



# AF in Hypertensive Patients: Prevention and Treatment

**Waleed Ammar MD.**

Associate professor of cardiology  
Cairo University

## Epidemiology and consequences of hypertension and atrial fibrillation

- Hypertension is the most common cardiovascular disorder and atrial fibrillation is the most common clinically significant arrhythmia.
- Both these conditions frequently coexist and their prevalence increases rapidly with aging.
- There are different risk factors predisposing to the development of atrial fibrillation, but due its high prevalence, hypertension is still the main risk factor for the development of atrial fibrillation.

## Epidemiology and consequences of hypertension and atrial fibrillation

- AF is associated with a five-fold increase in the risk of stroke, with approximately 25% of all patients presenting with a stroke shows AF.
- Other consequences of AF include increase in overall mortality, heart failure, hospitalization, reduced quality of life and impaired cognitive functions.
- The presence of AF per se increases the risk of stroke but its coexistence with HTN leads to an abrupt increase of cardiovascular complications
- Atrial fibrillation is still under-recognised and under-treated, as many patients remain asymptomatic.

## The Structural Effects of Hypertension and Development of Atrial Fibrillation

- Hypertension is present up to 70% of AF patients, making this the most common co-morbidity found in AF registries
- Long-standing hypertension may cause left atrial enlargement early, before any evidence of left ventricular hypertrophy (LVH) or atrial arrhythmia.
- The magnitude of atrial enlargement correlates with the degree of hypertension
- In the Framingham study, the risk of developing AF increased by 39% for each 5 mm increase in left atrial size, after adjustment for other risk factors

## PATHOPHYSIOLOGY

- Untreated or suboptimally treated hypertension leads to LV hypertrophy, which is one of the most important expressions of subclinical organ damage, and is an independent risk factor for cardiovascular events, including the development of atrial fibrillation.
- In the presence of LVH, left ventricular compliance is reduced, left ventricular stiffness and filling pressure increase, coronary flow reserve is decreased, wall stress is increased and there is activation of the sympathetic nervous system and of the renin–angiotensin–aldosterone system.

## PATHOPHYSIOLOGY

- In the atria, proliferation and differentiation of fibroblasts and enhanced connective tissue deposition and fibrosis are the hallmarks of this process.
- Structural remodelling results in electrical dissociation between muscle bundles and in local conduction heterogeneities facilitating the initiation and perpetuation of atrial fibrillation.
- This electroanatomical substrate permits multiple small re-entrant circuits that can maintain the arrhythmia.

## Atrial remodelling

1. Electrical remodelling: where at rapid atrial rates, intracellular changes in calcium handling lead to a reduction in the action potential duration.
2. Contractile remodelling: occurs rapidly. The abnormal calcium handling at the high rates of contraction may be responsible for loss of contractility. The contractile remodelling may be responsible for its most devastating consequence, which are thromboembolic events.
3. Structural tissue remodelling: occurs after weeks or months and in this case there are macroscopic and microscopic changes in the myocardium, which contribute to contractile dysfunction and decreased cardiac output

## Vascular function and new-onset AF

- The role of arterial stiffness appears key but poorly understood.
- In a study of patients aged  $\geq 45$  years from the Framingham Heart Study offspring.
- Higher augmentation index, baseline brachial artery diameter, and lower flow-mediated dilation were associated with increased risk of incident AF.

## Chronic kidney disease

- Hypertension is a risk factor for chronic kidney disease, and studies have shown that, the progression of renal dysfunction is a powerful predictor of new-onset atrial fibrillation in patients with hypertension, independently of LVH and left atrial dilatation .

## Antihypertensive agents and AF

- Antihypertensive drugs reduce the risk for atrial fibrillation mainly by lowering high blood pressure. However, some antihypertensive drugs may also reduce the risk for atrial fibrillation through other mechanisms
- There have been few prospective studies on the development of atrial fibrillation in hypertensive individuals, but there are several secondary analyses of large randomized trials and meta-analyses.

