

# Thrombosis and Haemostasis

## 2024 Chinese expert consensus guidelines on the diagnosis and treatment of Atrial Fibrillation in the Elderly. Executive Summary

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### Abstract:

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The writing committee members comprehensively reviewed updated evidence pertaining to elderly patients with AF, and formulated this 2024 update. The highlighted issues focused on the following: screening for AF, geriatric comprehensive assessment, use of the Atrial fibrillation Better Care (ABC) pathway for the elderly patients, and special clinical settings related to elderly patients with AF. New recommendations addressing smart technology facilitated AF screening, ABC pathway based management and optimal anticoagulation were developed, with a focus on the elderly.

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**2024 Chinese expert consensus guidelines on the diagnosis and treatment of Atrial Fibrillation in the Elderly, endorsed by Geriatric Society of Chinese Medical Association (Cardiovascular Group) and Chinese Society of Geriatric Health Medicine (Cardiovascular branch). Executive Summary**

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This is an executive summary of the full consensus guideline, which is published in Chinese Journal of Cardiac Arrhythmias (Chin J Cardiac Arrhythm 2024; DOI: 10.3760/cma.j.cn113859-20240130-00012)

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The writing committee members comprehensively reviewed updated evidence pertaining to elderly patients with AF, and formulated this 2024 update. The highlighted issues focused on the following: screening for AF, geriatric

comprehensive assessment, use of the Atrial fibrillation Better Care (ABC) pathway for the elderly patients, and special clinical settings related to elderly patients with AF. New recommendations addressing smart technology facilitated AF screening, ABC pathway based management and optimal anticoagulation were developed, with a focus on the elderly.

### **Keywords**

GSCMA, CSGHM, atrial fibrillation, elderly, management, consensus guideline, executive summary

### **Introduction**

The consensus guidelines of the Geriatric Society of Chinese Medical Association (GSCMA) on the management of atrial fibrillation (AF) in the elderly was first published in 2011 and updated in 2016,<sup>1, 2</sup> with endorsement by Chinese Society of Geriatric Health Medicine (CSGHM). Since then, many important studies regarding the screening and treatment in the elderly population have been reported, necessitating this updated expert consensus guidelines.

This is an executive summary of the full consensus guideline, which is published in Chinese Journal of Cardiac Arrhythmias.<sup>3</sup> The writing committee members comprehensively reviewed updated evidence pertaining to elderly patients with AF, and formulated this 2024 update. The highlighted issues focused on the following: screening for AF, geriatric comprehensive assessment, use of the Atrial fibrillation Better Care (ABC) pathway for the elderly patients, and special clinical settings related to elderly patients with AF. New recommendations addressing smart technology facilitated AF screening, ABC pathway based management and optimal anticoagulation were developed, with a focus on the elderly.

### **Epidemiology of elderly AF population**

Atrial fibrillation (AF) prevalence increases with increasing age, being 0.72% in population aged 55- 59 years, 6.52% in aged 80-84 years, and 8.18% in aged over 95 years.<sup>4</sup> The increasing aging population and chronic diseases increases the risk of AF and AF-related stroke in the elderly population in China. The lifetime risk of AF of the population aged over 75 years is doubled compared to those aged 50 years.<sup>5</sup> Thus it is estimated that there are currently 20 million adult AF patients in China.<sup>6, 7</sup> In the 2018 Blue Book on the Prevention and Treatment of Atrial Fibrillation in China, the elderly population with AF was modelled to exceed 9 million by the year 2050.<sup>4</sup>

The elderly AF population often have a variety of diseases, such as coronary heart disease (CAD), arteriosclerosis, heart failure (HF), valvular disease, pulmonary hypertension, chronic obstructive pulmonary disease, diabetes, chronic anemia,

chronic kidney disease, tumor, etc. Indeed, the optimal thromboprophylaxis in the Chinese elderly Patients with atrial Fibrillation (ChiOTEAF) Registry found that 73.2% of the elderly AF population aged over 75 years had  $\geq 2$  comorbidities and 35.7% were treated with over 5 or more drugs.<sup>8</sup> Such clinically complex phenotypes AF patients with multimorbidity, frailty and polypharmacy have important implications for treatment and prognosis.<sup>9-11</sup>

These comorbidities were independently associated with thromboembolic and bleeding risks, which results in poor adherence to anticoagulation amongst elderly patients with AF.<sup>12</sup> Some evidence suggests that Asian patients are more sensitive to anticoagulation, in terms of bleeding,<sup>13, 14</sup> but ethnic differences in thromboembolism and intracranial bleeding are evident.<sup>15, 16</sup>

### **Recommendations**

1. Aging and chronic disease increase the risk of AF and stroke in the elderly population.
2. The elderly population with AF often have multiple comorbidities, contributing to clinically complex phenotypes, with implications for AF-related complications, such as thromboembolism.
3. A geriatric general assessment and proactive management of comorbidities are needed in these elderly patients (Figure 1).

### **Atrial fibrillation stages**

AF is a progressive disease, contributed by an unhealthy lifestyle and risk factors over an individual patient's lifetime.<sup>17</sup> AF stages, defined as those at risk for AF, pre-AF, AF, and permanent AF, emphasizes prevention through addressing modifiable risk factors and the appropriate treatments based on AF burden.<sup>18</sup>

The population *at risk for AF* includes susceptible factors to AF, such as obesity, obstructive sleep apnea (OSA), physical inactivity, alcohol, diabetes, hypertension, and other nonmodifiable risk factors.<sup>19</sup> At *pre-AF stage*, there is the evidence of structural or electrical changes further predisposing to AF, such as atrial enlargement, frequent atrial ectopy, short bursts of atrial tachycardia, with HF, valve disease, CAD, hypertrophic cardiomyopathy, thyroid disease, etc. At the *AF stage*, AF burden can be ongoing monitored to track the progression of disease. At the *permanent AF stage*, rhythm control approaches are discontinued.

### **Recommendations**

1. AF stages can be classified into as at risk for AF, pre-AF, AF and permanent AF.
2. Holistic risk factor management is recommended to reduce naive or recurrent onset of AF at the earlier stages.
3. Appropriate stroke prevention and individualized patient-centred symptom

directed rate or rhythm management should be administered, as appropriate.

### **AF screening**

Screening techniques for AF include photoplethysmography (PPG), single/multi-lead electrocardiogram (ECG), and accelerometer, etc. There are a variety of screening devices, such as handheld devices, wristbands/watches, chest straps, and stickers. The common screening strategies are as follows: general population screening and "targeted" population screening, intermittent testing/continuous monitoring, consumer-led screening, or physician/nurse-led screening. The detected rate of targeted screening is higher than that of general population screening.

The more frequent and longer AF monitoring, the higher the sensitivity of AF detection.<sup>20</sup> Compared with intermittent testing of single-lead ECG, PPG-based wearables demonstrated the good detection of AF,<sup>21</sup> with the advantage of the continuous monitoring and low cost. Moreover, the wearables can detect the susceptible factors to AF (e.g. OSA, hypertension).<sup>22</sup> With the use of validated wearables, a consumer-led screening approach can be applied for the detection of AF<sup>23</sup> and its susceptible risk factors.<sup>24</sup>

Screening for AF with validated wearables in the elderly,<sup>25</sup> or the high-risk population, such as with OSA, hypertension, diabetes, and post-stroke, will facilitate the early detection and management of AF.

### **Recommendation**

1. With the updated evidence on the application of wearable device technology, the use of smart devices, with PPG or single/multiple-lead electrocardiogram, for AF screening is recommended in the elderly population, or in high-risk populations, eg. those with OSA, hypertension, diabetes, post-stroke, etc. (Figure 2)

### **Holistic or integrated care management for the elderly**

A holistic or integrated care approach, with the well-validated Atrial fibrillation Better Care (ABC) pathway is recommended for the elderly population with AF to improve clinical outcomes (Figure 3).

**“A”:** **Avoid stroke with anticoagulation** using non-vitamin K antagonist oral anticoagulants (NOAC) or well-managed warfarin (International normalized ratio, INR 2.0-3.0 with time in therapeutic range  $\geq 70\%$ ) in patients at high-risk of stroke. An INR 1.6-2.5 may be considered in frail elderly patients aged over 75 years or HAS-BLED score  $\geq 3$ , as lower INR targets appear to reduce bleeding but increases thromboembolism in AF.<sup>26</sup> Good quality anticoagulation control with time in target range (TTR)  $\geq 70\%$  is associated with low thromboembolism and bleeding risks.

In patients at intermediate risk for stroke (ie. stroke prevalence of 1%-2%/year, ie. CHA<sub>2</sub>DS<sub>2</sub>-VASc =1 in male or =2 in female) could benefit from the modification of risk factors. No antithrombotic therapy is recommended in low-risk subjects, ie. CHA<sub>2</sub>DS<sub>2</sub>-VASc =0 in male or =1 in female, but elderly AF patients would not be in this category, being at age ≥ 65 years.

