation then they can block the blood vessels that supply the organs, such as the brain, and cause a stroke.

AF increases the risk of stroke by 500%, a five-fold increase. It is imperative that an AF patient classed as 'at risk' is prescribed anticoagulant medication to inhibit the coagulation of the blood. This reduces the risk of clots and stroke. You can check your personal AF related stroke risk using the CHA2DS2-VASc scoring system below. The CHA2DS2-VASc score allows you to understand your risk of stroke due to your AF. If you have a score of Zero (or One due to gender alone) then national and international guidelines suggest you do not require any intervention. If you have a score of One due to anything other than gender, then you should consider an oral anticoagulant to reduce the risk of an AF-related stroke. If you have a score of 2 or greater, then oral anticoagulation is recommended to reduce the stroke risk due to your AF.

CHA2DS2-VASc scoring criteria to determine need for blood thinning based on AF-related stroke risk

Congestive heart disease	1 point
Hypertension	1 point
Age (75 years +)	2 point
Diabetes	1 point
Stroke or previous TIA	2 point
Vascular heart disease	1 point
Age (65-74 years)	1 point
Sex category - female	1 point
SCORE	

score	risk level	necessity for anticoagulant
0	low risk	anticoagulant not suggested
1	at risk	anticoagulant suggested dependent on personal preferences
2+	at risk	

Clots are made up of two main components, platelets and fibrin.

Platelets are small sticky cells that exist in large numbers in the blood. They are involved in forming scabs or sticking together. They are beneficial when you cut yourself in stopping the bleeding, but if working incorrectly, or present in too high a number, then your blood becomes clumpy and clots form when they should not.

The clotting of the blood is a complex process as blood should clot rapidly when required, but also remain fluid at other times. The process is referred to as the 'clotting cascade' by clinicians. This term is used to explain how the stimulation to form a clot triggers a series of steps before producing the blood enzyme thrombin. The enzyme thrombin changes the soluble protein fibrinogen to the insoluble protein fibrin. Clots are made of fibrin.

Antiplatelet drugs such as aspirin and clopidogrel, stop the activation of platelets. Although antiplatelet medication has been used for many years to prevent stroke, as of 2014, the National Institute for Health and Care Excellence (NICE) no longer recommends the use of aspirin for AF-related stroke prevention as OAC attains better results with greater safety.

What anticoagulation options are available?

Anticoagulants will not reduce or take away any symptoms of AF as they do not treat the condition. Anticoagulants are prescribed to prevent blood clots from forming inside your heart and to reduce your risk of having an AF-related stroke.

It is important to understand the effect of an anticoagulant on your body to ensure you receive the best therapy to suit you. It is also very important that you take your anticoagulant as prescribed by your doctor whether or not you are experiencing symptoms of AF.

Thanks to a number of medical advances, there are more anticoagulant options available than there were a few years ago. They all help to prevent the risk of an AF-related stroke by slowing down and reducing the formation of blood clots. Your doctor will work with you to find the right therapy, taking into account your individual risk of an AF-related stroke, any other medicines that you might be taking and your medical history.

Anticoagulant therapy options currently available for reducing the risk of an AF-related stroke can be divided into two groups; Direct Oral Anticoagulants (DOACs) and Vitamin K antagonists (VKAs).

Direct Oral Anticoagulants (DOACs)

DOACs work in a different way to VKAs to prevent the blood from clotting. There are four DOACs currently available in Europe: apixaban (Eliquis), dabigatran (Pradaxa), edoxaban (Lixiana), and rivaroxaban (Xarelto).

DOACs are proven to be safer than VKAs whilst being as effective or even more so. DOACs do not require monitoring with regular blood tests. Unlike VKAs, there are no interactions with foods. DOACs have fewer interactions with other medicines compared with VKAs and they are given at a fixed dose. DOACs start to work quicker than VKAs and the effect of DOACs wears off faster if therapy is stopped.

