

## ANTICOAGULANTS IN FRAIL OLDER PEOPLE

Atrial fibrillation (AF) is the most common cardiac arrhythmia or irregular heartbeat. Atrial fibrillation is an independent risk factor for stroke, increasing the risk 5-fold and even higher in those aged 65 years or more.

Oral anticoagulants are recommended for stroke prevention in people with atrial fibrillation. Frail older people with atrial fibrillation have an increased stroke incidence, mortality, symptom severity and length of hospital stay. Frail older people are therefore more likely to benefit from oral anticoagulants; however, they tend to be under-prescribed due to concerns about bleeding.

### Atrial fibrillation

In AF, the heart beats irregularly and often fast. This reduces the heart's ability to pump blood properly and increases the chance of a blood clot forming in the heart and travelling up to the brain, where it can cause a stroke.

Risk factors for AF include advancing age, heart disease, high blood pressure, excessive alcohol intake, obesity, and family history. Older persons with AF are four times more likely to be frail and twice as likely to have cognitive impairment than older patients without AF.

Common symptoms of atrial fibrillation include:

- Feeling breathless
- Feeling faint, dizzy, or lightheaded
- Racing heart (palpitations)
- Tiredness or weakness
- Chest pain or discomfort
- Difficulty exercising

### Anticoagulants

Oral anticoagulants are indicated for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation (NVAF).

They reduce the risk of stroke by about two-thirds, from around 12% to 4%. Oral anticoagulants are more effective in preventing recurrent stroke than antiplatelet agents and have a similar risk of bleeding.

Oral anticoagulants include warfarin (Coumadin, Marevan) and the newer direct-acting oral anticoagulants (DOACs):

- Apixaban (Eliquis)
- Dabigatran (Pradaxa)
- Rivaroxaban (Xarelto)

DOACs are also indicated for prevention of venous thromboembolism (VTE) following elective hip or knee replacement and for treatment of acute VTE and prevention of subsequent VTE.

Warfarin can be a challenging medicine to use, requiring frequent blood tests (INRs) to determine appropriate doses. Warfarin also interacts with many other medicines, leading to an increased risk of bleeding.

Monitoring of renal and liver function is required with DOACs, and several drug interactions are important. All DOACs require renal dose adjustment, in particular dabigatran. In people with reduced renal function (eGFR 30-50mL/min), the dose of dabigatran should be reduced from 150mg twice daily to 110mg twice daily.

The dose should also be reduced to 110mg twice daily in people older than 75 years.

The usual dose for apixaban is 5mg twice daily.

The dose should be lowered to 2.5mg twice daily in people if at least 2 of these factors:

- Weight less than 60kg
- Age greater than 80 years
- Serum creatinine greater than 133 micromol/L

Rivaroxaban dose is usually 20mg once daily, reduced to 15mg once daily if eGFR is 15-49 mL/min. Rivaroxaban is the only DOAC approved for use in Australia in patients with creatinine clearance down to 15mL/min.

### Stroke prevention

Large clinical trials have shown DOACs are just as good as warfarin for stroke prevention, including in people aged 75 years and older. In real life studies, all DOACs have been associated with a lower risk of stroke and systemic embolism, and all-cause mortality compared with warfarin.

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Apixaban is associated with a lower risk of all-cause mortality compared with rivaroxaban in the large ARISTOPHANES study; however, there is no significant difference between apixaban and dabigatran or dabigatran and rivaroxaban for all-cause mortality.

Ischaemic stroke is the most prevalent type of stroke, with a lower risk in apixaban and rivaroxaban compared to warfarin. Apixaban, dabigatran, and rivaroxaban are associated with a lower risk of haemorrhagic stroke compared to warfarin.

### Age and frailty

Age is a major risk factor for both AF and VTE. Older people are also at an increased risk of bleeding, and an increased falls and fracture risk. Whilst chronological age is not the main indicator for frailty, frailty increases vulnerability to stressors which can result in poor health outcomes, increased bleeding risk and mortality.

Frail people with atrial fibrillation are more susceptible to stroke and major bleeding due to multimorbidity, polypharmacy and low body weight. Frail older people are likely to receive greater benefit from stroke prevention but potentially higher risk of bleeding by taking anticoagulants.

However, evidence supports the use of oral anticoagulants among frail older people with atrial fibrillation as the benefits usually outweigh the risks.

The incidence of adverse events in frail people tends to occur early in treatment with DOACs, so careful follow-up is necessary during the initial 3 months.

### Major bleeding

All oral anticoagulants increase the risk of bleeding. There is no difference in bleeding complications in people older than 75 years compared to younger. Bleeding history and concurrent use of antiplatelet medicines or non-steroidal anti-inflammatory drugs (NSAIDs) need to be considered when prescribing oral anticoagulants. Other conditions that may predispose to bleeding complications such as high falls risk need to be considered.

Apixaban and dabigatran are associated with a lower risk of major bleeding compared with warfarin.

Rivaroxaban is associated with a higher risk of major bleeding and gastrointestinal bleeding compared with warfarin.

Compared to dabigatran and rivaroxaban, apixaban is associated with a lower risk of major bleeding and gastrointestinal bleeding. Dabigatran is associated with a lower risk of major bleeding and gastrointestinal bleeding compared to rivaroxaban.

For residents with a previous episode of gastrointestinal bleeding or at high risk of bleeding, apixaban may be the safest choice of oral anticoagulants.

### Intracranial haemorrhage

All DOACs are associated with a significantly lower risk of intracranial haemorrhage compared with warfarin. Apixaban has a similar risk of intracranial haemorrhage as aspirin.

### Conclusions

Careful assessment of the risks and benefits of anticoagulation is necessary in frail older people with atrial fibrillation. However, the favourable balance between risks and benefits of DOACs is usually preserved in this population. DOACs should be preferred to warfarin as oral anticoagulants for stroke prevention.

Frailty is a strong indicator of adverse events, so close monitoring is required, particularly in the initial few months.

### References

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