For the patients with intermediate- or high- risk stroke, but with long-term oral anticoagulant contraindications due to irreversible causes, percutaneous left atrial appendage closure (LAA) is recommended.

If the patients with high-risk for AF, e.g. left atrial enlargement, chronic obstructive pulmonary disease, chronic obstructive pulmonary disease (COPD), HF, stroke prevalence of >2%/year, it is recommended to monitor for AF occurrences and consideration of oral anticoagulation.

In a systematic review, patients with atrial high-rate episode (AHRE) detected by cardiac implantable electronic devices (CIEDs), the risk ratio (RR) for thromboembolic events in AHRE patients was 2.13 (95% CI: 1.53-2.95, I<sup>2</sup>: 0%), while the RR for incident clinical AF was 3.34 (95%CI: 1.89-5.90, I<sup>2</sup>: 73%).<sup>27</sup> In other studies, AHRE ≥24 h developed more ECG-diagnosed AF (17.0%/patient-year) than patients with shorter AHRE (8.2%/patient-year, detected by implanted cardiac device in recent trials).<sup>28, 29</sup>

In a real world cohort of CIED patients with median follow-up of 24.3 (10.6-40.3) months, 29.8% patients experienced the composite outcome of clinical AF or AHRE episodes lasting ≥24 h.<sup>30</sup> Baseline CHA<sub>2</sub>DS<sub>2</sub>-VASc score and the longest AHRE episode at enrollment lasting 12 h-23 h 59 min were independently associated with the composite outcome (hazard ratio, HR; 95% confidential interval, CI: 1.40; 1.07-1.83 and HR: 8.15; 95% CI 2.32-28.65, respectively).<sup>30</sup> Thus, baseline patients' characteristics (CHA<sub>2</sub>DS<sub>2</sub>-VASc score) and AHRE duration may help to intensify monitoring and decision-making, being independently associated with clinical AF at follow-up.

Two randomized trials, the NOAH-AFNET 6 and ARTESiA trials, provides high-quality evidence on the anticoagulation for patients with device-detected AF.<sup>28, 31</sup> Among patients with subclinical AF, with at least one episode lasting 6 minutes or longer but no episodes lasting longer than 24 hours, detected by implanted cardiac device, apixaban resulted in a lower risk of stroke or systemic embolism than aspirin but this was with a higher risk of major bleeding.<sup>31</sup> For the patients with AHRE also detected with implanted cardiac device in the NOAH-AF trial, anticoagulation with edoxaban did not significantly reduce the incidence of a composite of cardiovascular death, stroke, or systemic embolism as compared with placebo in NOAH-AFNET 6.<sup>28,</sup>

<sup>29</sup> Meta-analysis of NOAH-AFNET 6 and ARTESiA trials demonstrated that oral

anticoagulation reduced the risk of stroke in patients with device-detected AF and increased the risk of major bleeding.<sup>32</sup> Taking into account these results, dynamic monitoring AHRE/AF progression and CHA<sub>2</sub>DS<sub>2</sub>-VASc, considering the benefits and related risks of oral anticoagulants, and individualized decision making of stroke prevention approach, is proposed for patients with CIED and AHRE.

**“B”:** **Better patient-centered symptom-directed rate or rhythm control strategies** are recommended to reduce AF burden, as well as improve clinical outcomes with early rhythm control for selected patients.

**“C”:** **Cardiovascular risk and comorbidity management** (OSA, diabetes, hypertension, HF, CAD, COPD, pulmonary hypertension, etc.) **as well as lifestyle changes** (obesity reduction, regular exercise, reducing alcohol/stimulants, psychological morbidity, etc.).

Digital health technology can be used to facilitate AF care pathways.<sup>33</sup> In the mAFA-II randomised trial, smart technology facilitated ABC pathway (mobile Atrial Fibrillation, mAFA) reduced clinical adverse in the elderly patients with AF, reducing the composite endpoints of all-cause death, thromboembolism and rehospitalization in the elderly patients aged over 75 years, or HF, diabetes, prior thromboembolism, or with multiple morbidity (Figure 4).<sup>34-38</sup> In a systematic review and meta-analysis, adherence to the ABC pathway was associated with a reduction in mortality, stroke and bleeding.<sup>39</sup> The potential cost-effective use of streamlining and integrating care via the Atrial fibrillation Better Care (ABC) pathway for AF has been reported.<sup>40</sup> The substantial healthcare burden associated with AF, from strokes, bleeds and mortality over the next decades can be reduced if patients are managed with a holistic or integrated care approach based on the ABC pathway, equating to substantial healthcare cost reductions.<sup>41</sup>

### **Recommendation**

1. The Atrial fibrillation Better Care (ABC) pathway is recommended for the elderly population with AF.
2. Validated smart technology facilitated ABC pathway management, e.g. mAFA, is a cost-effective tool for the elderly AF population to reduce all-cause death, thromboembolism, and other clinical adverse events.

### **Risk assessment for the elderly patients**

The risk assessment for the elderly AF patients includes assessment of stroke risk, bleeding risk, and comprehensive geriatric assessment.

In our 2016 consensus document, we recommended the use of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score for stroke risk assessment for the elderly AF patients. In this 2024 update, we still recommend the use of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score as the most validated stroke risk



prediction scheme. The assessment of dynamic changes on stroke risk with re-evaluation of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score is recommended at least annually.<sup>42</sup> For the patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of low or intermediate risk at baseline, more frequent stroke risk evaluation,<sup>43</sup> e.g. every 4 months, is proposed.

The HAS-BLED score is recommended for the bleeding risk for the elderly patients with AF, with the advantage of simplicity, as well as a better predictive ability of hemorrhage and major bleeding (including intracranial bleeding).<sup>44</sup> The HAS-BLED score has been extensively validated in patients without anticoagulant, with oral anticoagulants, and NOAC.<sup>45-47</sup> With the initiation of anticoagulant, regular bleeding risk assessment with HAS-BLED score helps to mitigate modifiable bleeding risk factors, schedule high bleeding risk patients for early review and follow-up, and to improve oral anticoagulant uptake.<sup>48</sup>

The comprehensive geriatric assessment, including disability assessment (ADL scale),<sup>49</sup> frailty screening (FRAIL scale),<sup>50</sup> gait abnormality and fall risk assessment (TUGT scale),<sup>51</sup> fall scale screening, cognitive function assessment (Mini-Cog scale),<sup>52</sup> renal function [eGFR, CKD-EPI (Scr/Cys-c) formula], nutritional status, diet and weight, depressive status, comorbidities, and combined with multiple drugs, is recommended.

### **Recommendation**

1. The CHA<sub>2</sub>DS<sub>2</sub>-VASc score for stroke risk and HAS-BLED for bleeding risk are recommended for risk stratification in elderly AF patients.
2. The Comprehensive Geriatric Assessment should be performed to improve the adherence to the anticoagulant.

### **Rhythm/rate control with drugs**

The purpose of rhythm or rate control for the elderly patients with AF is to relieve the symptoms, reduce the frequency and duration of AF episodes, maintain cardiac function, prevent from the tachycardia cardiomyopathy, improve quality of life, and reduce the hospitalization.

The antiarrhythmic drugs for cardioversion include Class I c (propafenone) and Class III (amiodarone, ibutilide). Amiodarone can effectively convert AF to sinus rhythm, with the successful rate of 35%-90% during 8-24 hours. However, the concurrent use of amiodarone and NOACs might increase the risk of major bleeding among older patients.<sup>53, 54</sup> Ibutilide is an effective drug for conversion of recent-onset AF and flutter in elderly patients, with the overall rate of successful conversion was 59%.<sup>55</sup> There is up to a 4% risk of torsade de pointes and a 4.9% risk of monomorphic ventricular tachycardia, especially for the elderly patients, female, low weight, or with HF. In addition, propafenone can increase the blood concentration of warfarin and digoxin.

Hence, close monitoring is warranted during and after drug infusion for the elderly patients receiving cardioversion.

Intravenous sotalol is less effective than ibutilide in AF, with the underlyingly increased risk of mortality for maintaining sinus rhythm.<sup>56</sup> Dronedaron was less sufficient than amiodarone in converting AF. Therefore, we don't recommend the use of sotalol and dronedarone for the cardioversion in elderly patients with AF.

### **Recommendation**

1. A patient-centered symptom-directed rhythm or rate control approach is recommended for the elderly population with AF.

### **Rhythm/rate control with invasive procedures**

#### *Cardioversion:*

Early rhythm-control therapy was associated with a lower risk of adverse cardiovascular outcomes than usual care among elderly patients with early AF and cardiovascular conditions.<sup>57, 58</sup> For elderly patients with AF diagnosed  $\leq 12$  months, or the uncontrolled ventricular rate, or severe symptom with controlled ventricular rate, or patient's willing to restore sinus rhythm, cardioversion is recommended. However, in patients with left atrial thrombosis, or sick sinus syndrome without pacemaker, atrioventricular block, or QT interval correction prolongation ( $>500$  ms) are contraindications to cardioversion.