Apixaban:

In February 2013, apixaban was approved by The National Institute for Health and Care Excellence (NICE) for use within the UK. It is prescribed for reducing AF-related stroke risk in people with AF where the cause is not a heart valve problem. Apixaban is a medication that has a direct effect on the enzyme called 'Ten A', often written 'Xa'. This is part of the clotting cascade that leads to the soluble fibrinogen being converted to the fibrous fibrin, then causing clots (thrombus). This controlled blocking of Xa stops the blood clotting as quickly, which helps to prevent the formation of clots in the heart that cause strokes.

The recommended dose of apixaban is 5mg twice daily. If you are over 80, have low body weight, or impaired kidney function, you may be offered a lower dose of 2.5mg twice daily.

You should inform your doctor and dentist that you take apixaban before having any operation or procedure, or before changing or starting other medications including herbal remedies.

Apixaban is rapidly metabolised by the body, requiring a twice daily dose.

In clinical trials, apixaban was shown to be at least three times more effective than aspirin in preventing AF-related stroke. There are no known lifestyle issues like those that apply to warfarin, and apixaban does not involve frequent blood monitoring.

There are few identified interactions between apixaban and other medications. Trials have suggested that there may be fewer bleeds in the brain (intracranial haemorrhages) and fewer fatal bleeds when compared with warfarin.

Apixaban's anticoagulation effects last about 12 hours which is why you need to take this medication twice a day. Its effects can however be reversed if needed - a medication called Andexxa can do this.

Rivaroxaban:

In May 2012, NICE published a recommendation for rivaroxaban as a possible treatment to reduce the risk of stroke in AF patients who are already assessed as being at increased risk of stroke and systemic embolism.

Rivaroxaban interferes with Factor Xa that is involved in the development of blood clots. Unlike warfarin, it does not require regular INR monitoring.

Rivaroxaban is licensed in the UK for use in non-valvular AF patients to reduce the increased risk of stroke caused by AF. Rivaroxaban is approved for other indications including reducing the risk of clots in adults who have hip or knee replacement surgery, and treating thrombosis due to a clot formation in the body (e.g. the leg), also known as DVT (deep vein thrombosis).

For stroke prevention in AF, rivaroxaban is administered at a fixed dose of 20mg once daily, although the dose may need to be reduced if kidney function is impaired. If your kidney function is impaired, you have low body weight, or you are taking other medication that affects the amount of rivaroxaban required to be effective, you may be offered a lower dose of 15mg once daily. Rivaroxaban should be taken once a day with your main meal so that it will be completely absorbed. Like apixaban, rivaroxaban can be reversed with Andexxa.

Dabigatran:

NICE approved the use of dabigatran in March 2012 for the prevention of stroke and systemic blood clots in patients with AF. Dabigatran is a medication that has a direct effect on the enzyme thrombin - it is called a direct thrombin inhibitor. It has its effects on the final step of the 'clotting cascade'.

Dabigatran is specifically licensed in patients with non-valvular AF without underlying heart valve disease, who have at least one or more risk factors.

It is also licensed for the treatment of deep vein thrombosis and pulmonary embolism, and as a preventative measure for these conditions. Unlike warfarin, dabigatran doesn't require regular blood tests to determine the dose. Dabigatran is also used in medical practice to reduce the risk of clots forming after orthopaedic surgery, such as a hip or knee replacement.

The recommended dose of dabigatran is 150mg twice daily. If you are over 80, have low body weight, or impaired kidney function, you may be offered a lower dose of 110mg twice daily. Unlike warfarin, dabigatran is rapidly metabolised by the body, requiring a twice daily dose. If a tablet is missed or overlooked then it should be taken as soon as possible after the mistake is noticed, unless it is almost time for your next dose. Dabigatran requires acidic surroundings to aid absorption and is manufactured to enhance this which is why it often causes indigestion. You are advised to swallow the capsules whole with a glass of water.

In December 2015, idarucizumab (Praxbind); a dabigatran-specific reversal agent was launched in the UK for emergency surgery or urgent procedures; and in uncontrolled bleeding. The use of Praxbind is restricted to hospital use only.

Edoxaban:

Edoxaban is an anticoagulant drug that helps to reduce the risk of blood from clotting inappropriately. It does this by inhibiting factor Xa with a substance in the body (Factor Xa, 'ten A') that is involved in the development of blood clots. Unlike warfarin, it does not require regular INR monitoring.