## RAAS

- In a large meta-analysis, the use of an angiotensin converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB) was associated with an average 49% relative reduction in new-onset atrial fibrillation, a 53% lower failure rate of electrical cardioversion of atrial fibrillation, and a 61% lower rate of recurrence of atrial fibrillation after electrical cardioversion

## RAAS

- There are different mechanisms explaining the beneficial effects of RAS blockers in patients with hypertension and atrial fibrillation.
- Blockade of the RAS may prevent left atrial dilatation, atrial fibrosis, dysfunction and slowing of conduction velocity, with some studies also indicating direct antiarrhythmic properties.

## Beta-blockers

- Beta-blockers are effective in atrial fibrillation rate-control and possibly in maintaining sinus rhythm, especially in heart failure and in cardiac postoperative settings
- AF with systolic heart failure or post MI may represent specific indications for using beta-blockers.
- In a systematic review including almost 12 000 patients with systolic heart failure, the incidence of new-onset atrial fibrillation was significantly lower in the patients treated with beta-blockers compared with those assigned to placebo with a RR reduction of 27% (14–38%,  $P < 0.001$ )

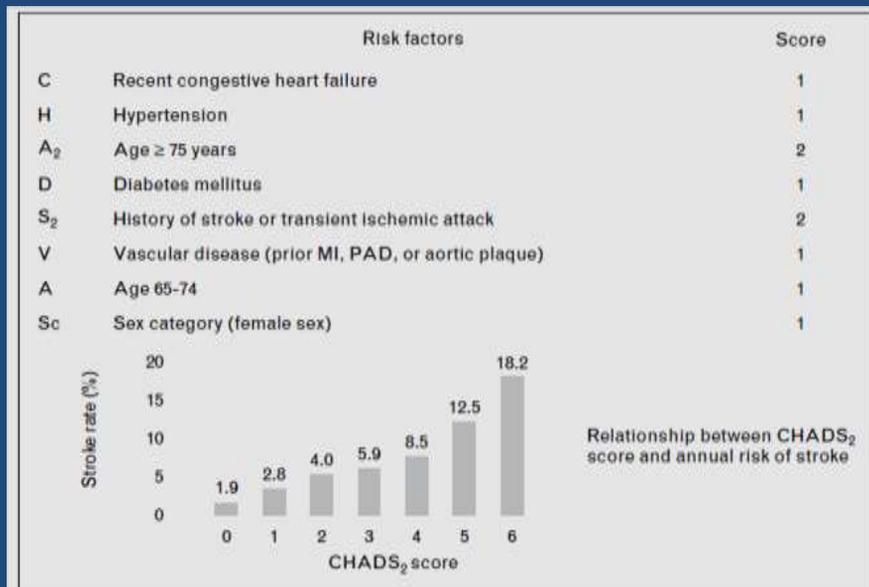
## Calcium channel blockers (CCBs)

- Calcium channel blockers could theoretically attenuate the calcium overload in tachycardia-induced electrical remodelling of the atria
- However, In the VALUE trial the ARB valsartan was more effective than the CCB amlodipine in preventing new-onset atrial fibrillation

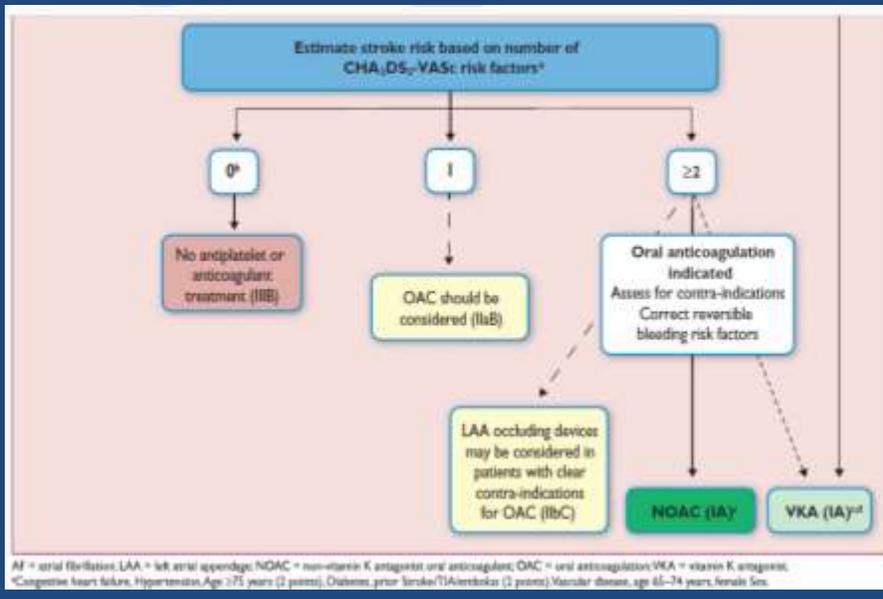
## Atrial Fibrillation and Hypertension: Preventive and Therapeutic Implications