Electrocardioversion can be used as an effective means of emergency management for patients with AF with obvious hemodynamic disturbance, myocardial ischemia, or preexcitation syndrome with rapid ventricular rate, and can also be used for selective cardioversion treatment for patients with persistent and long-duration persistent AF. Electrocardioversion may lead to complications in the elderly population, including sedation-related complications, cardiac arrest, skin burn, etc., and there is a risk of inducing pulmonary edema in patients with left ventricular dysfunction or HF.

Oral anticoagulant during peri-procedure significantly reduces the risk of thromboembolism. In patients with AF of  $\geq 48$ h or unknown duration, warfarin (INR 2.0 -3.0, or 1.6 to 2.5 for those aged  $\geq 75$  years) or NOAC therapy should be used for at least 3 weeks prior to cardioversion. For those with AF  $< 48$  h, cardioversion may be performed with heparin, low molecular weight heparin, or NOAC during the peri-procedure. Anticoagulation therapy is required for 4 weeks after cardioversion, regardless of the duration of pre-cardioversion. After 4 weeks, long-term anticoagulation therapy can be determined based on the stroke risk.

Those who need early cardioversion should be performed after transesophageal ultrasound to rule out intra-atrial thrombus. In patients with hemodynamic instability, cardioversion should be initiated immediately while anticoagulant therapy is initiated

with heparin or low molecular weight heparin.

#### *Pacemakers:*

The elderly AF patient with bradyarrhythmias can be a candidate for pacemaker therapy. For elderly patients with AF and HF, cardiac resynchronization therapy improves left ventricle ejection fraction, quality of life, and all-cause mortality.

#### *Catheter ablation*

Left atrial enlargement and fibrosis increased with aging. AF ablation-related complications showed the increased trend over aging, such as cardiovascular adverse events, death, AF recurrence, and postoperative atrial flutter, etc. Therefore, catheter ablation in elderly patients needs to fully weight the benefits and risks. Catheter ablation should not be proposed for the patients with contraindications to anticoagulant therapy.

Appropriate measures should be taken to reduce AF recurrence after the ablation for the elderly patients (Figure 5). The decision on long-term anticoagulation after ablation depends on the individual's risk profile.

#### **Recommendation**

1. The risk and benefits should be weighted for the elderly patients receiving invasive rhythm or rate control.
2. Long-term anticoagulation should be considered for patients at high-risk stroke.

#### **Antithrombotic treatment**

The elderly patients with AF often clinically complex, with the cardiac, venous, and arterial thromboembolic risks. The ChiOTEAF demonstrated that elderly patients with AF were often at risk of falls, with associated atherosclerosis, chronic kidney disease/liver disease, or malignancy, increasing the risks of thrombosis and bleeding (Figure 6).<sup>59</sup>

Nonetheless, oral anticoagulation therapy for high-risk elderly AF patients, even with fall risk, HF, chronic kidney disease/liver disease, and malignant tumor, is associated with a reduction in the composite end points of acute myocardial infarction, ischemic stroke, cerebral hemorrhage, and all-cause death (Figure 6).<sup>60</sup> In elderly patients aged over 85 years of age, optimized oral anticoagulant therapy decreased the composite end point of thrombosis and all-cause death by 54% without increasing the risk of major bleeding events (OR 0.46; 95%CI 0.32~0.66; P<0.001).<sup>34</sup>

However, less than half of elderly Chinese patients with AF at high-risk for stroke receive oral anticoagulation.<sup>59</sup> In the ChiOTEAF registry, for example, only 26.4% received oral anticoagulation therapy in Chinese elderly patients aged over 85 years

old.<sup>60</sup> Chronic kidney disease, liver disease, dementia, and prior bleeding were independent risk factors for the poor adherence to oral anticoagulant therapy. Such poor adherence to the anticoagulant therapy increased the risk of thromboembolism and all-cause death by 2- and 4- fold, respectively (Figure 6).<sup>61</sup>

A meta-analysis of 22 studies confirmed that NOACs, compared to warfarin, reduced the risk of stroke and systemic embolism, intracranial bleeding, haemorrhagic stroke and fatal bleeding in the elderly patients aged over 75 years.<sup>62</sup> Even for the extremely-high-risk, very elderly (> 90 years) patients, NOACs were associated with a lower risk of composite endpoint of ischemic stroke, intracranial haemorrhage, major bleeding, or mortality compared to warfarin or non-oral anticoagulants.<sup>63</sup> However, the bleeding risk associated with anticoagulant still needs to be monitored and proactive management, especially gastrointestinal bleeding among elderly patients.<sup>62</sup>

Moreover, inadequate off label underdosing of oral anticoagulants is common in elderly patients with AF. In China, for example, one in five elderly aged over 75 years old received inadequate dosage of oral anticoagulant (warfarin or NOAC), with a higher risk of the composite outcome and thromboembolic events compared with standard dose NOAC.<sup>61</sup>

In AF patients over 80 years in high-risk elderly AF patients at increased bleeding risk, use of very low dosage (edoxaban 15 mg o.d., dabigatran 110 or 150 o.d., apixaban 2.5 mg o.d., or rivaroxaban 10 mg) was associated with a greater risk of arterial (major adverse limb events requiring lower limb revascularization or amputation, hazard ratio, HR: 1.54, 95% confidential interval, CI: 1.09-2.18; P = 0.014) and venous thrombosis (HR: 3.75, 95% CI: 1.56-8.97; P = 0.003), death (HR: 1.21, 95% CI: 1.15-1.29; P <0.001), when compared with that of regular-dosage NOAC.<sup>64</sup>

Adherence to the ABC pathway was associated with a lower composite outcome of all-cause death and any thromboembolism event (stroke, TIA, peripheral embolism) even amongst the elderly patients with AF.<sup>65</sup>

### **Recommendation**

1. Elderly patients, especially high-risk patients, would benefit from the optimal label or guideline recommended oral anticoagulant after balancing bleeding risk, with a preference for NOACs. More intensive follow-up, e.g. risk factor monitoring, the intensity and safety of anticoagulant, liver/renal function, etc should be taken to improve poor adherence to oral anticoagulant. Cognitive function should be assessed, and patient's education encouraged to avoid missing doses or noncompliance.

2. NOACs are preferred for the elderly patients with AF than warfarin, except those with mechanical valve or severe mitral stenosis. If on warfarin, INR should remain between 2.0-3.0, or 1.6-2.5 for those aged over 75 years old. Good quality anticoagulation control (TTR  $\geq$  65%) should be aimed for.
3. Minor bleeding associated with NOAC can be managed conservatively and if necessary, the NOAC could be discontinued for 12-24h. Moderate bleeding requires blood products, etc., depending on the type of oral anticoagulant. The specific antagonists (vitamin K, idarucizumab, or andexanet $\alpha$ , etc.) can be used for the life-threatening bleeding. Whether or when to resume anticoagulant therapy after bleeding events should be weighted, balancing the risk of thrombosis and bleeding.

### **Elderly patients with CAD**

PIONEER-AF,<sup>66</sup> REDUAL,<sup>67</sup> AUGUSTUS,<sup>68</sup> ENTRUST<sup>69</sup> trials confirmed that the double or triple antithrombotic approach with NOAC were at low risk of major bleeding, especially cerebral haemorrhage, compared with warfarin. Compared to triple antithrombotic approach (NOAC plus dual antiplatelet), there was a similar stroke risk for patients receiving NOAC with single antiplatelet. Nonetheless, myocardial infarction and stenosis thrombus may be slightly increased in patients with NOAC plus single antiplatelet.<sup>70</sup> The duration of dual or triple antithrombotic approach should be based on the risk of arterial thrombosis, cardiogenic thrombosis, and bleeding.

### **Recommendation**

1. For patients undergoing elective percutaneous coronary intervention (PCI), it is recommended to stop aspirin within 1 week, continue to "double therapy" (clopidogrel + oral anticoagulant), and with single oral anticoagulant (ideally a NOAC) after one year. For the patients at high risk of bleeding, anticoagulant monotherapy can be considered after 6 months.
2. For patients with acute coronary syndrome (ACS) and PCI, triple therapy should be used for 1 month, followed by double therapy, and single anticoagulant therapy 1 year later. Standard-dose single anticoagulant is recommended for stable coronary heart disease or chronic coronary syndrome.