Edoxaban is licensed in the UK for use in nonvalvular AF patients to reduce the increased risk of stroke caused by AF. It is also approved for other indications, specifically treatment and prevention of deep vein thrombosis (DVT) and a pulmonary embolism which is a blood clot in the lungs.

The recommended dose of edoxaban is 60 mg once daily and should be swallowed preferably with water. It can be taken with or without food. If your kidney function is impaired, you have low body weight, or you are taking other medication that affects the amount of edoxaban required to be effective, you may be offered a lower dose of 30mg once daily. Talk to your doctor who will advise on the best dose for you.

The effectiveness and safety of edoxaban was assessed in the largest and longest trial with any novel oral anticoagulant in patients with AF performed to date. The trial was conducted in 21,105 patients and showed that edoxaban had similar efficacy to warfarin for stroke prevention.

Vitamin K antagonists (VKAs):

VKAs affect how the liver uses Vitamin K to form proteins which regulate blood clotting. VKA therapy takes a few days to have an effect and it takes a few days for the effect to wear off when treatment is stopped, unless an antidote is given. Vitamin K is obtained in the body from food intake and is essential for the functioning of several proteins involved in the regulation of blood clotting. Vitamin K is found in many everyday foods, particularly green leafy vegetables.

The most commonly used VKA is warfarin. VKAs have been used as anticoagulants for more than 60 years. Two out of three AF-related strokes are prevented with warfarin compared to those not taking anticoagulant therapy.

The effectiveness of VKAs is impacted by the amount of vitamin K in your diet. If your diet is reasonably consistent, then the amount of vitamin K in your body will be matched by the warfarin dose. If the amount of vitamin K in your diet changes, it can affect the ability of the VKA to prevent clot formation and the dose will need to be adjusted. Taking other medicines and consuming alcohol can also have an impact on how VKA works in the body.

Regular monitoring with blood tests is needed with VKAs by taking a blood sample. The specific test used to measure the blood's clotting capability is called the INR (International Normalised Ratio). By measuring the INR, anticoagulant clinics and healthcare teams can optimise the amount of VKA therapy given to a patient. Too little warfarin reduces the therapy's ability to prevent an AF-related stroke whereas too much warfarin can put you at increased risk of bleeding. The dose of warfarin might need to be adjusted to ensure your INR remains within the target required for your condition. It might take a little while to get the dose right for you and initially your monitoring will be frequent. Once your INR is more stabilised your monitoring can become a little less frequent however, it will still need to be done on a regular basis.

Regular monitoring can be done at your doctor's surgery or there may be the possibility for you to self-monitor. Self-testing involves the use of a handheld device to measure the INR in a drop of blood, rather like monitoring blood sugar levels in diabetes. This testing can be undertaken in the comfort of your own home, at work or while away on business or holiday.

Are there any drugs I should not take with my anticoagulant?

Do not start any new medicine (prescribed and/or over the counter), supplements such as vitamins or herbal remedies without first checking with your healthcare provider or pharmacist.

Each anticoagulant is different so it is important to ask your doctor or pharmacist in relation to the anticoagulant you are taking. VKAs such as warfarin interact with other medicines more than the DOACs.

Before a Procedure:

Patients should be guided by their clinicians as to if and when to stop their usual oral anticoagulant. If heparin is required to provide anticoagulant cover before, during, and after their procedure, guidance around in what form should be given. Sometimes, those already on anticoagulation may be asked to discontinue this temporarily for a few days before an invasive procedure, surgery, an exploratory investigation like a colonoscopy, or a catheter ablation. For people on warfarin, their international normalised ratio (INR) will typically drop from 2.5 to around 1.5 after about three days. However, many centres perform cardiac catheter ablations with patients continuing to take their warfarin.

"I was surprised when my Consultant told me I should not stop taking the anticoagulants before the procedure"

Carole, Ipswich

Risk of bleeding whilst taking anticoagulants

Anticoagulants do not cause bleeding. Bleeding can occur from an injury or can develop internally, for example in the stomach or gut. The role of anticoagulants is to help prevent potentially dangerous clots from forming in your body, so you may have an increased risk of bleeding whilst taking it. The risk of major bleeding in people taking anticoagulants is low and can affect about 3 in 100 people a year. If you experience a major bleed (with severe blood loss and/or symptoms requiring treatment in hospital) and you are on an anticoagulant, it can be treated successfully in approximately 90% of cases.