- Although antiarrhythmic drugs and ablative therapies reduce AF burden and improve symptoms, no cure exists and they often have narrow therapeutic-to-toxic indices.
- This has led many to search for “upstream” or preventative therapies to delay the onset of AF (primary prevention) and prevent recurrent AF (secondary prevention)
- Since hypertension is a key contributor to the generation of a substrate vulnerable to AF, Hence, antihypertensive therapies may reduce atrial remodeling and hold promise as “upstream” therapies for AF.

## Prevention of thromboembolic events



## Prevention of thromboembolic events



## Antithrombotic agents : VKA

- A meta-analysis of more than 28 000 patients showed that adjusted-dose warfarin results in a reduction in ischemic stroke by 64% and in all cause mortality by 26%.
- This reduction was similar for both primary and secondary prevention and for both disabling and nondisabling strokes. By on-treatment analysis, the prevention efficacy of oral anticoagulation ( warfarin) exceeded 80%.

## Non-vitamin K antagonist oral anticoagulants



### Randomized Evaluation of Long-term anticoagulant therapy

*Dabigatran Compared to Warfarin in 18,113 Patients with Atrial Fibrillation at Risk of Stroke*

**R**ivaroxaban **O**nce-daily oral direct factor Xa inhibition  
**C**ompared with vitamin **K** antagonism for prevention  
of stroke and **E**mbolism **T**rial in **A**trial **F**ibrillation

Kenneth W. Mahaffey, MD and Keith AA Fox, MB ChB  
on behalf of the ROCKET AF Investigators



**Apixaban versus Warfarin in  
Patients with Atrial Fibrillation**  
Results of the ARISTOTLE Trial

Presented on behalf of the ARISTOTLE Investigators  
and Committees

## !! Aspirin ...

- Aspirin offers only modest protection against stroke for patients with atrial fibrillation and in a large meta-analysis, aspirin resulted in non-significant 19% reduction in stroke and insignificant impact on mortality.
- Nine studies compared the effects of VKA versus aspirin and found significant reduction of primary endpoint 39% in favour of treatment with VKA.

## !!! Clopidogrel....

- The atrial fibrillation Clopidogrel Trial with Irbesartan for the prevention of Vascular Events-Warfarin arm trial (ACTIVE-W), compared (clopidogrel plus aspirin) versus warfarin for prevention of vascular events in atrial fibrillation with an average of two stroke risk factors.
- Anticoagulation therapy was superior to the combination of clopidogrel plus aspirin (RR reduction 40%) with no differences in bleeding events between treatment arms

**Table 10** Clinical characteristics comprising the HAS-BLED bleeding risk score

Letter	Clinical characteristic <sup>a</sup>	Points awarded
<b>H</b>	Hypertension	1
<b>A</b>	Abnormal renal and liver function (1 point each)	1 or 2
<b>S</b>	Stroke	1
<b>B</b>	Bleeding	1
<b>L</b>	Labile INRs	1
<b>E</b>	Elderly (e.g. age >65 years)	1
<b>D</b>	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

## Conclusion

- As the population ages, the burden of HTN and AF will continue to rise. Systemic HTN is the most common and modifiable risk factor for development of AF.
- Early treatment of HTN represents a potential opportunity for AF prevention.
- Antihypertensive medications, including those that block the RAAS pathway, may decrease the risk of incident and recurrent AF.
- Hypertension is an integral component of both stroke and bleeding risk scores in AF patients

Thank you