### **Elderly patients with comorbidities**

The prevalence of multimorbidity was reported as 31.8% among the Chinese population aged over 60 years, increasing with the aging.<sup>71</sup> Multimorbidity leads to increased risks of functional decline, polypharmacy, disability and hospitalization. Cardiovascular disease (hypertension, CAD, HF, etc), non-cardiovascular disease

(diabetes, COPD, OSA, chronic kidney/liver disease, cancer, etc.) and mental disorders are common in the elderly population, which raising the risk of AF onset and AF-related complications.<sup>72</sup>

Lifestyle factors and comorbidities cannot be considered in isolation in relation to the progression of AF.<sup>73</sup> Thus, lifestyle modification may not just decrease AF risk and common comorbidities of AF in the 'naïve-AF' general population, but can also effectively reduce recurrent AF in patients receiving AF ablation and its related complications. Such lifestyle and risk factor modification interventions are related to the prevention and treatment of AF and AF-related complications.<sup>19</sup>

Polypharmacy, with the use of more than five drugs at the same time, is common in elderly patients with AF, especially those over 75 years (Figure 7). The presence of polypharmacy in AF patients is associated with adverse clinical outcomes.<sup>74</sup> The risk of major bleeding and non-major bleeding also increased significantly.<sup>75</sup>

Smart tools might help the elderly patients with AF for the cardiovascular risk and comorbidities management.<sup>33</sup> A web-based integrated management program improved medication adherence and quality of Life, and reduced readmission in AF patients with mean age of 73 years.<sup>76</sup> In the mAFA II trial, the hazard risk for the acute coronary syndrome, heart failure, and uncontrolled blood pressure, as the C criterion of the ABC pathway, reduced 71%, compared to the usual care group ( HR, 0.29; 95% CI, 0.19-0.45; P <0 .001).<sup>35</sup>

### **Recommendation**

The elderly population is commonly associated with multimorbidity and polypharmacy, leading to the risk of AF and AF-related complications. Lifestyle modification and appropriate measures should be taken to reduce AF progression and inappropriate use of the drugs. Smart tools might be used to facilitate risk factor and comorbidities management for the elderly patient.

### **Elderly patients with stroke**

The annual prevalence of ischaemic stroke is 1-2% among AF patients on NOAC.<sup>77</sup> Older patients with acute ischemic stroke have a worst prognosis, with higher bleeding risk and mortality than younger patients, but can still benefit from the thrombolysis.

AF patients with ischemic stroke or transient ischemic attack have a high risk of recurrent stroke. Infarct size, NIHSS score, CHA<sub>2</sub>DS<sub>2</sub>-VASc and HAS-BLED score should be taken into the account to decide the anticoagulant approach. For patients with NIHSS score <15 and low bleeding risk, oral anticoagulant can be initiated 2-14 days. For patients with NIHSS score ≥15 and high risk of bleeding, oral anticoagulant

should be restarted after 14 days. During the initial period <14 days, aspirin can be used before initiation of oral anticoagulant therapy.<sup>78</sup>

In addition to cardiogenic factors, ischaemic stroke in patients with AF may be caused by large atherosclerosis diseases (such as symptomatic intracranial vascular stenosis). If a patient has recently undergone carotid stent implantation and the risk of bleeding is low, oral anticoagulant therapy in conjunction with antiplatelet drugs may be considered.

AF patients receiving carotid endarterectomy can receive only aspirin before and for a few days after surgery, and discontinue aspirin after resuming NOAC therapy. Patients with AF who have asymptomatic atherosclerosis and narrow internal carotid and/or intracranial arteries should be treated with statins and oral anticoagulant without additional antiplatelet therapy.

The intracranial hemorrhage (ICH) rate is about 0.23-0.55%/year in patients with NOAC. Based on the available evidence, the restart of NOAC can be cautiously considered 4 weeks after ICH after a multidisciplinary review, including cardiologists, stroke neurologists, etc. For the elderly patients at high risk, the potential ICH risk factors, such as cerebral amyloidosis, cerebral microbleeds, should be assessed with Magnetic Resonance Imaging (e.g. susceptibility weighted imaging), prior to deciding on oral anticoagulation.

### **Periprocedural and perioperative management**

About 10% of patients with AF undergo invasive procedure or surgery each year. The common operation received by the elderly patients with AF were cardiovascular, gastrointestinal, and mouth. Patients aged over 75 years were more likely to receive orthopedic and ophthalmic operations.<sup>79</sup> The comorbidities, liver/ renal dysfunction of the elderly patients was associated with the time of stopping and restarting anticoagulants during peri-operation. The perioperative anticoagulation strategy in elderly patients with AF should consider the patient's factors, the type of the operation (interventions with minor bleeding risk, low bleeding risk, or high bleeding risk)<sup>80</sup> and the anticoagulant drugs (Figure 8).

Warfarin is usually stopped at least 5 days prior to the procedures with low/high bleeding risk with the obvious clinical impact. The elderly with comorbidities, patients with very low-dose warfarin requirements, and those with a higher target INR range, a longer period of warfarin interruption may be needed.

NOACs can be stopped close to the procedure usually without bridging. There was no significant difference of continuing NOAC on the thromboembolic or bleeding rates, compared to a bridging approach.<sup>81 82</sup> Also, if NOACs are interrupted for >72 h the

likelihood of any residual NOAC level appears very low.<sup>83, 84</sup>

The continuation, discontinuation, bridging, and resumption of anticoagulation, with regarding to the time points in the perioperative period is illustrated in Figures 9, 10.

### **Recommendation**

1. Warfarin is stopped at least 5 days prior to the intervention with low/high bleeding risk, depending on the INR range, and restart with the bridging of low weight molecular heparin (Figure 9).
2. NOACs should be stopped at least 24 h and up to 96 h depending on the bleeding risk and the urgency of surgery/operation (Figure 10).

### **Elderly patients with cancer**

Both AF and tumors increase the risk of thrombosis. Gastrointestinal or hematological tumors also raise the risk of bleeding. Warfarin, low molecular weight heparin or NOAC can be considered when CHA<sub>2</sub>DS<sub>2</sub>-VASc score is  $\geq 2$  and platelet count is  $>50 \times 10^9/L$ . Careful and regular monitoring is advised.

### **Frailty**

Both AF and frailty increase with aging. The reported rate of the frailty ranges from 4.4% to 75.4%.<sup>85</sup> AF contribute to the risk of frailty, while frailty results in poor adherence to anticoagulant.

### **Recommendation**

NOACs are recommended for the elderly patients with AF and frailty.

The management of chronic conditions in the elderly population with AF is summarized in Figure 11.

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## **Acknowledgement**

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## **Competing financial interests**

GYHL: Consultant for Bayer/Janssen, Astellas, Merck, Sanofi, BMS/Pfizer, Biotronik, Medtronic, Portola, Boehringer Ingelheim, Microlife and Daiichi-Sankyo. Speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Microlife, Roche and Daiichi-Sankyo

Other authors: None declared.



**Figure 1 Risk assessment of the elderly patients with AF**

\* AF = atrial fibrillation; BP = blood pressure; CAD = coronary artery disease; CHA<sub>2</sub>DS<sub>2</sub>-VASc = Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65-74 years, Sex category (female); EF = ejection fraction; HCM = hypertrophic cardiomyopathy; HF = heart failure; LV = left ventricular; LVEF = left ventricular ejection fraction; PAD = peripheral artery disease; TIA = transient ischaemic attack. ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; SBP = systolic blood pressure; INR = international normalized ratio; NSAID = Non-steroidal anti-inflammatory drug; TTR = time in therapeutic range; VKA = vitamin K antagonist. CKD-EP= Chronic Kidney Disease Epidemiology Collaboration.

For the patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of low or intermediate risk at baseline, more frequent stroke risk evaluation, e.g. every 4 months, is proposed.

**Figure 2 AF screening and monitoring for the elderly population**

\* AF = atrial fibrillation. OSA = obstructive sleep apnea.

**Figure 3 An integrated care ABC pathway for the elderly population with Atrial Fibrillation**

\* F = female; m = male; NOAC = non-vitamin K antagonist oral anticoagulant; INR = international normalized ratio; OAC =oral anticoagulant; OSA = obstructive sleep apnea; COPD = chronic obstructive pulmonary disease.



**Figure 4 Mobile health technology facilitated integrated care for the elderly patients with AF**

**Figure 5 Appropriate measures to reduce AF recurrence for the elderly patients receiving ablation**

\* Clinical recurrence of AF □ late recurrence or very late recurrence

**Figure 6 Risk reductions in elderly patients with AF on OACs in special clinical setting (very elderly, multimorbidities, with CAD) and the increased risk of those without OACs or with underdosing of OACs**

\* TE and all-cause death reduced among the very elderly patients and with multimorbidities on OACs. The composite of all-cause death, TE, major bleeding and acute coronary syndrome was reduced in the elderly patients with OACs. \*\* □ For elderly patients with AF without OACs, the thromboembolic risk increased by 2.2 fold in those with CHA2DS2-VASc  $\geq 1$  in male, or  $\geq 2$  in female and by 2.5 fold in those with the underdoing of OACs. TE = thromboembolism; CAD = coronary artery disease. OACs = oral anticoagulants. Cited from Optimal Thromboprophylaxis in Elderly Chinese Patients with Atrial Fibrillation (ChiOTEAF) registry. Eur Heart J Qual Care Clin Outcomes. 2023 J Arrhythm. 2022; Int J Stroke. 2022; Int J Stroke. 2021.