It is very important to inform doctors and dentists that you take an anticoagulant before starting any new medication or before having a procedure or operation.

What to do if you notice bleeding:

Speak to your doctor immediately if you experience any of the following signs of bleeding:

- Bruising or bleeding under the skin
- Nose bleeds or cuts that take a long time to stop bleeding
- Red or dark brown urine
- Coughing up or vomiting blood or ground coffee-like material
- Red or black stools
- Bleeding gums
- Bleeding that does not stop by itself
- Abnormally heavy periods

Bleeding is not always obvious. If you experience any side effects talk to your doctor or pharmacist. It is important to not stop taking your anticoagulants before speaking to them first.

Minimising bleeding risks

There are things to keep in mind to help you minimise the risk of bleeding if you are on an anticoagulant. This is called The HAS-BLED system which can be used to estimate the risk of bleeds.

Risk factor		Score
H	Hypertension (high blood pressure)	1
A	Abnormal renal and liver function	1 point each
S	Stroke and TIA	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age is over 65 years)	1
D	Drugs or alcohol	1 point each

A HAS-BLED score of three or more indicates 'high risk'. High risk is not necessarily a reason to deny offering oral anticoagulants, neither is a previous intracranial haemorrhage (ICH), the risk of which decreases with time. The risk of ischaemic stroke from not being prescribed oral anticoagulants is likely to outweigh the risk of ICH from taking them.

How long do I need to take anticoagulants?

The medicines prescribed are intended to provide you with ongoing protection against the risk of an AF-related stroke. Therefore, you should expect to continue anticoagulation therapy indefinitely unless your doctor changes or recommends another form of therapy.

My AF symptoms have improved. Can I stop taking my anticoagulant?

Never stop your anticoagulant therapy without having consulted your doctor as this could put you at risk of having an AF-related stroke. If you wish to stop taking your medicine, please speak to a doctor first to discuss your reasons and to agree the best course of action for you.

Remember that some people do not have any symptoms of AF, yet the risk of an AF-related stroke is still there. Anticoagulant therapy should be taken continuously, independent of any obvious AF symptoms.

Transcatheter Closure of the Left Atrial Appendage or Left Atrial Appendage Occlusion (LAAO)

Figure 2. LAA device

Unfortunately, some patients at high risk of an AF-related stroke are either unable or unwilling to take anticoagulants because of associated risks, or side effects. An alternative to medication for patients with AF at high risk of an AF-related stroke is to close off the appendage with a medical closure device (see Figure 2).

The device is designed to close the left atrial appendage (which is known to be the main source of blood clots in patients with AF), preventing clots from forming in the LAA, or breaking free from it and travelling to the brain.

Transcatheter closure of the LAA is carried out in a cardiac catheterisation laboratory, a specially equipped cardiology room where patients with heart rhythm disorders are examined and treated, or in an electrophysiology laboratory. The procedure lasts about 45-90 minutes. The procedure is usually done under general anaesthesia (but may also be done under sedation in some instances).

During the procedure, a cardiac ultrasound (echocardiogram) examination is undertaken (to get clear pictures of the heart) by placing a probe in the oesophagus.

A small cut (or incision) is made in the groin and through this opening a small plastic tube (catheter) is inserted into a vein in the leg. This catheter contains the compressed umbrella shaped device which is used to close the opening of the left atrial appendage.

Using X-rays and ultrasound images, the catheter is guided into the heart. The umbrella-like device is then passed through the catheter and into position within the LAA. As the compressed device is pushed from the end of the catheter tip, it expands thereby blocking the mouth of the left atrial appendage (see Figure 3).

The patient may need to return to their doctor for periodic follow-up visits over the next year. The doctor will also advise the patient when normal daily activities can be resumed. Typically, all strenuous activity should be avoided for one month following the procedure. If the patient experiences shortness of breath or chest pain, they should seek medical help immediately.