**Figure 7 Multimorbidity, polypharmacy and high-risk thromboembolism and bleeding in the elderly population with AF**

\*F = female; M = male. Cited from Optimal Thromboprophylaxis in Elderly Chinese Patients with Atrial Fibrillation (ChiOTEAF) registry. J Am Heart Assoc. 2022; J Arrhythm. 2022.

**Figure 8 Periprocedural and perioperative risk assessment of the elderly population with AF**

\* Intervention with minor bleeding: e.g. Dental extractions (1–3 teeth), paradental surgery, implant positioning, subgingival scaling/cleaning Cataract or glaucoma intervention Endoscopy without biopsy or resection Superficial surgery (e.g. abscess incision; small dermatologic excisions, skin biopsy) Pacemaker or ICD implantation (except complex procedures) Electrophysiological study or catheter ablation (except complex procedures) Routine elective coronary/peripheral artery intervention (except complex procedures) Intramuscular injection (e.g. vaccination)

Intervention with low-risk bleeding: e.g. Complex dental procedures Endoscopy with simple biopsy Small orthopaedic surgery (foot, hand, arthroscopy.

Intervention with high-risk interventions: e.g. Cardiac surgery Peripheral arterial revascularization surgery (e.g. aortic aneurysm repair, vascular bypass) Complex invasive cardiological interventions, including lead extraction, (epicardial) VT ablation, chronic total occlusion PCI etc. Neurosurgery Spinal or epidural anaesthesia; lumbar diagnostic puncture Complex endoscopy (e.g. multiple/large polypectomy, ERCP with sphincterotomy etc.) Abdominal surgery (incl. liver

biopsy) Thoracic surgery Major urologic surgery/biopsy (incl. kidney) Extracorporeal shockwave lithotripsy Major orthopaedic surgery. Cited from 2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation. Europace. 2021.

**Figure 9 Continuation, discontinuation, bridging, or resumption of anticoagulation with warfarin, with regarding to the time points in the perioperative period**

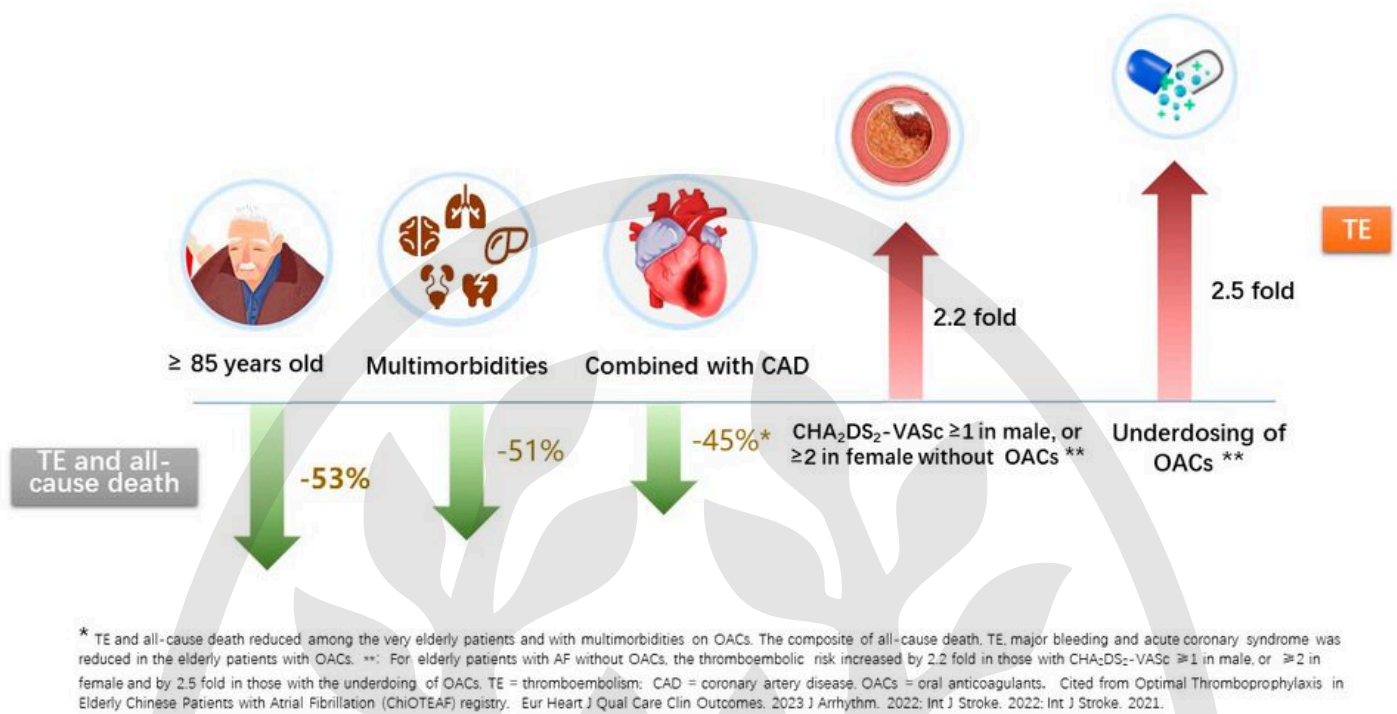
\* LMWH = Low molecular weight heparin. INR = international normalized ratio. OAC = oral anticoagulant.

**Figure 10 Continuation, discontinuation, bridging, or resumption of anticoagulation with NOACs, with regarding to the time points in the perioperative period**

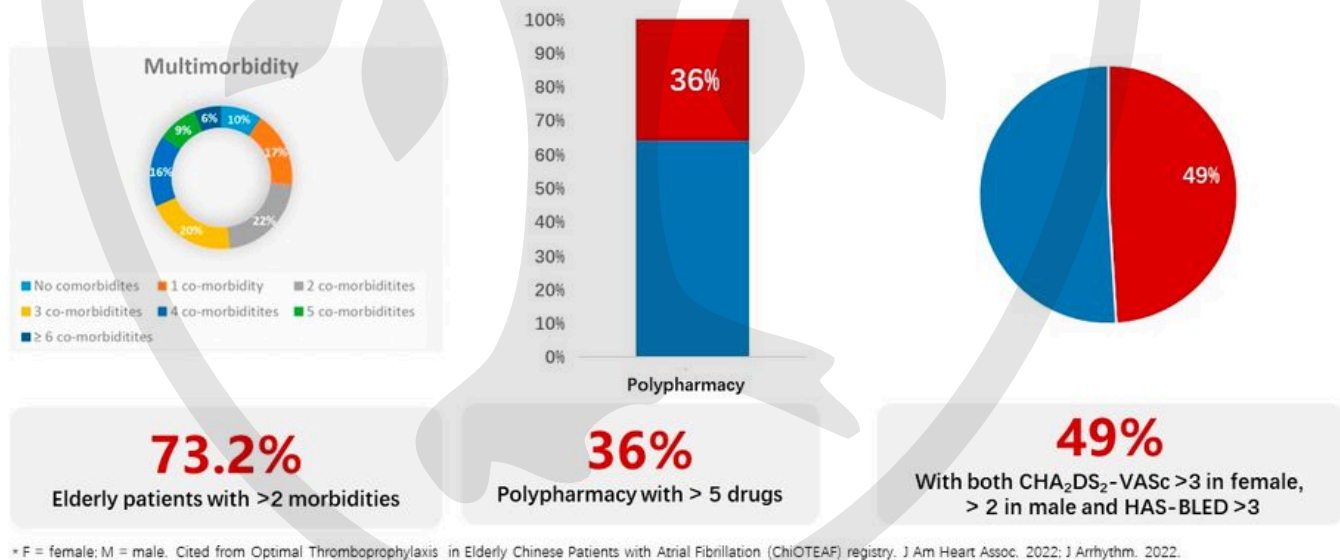
\* NOAC = non-vitamin k antagonist oral anticoagulant.

**Figure 11 Management of chronic conditions in the elderly population with AF**

\* AF = atrial fibrillation. ARBs = angiotensin receptor blockers ; ACE inhibitors = angiotensin-converting enzyme inhibitors. NOACs = non-vitamin K oral antagonist anticoagulants.