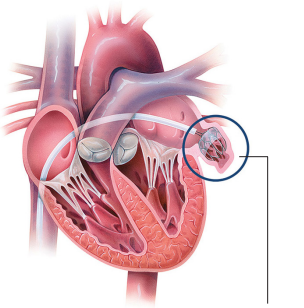


Figure 3. Position of the LAA device

What happens after the procedure?

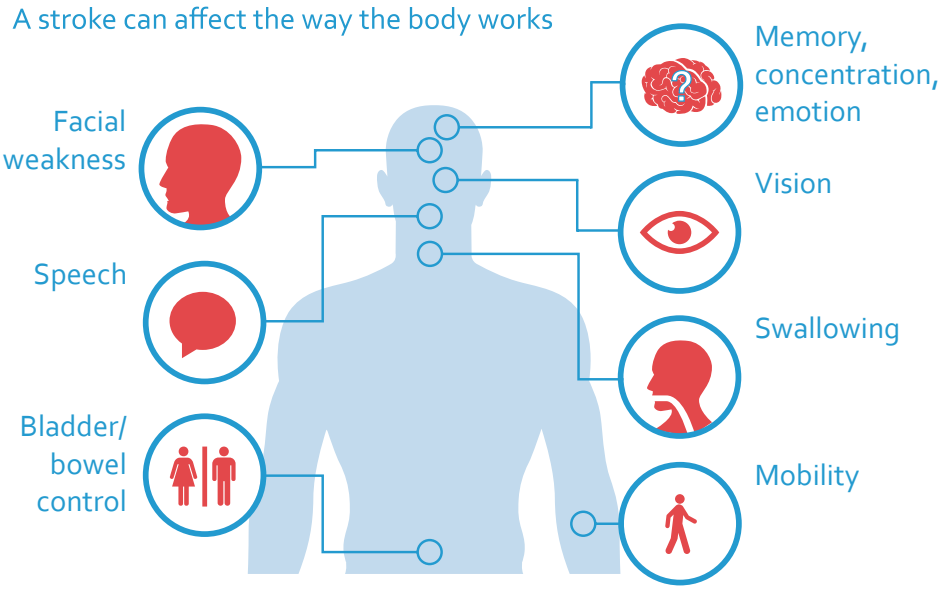
Recovery following the procedure will take about 24 hours. After recovery from anaesthesia and with adequate bed rest the patient should be able to sit up and walk around. Before leaving the hospital, tests such as an echocardiogram (ultrasound scan of the heart) may be performed to make sure the device is still positioned correctly. As the procedure is minimally invasive, the recovery process is likely to be quick and easy. There may be an adhesive plaster used in the groin where the catheter was inserted. The patient may also have a sore throat due to the use of imaging probe (transoesophageal echo).

What are the benefits of the LAAO closure?

The main benefit of this procedure is that it potentially eliminates the need to take anticoagulants. In the majority of patients who undergo the procedure, warfarin is continued for a minimum period of six to eight weeks post procedure as time has to be allowed for the implanted device to bed in. During this time the body will form a new layer of natural tissue over the device, sealing it into place.

Antiplatelet therapy will have to be taken e.g aspirin or clopidogrel following cessation of OAC with detailed advice from your doctor.

Conclusion



All strokes, including AF-related strokes, can cause life changing, disabling effects to your body and mind and greatly impact everyday life. Those affected by an AF-related stroke may not be able to look after themselves and interact as they did before the stroke, so family and friends are usually affected too. Strokes, including AF-related strokes, can also be life threatening.

It is therefore important to take anticoagulation medication as prescribed if you are considered at risk by your GP or consultant.

If you have any questions or concerns regarding anticoagulants, please contact AF Association on info@afa.org.uk or +44 (0)1789 867502

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"This booklet was so helpful in explaining why it is so important to take the anticoagulants I was prescribed by the doctor, I didn't have any symptoms, but I was still at risk of a having a stroke"

Jane, Kent

To view our patient resources, scan the QR code below:

Please remember that this publication provides general guidelines only. Individuals should always discuss their condition with a healthcare professional. If you would like further information or would like to provide feedback, please contact AF Association.

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If you would like further information or would like to provide feedback please contact AF Association.