**Figure 6 Risk reductions in elderly patients with AF on OACs in special clinical setting (very elderly, multimorbidities, with CAD) and the increased risk of those without OACs or with underdosing of OACs**



**Figure 7 Multimorbidity, polypharmacy and high-risk thromboembolism and bleeding in the elderly population with AF**



Stroke risk



Bleeding risk

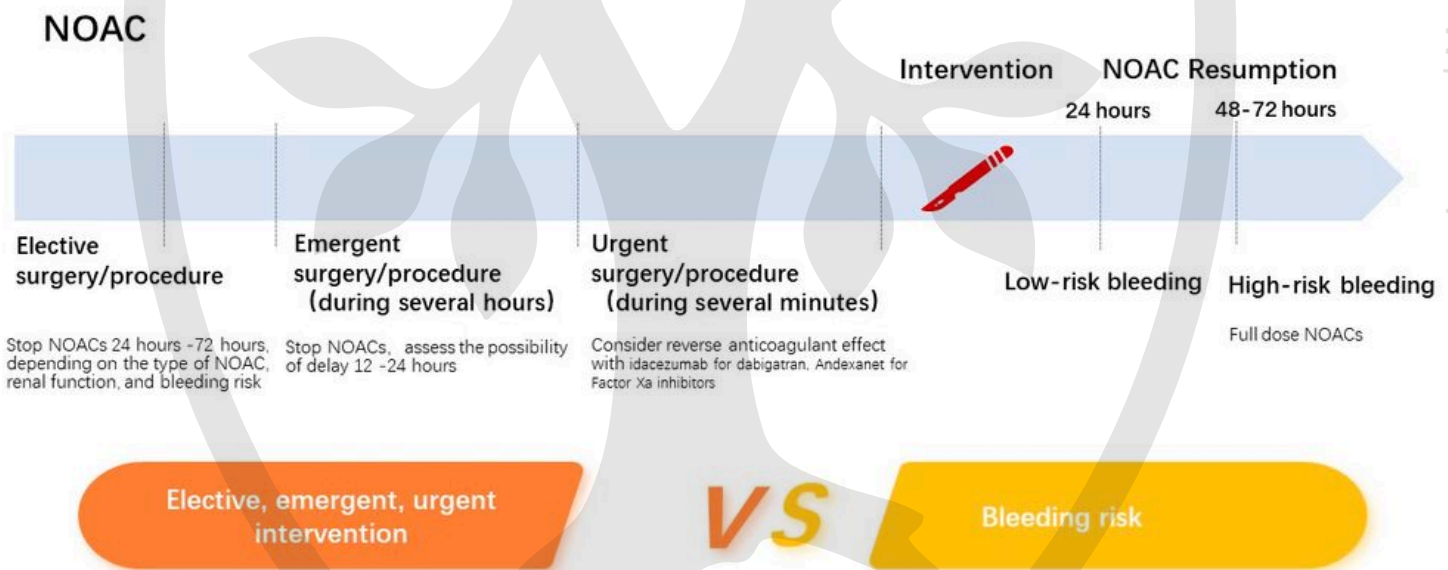


Geriatric assessment

| CHA <sub>2</sub> DS <sub>2</sub> -VASc score |                          |  | HAS-BLED score |            |  | Geriatric General Evaluation   |                  |   |                          |
|--|--------------------------|--|----------------|------------|--|--|------------------|---|--------------------------|
| Risk factors                                 | Definition               | Points   | Risk factors   | Definition | Points                                 | Items  | Scores           |   |                          |
| C  | Congestive heart failure | Clinical HF, or objective evidence of moderate to severe LV dysfunction, or HCM                      | 1              | H          | Uncontrolled hypertension              | SBP >160 mmHg  | 1                | Disability assessment   | ADL scale                |
| H  | Hypertension             | or on antihypertensive therapy   | 1              | A          | Abnormal and/or renal hepatic function | Dialysis, transplant, serum creatinine >200 µmol/L, cirrhosis, bilirubin > × 2 upper limit of normal, AST/ALT/ALP >3 × upper limit of normal | 1 point for each | Frailty screening   | FRAIL score              |
| A  | Age                      | Age 75 years or old  | 2              | S          | Stroke                                 | Previous ischaemic or hemorrhagic stroke   | 1                | Gait abnormality and fall risk                                    | TUGT scale               |
| D  | Diabetes mellitus        | Treatment with oral hypoglycaemic drugs and/or insulin or fasting blood glucose >125 mg/dL (7mmol/l) | 1              | B          | Bleeding history or predisposition     | Previous major haemorrhage or anaemia or severe thrombocytopenia   | 1                | Cognitive function assessment                                     | Mini-Cog scale           |
| S  | Stroke                   | Previous stroke, TIA, or thromboembolism   | 2              | L          | Labile INR                             | TTR <60% in patient receiving VKA  | 1                | Renal function  | eGFR, CKD-EP (Scr/Cys-c) |
| V  | Vascular disease         | Angiographically significant CAD, previous myocardial infarction, PAD, or aortic plaque              | 1              | E          | Elderly                                | Aged >65 years or extreme frailty  | 1                | Nutritional status, diet and weight,                              | -                        |
| A  | Age                      | Age 65 - 74 years  | 1              | D          | Drugs or excessive alcohol drinking    | Concomitant use of antiplatelet or NSAID; and/or excessive alcohol per week  | 1 point for each | Depressive status, comorbidities, and combined with multiple drug | -                        |
| Sc   | Sex                      | Female   | 1              |            |  |  |                  |   |                          |

\* AF = atrial fibrillation; BP = blood pressure; CAD = coronary artery disease; CHA<sub>2</sub>DS<sub>2</sub>-VASc = Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65-74 years, Sex category (female); EF = ejection fraction; HCM = hypertrophic cardiomyopathy; HF = heart failure; LV = left ventricular; LVEF = left ventricular ejection fraction; PAD = peripheral artery disease; TIA = transient ischaemic attack; ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; SBP = systolic blood pressure; INR = international normalized ratio; NSAID = Non-steroidal anti-inflammatory drug; TTR = time in therapeutic range; VKA = vitamin K antagonist; CKD-EP = Chronic Kidney Disease Epidemiology Collaboration. For the patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of low or intermediate risk at baseline, more frequent stroke risk evaluation, e.g. every 4 months, is proposed.

Figure 1 Risk assessment of the elderly patients with AF



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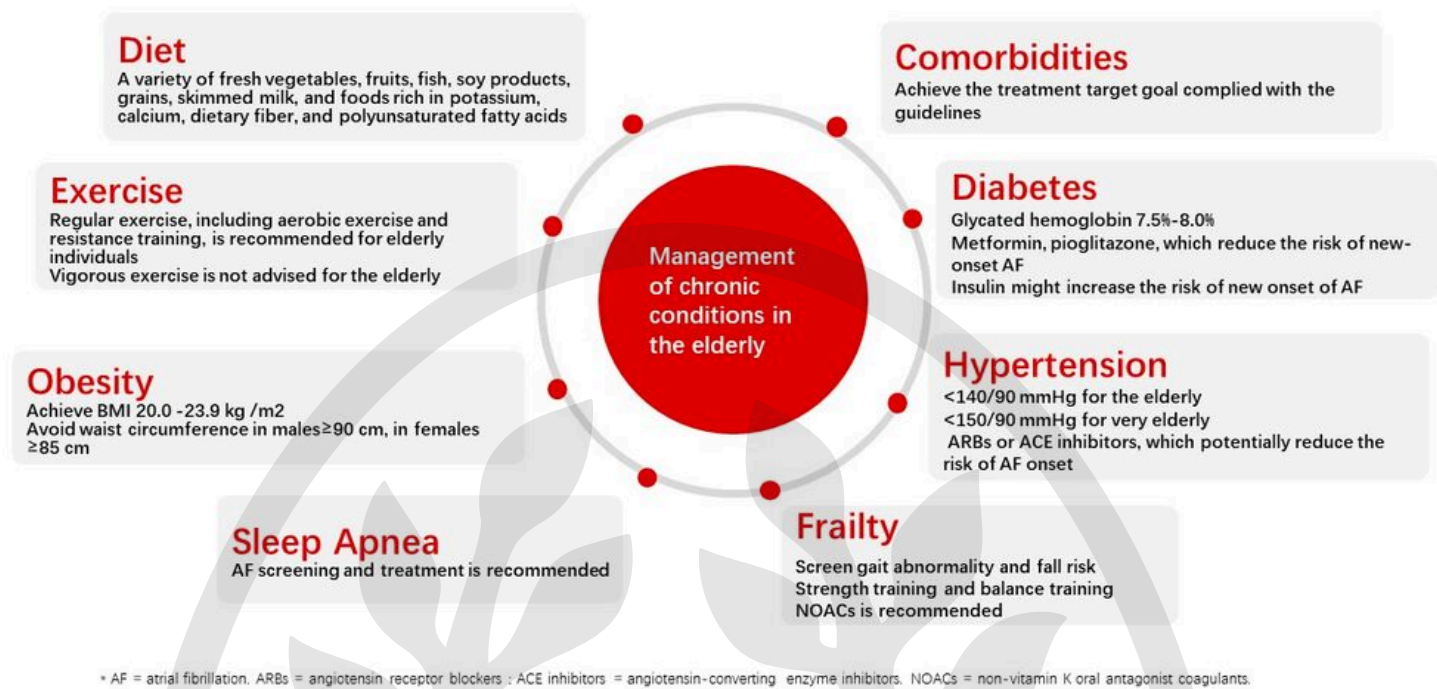


Figure 11 Management of chronic conditions in the elderly population with AF

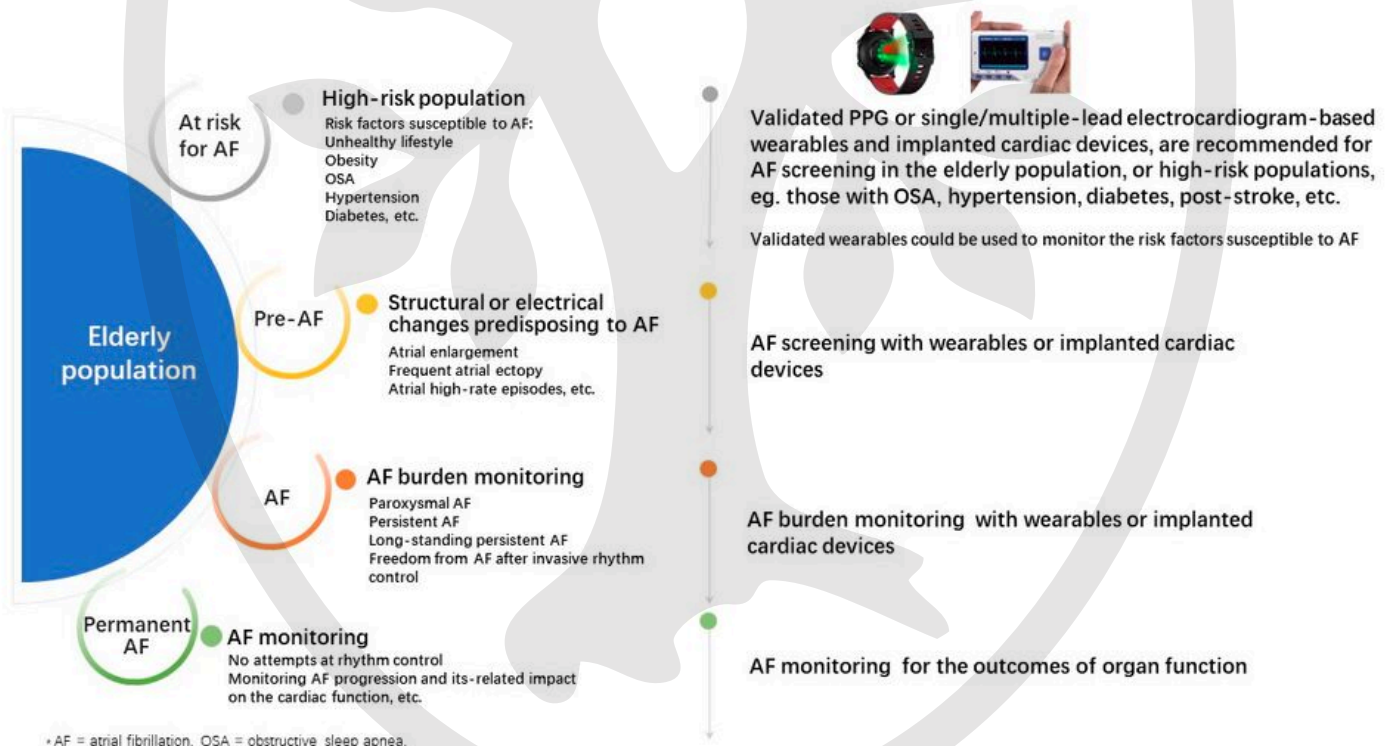


Figure 2 AF screening and monitoring for the elderly population

Integrated care: ABC Pathway for the elderly population with AF



\* F = female; m = male; NOAC = non-vitamin K antagonist oral anticoagulant; INR = international normalized ratio; OAC = oral anticoagulant; OSA = obstructive sleep apnea; COPD = chronic obstructive pulmonary disease.

Figure 3 An integrated care ABC pathway for the elderly population with Atrial Fibrillation

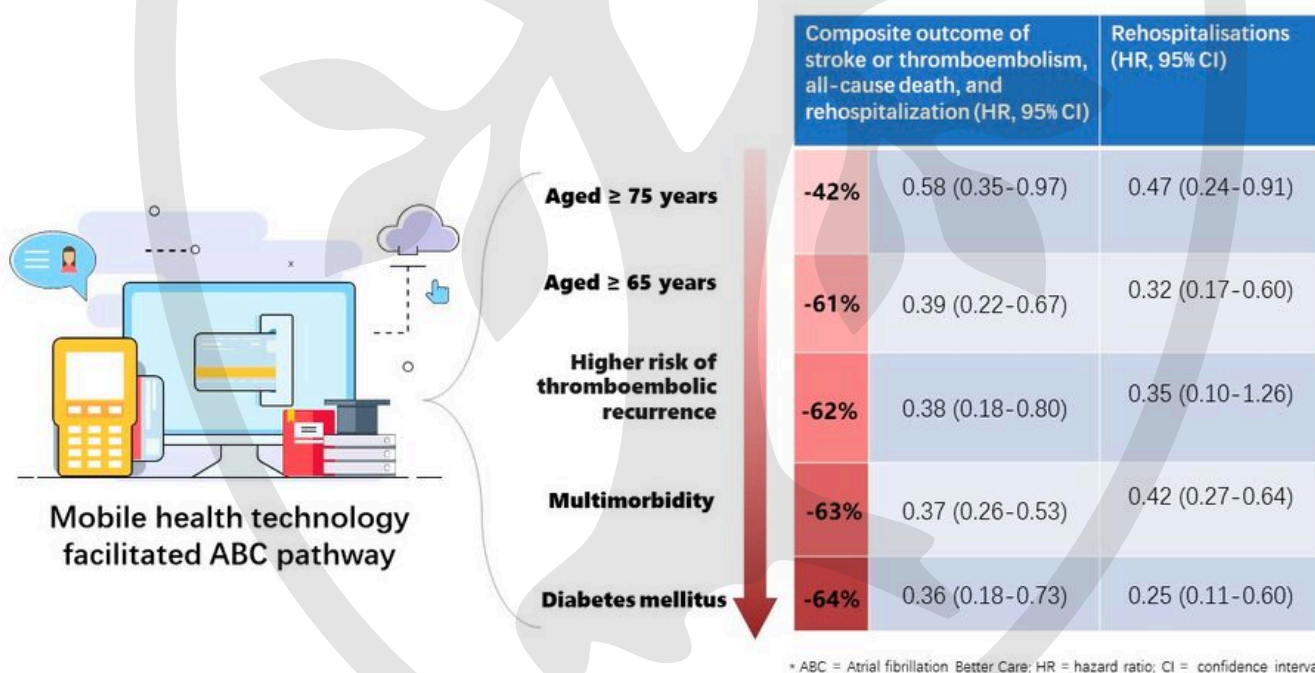


Figure 4 Mobile health technology facilitated integrated care for the elderly patients with AF

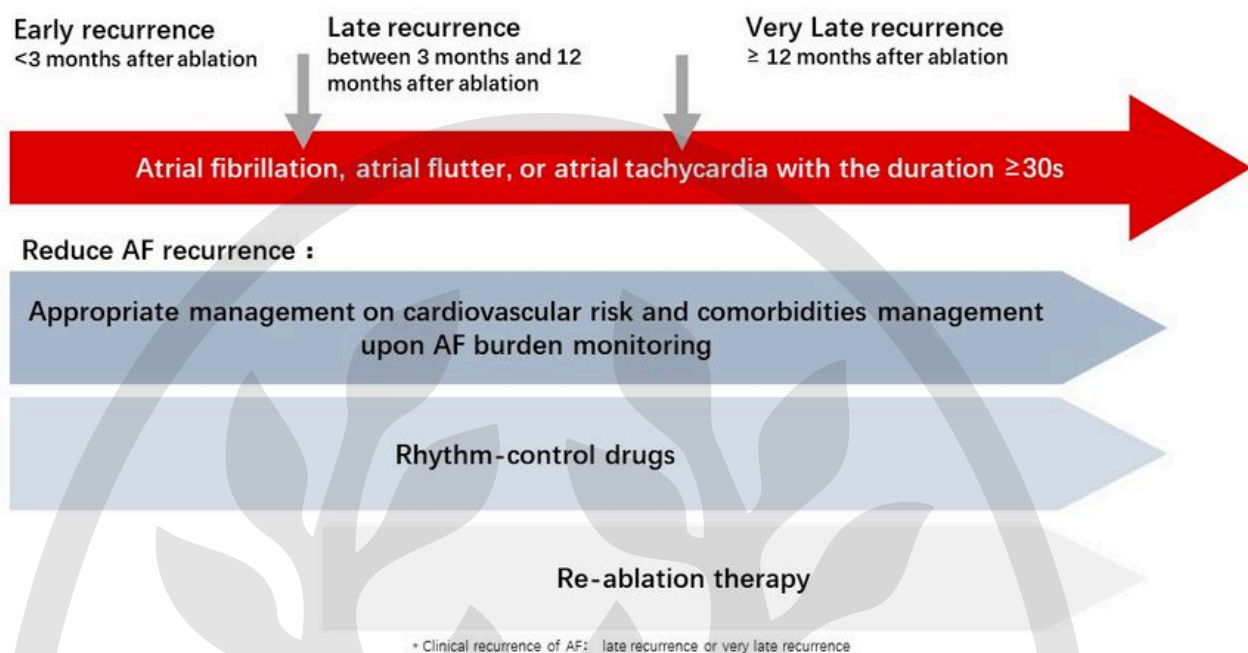
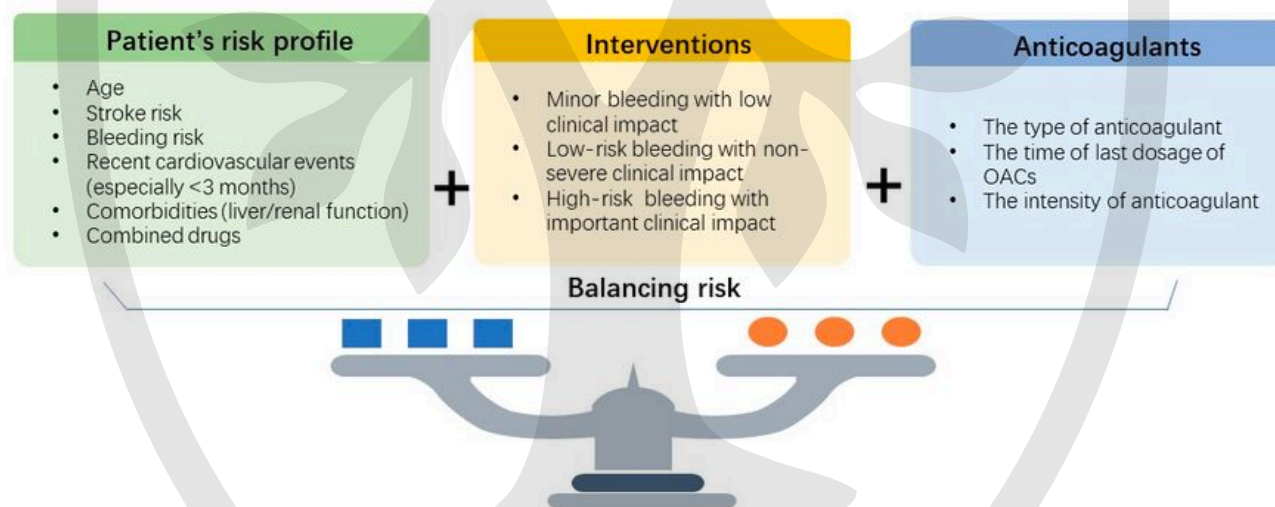


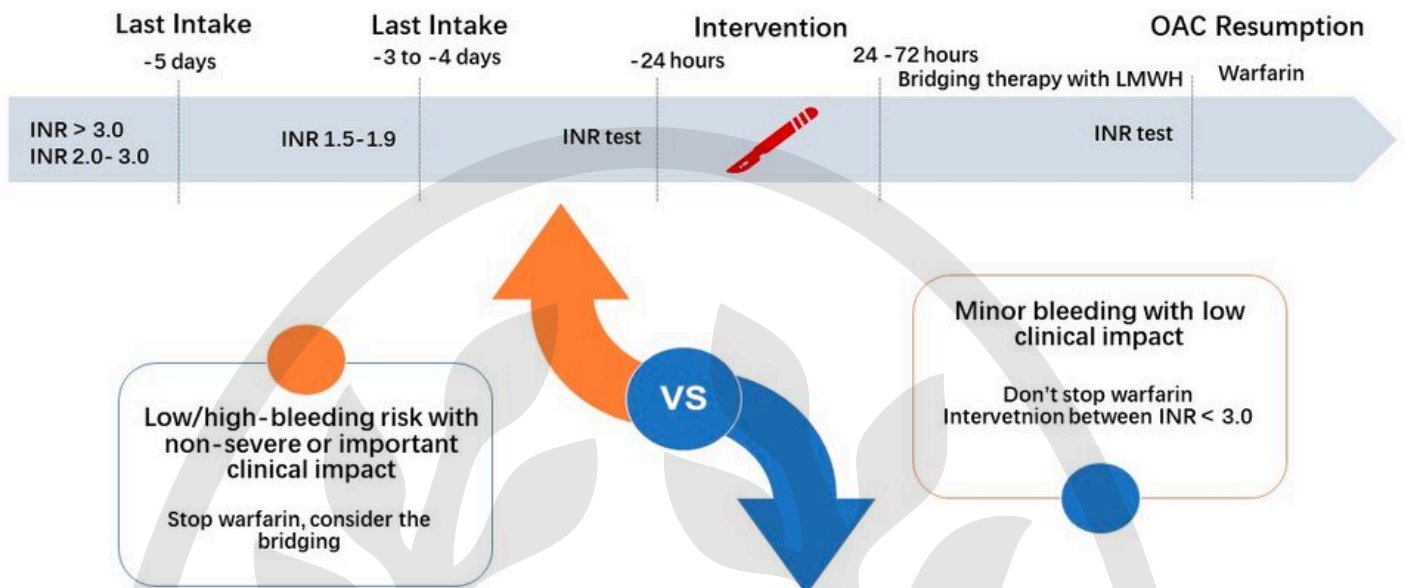
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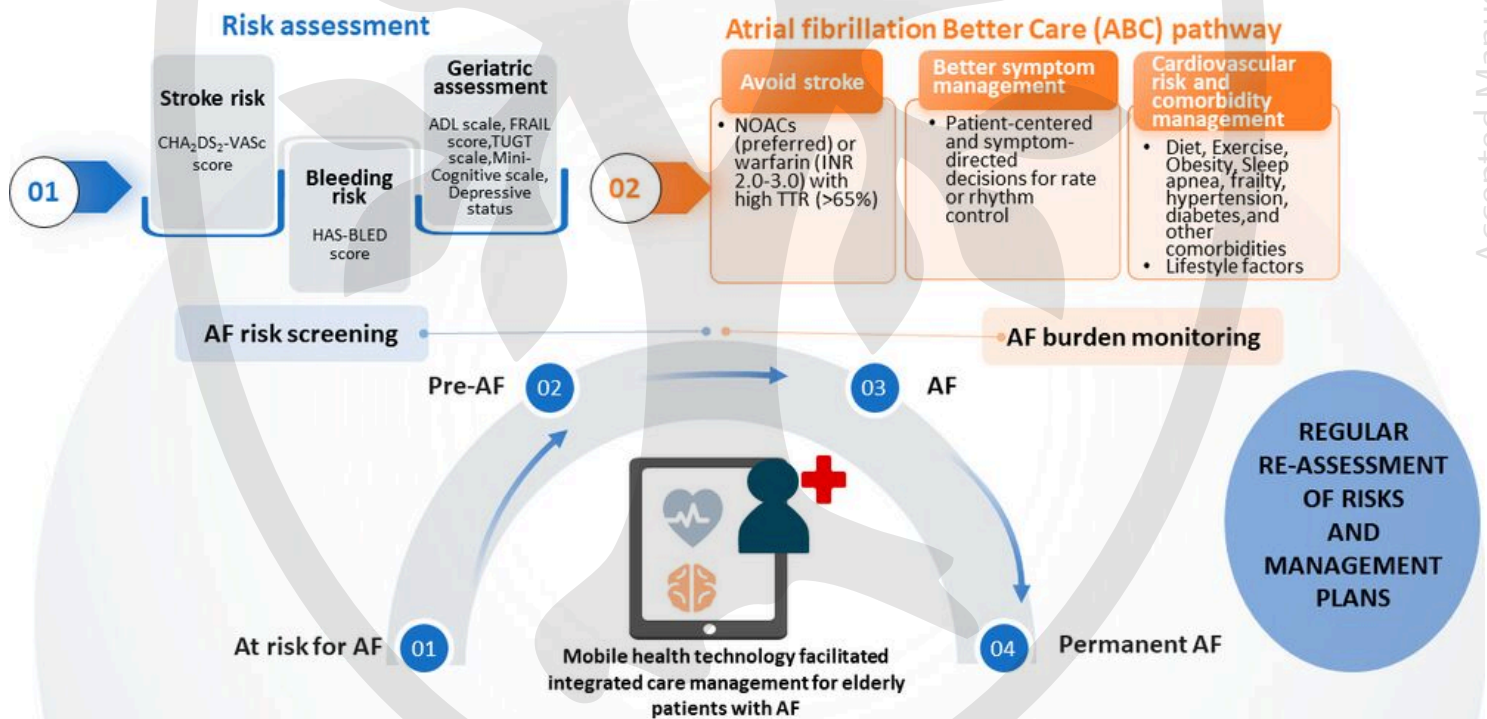
Figure 8 Periprocedural and perioperative risk assessment of the elderly population with AF

# Warfarin



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## Chinese expert consensus guidelines on the diagnosis and treatment of Atrial Fibrillation in the Elderly

\* AF = Atrial fibrillation; CHA2DS2-VASc = Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65-74 years, Sex category (female); ADL scale = Activities Daily Living; TUGT scale = Timed Up and Go Test.