Atrial Fibrillation and Heart Failure: How Should We Manage Our Patients?

Atrial fibrillation (AF) and heart failure (HF) are global epidemics that began more than a century ago, and their association with an ageing general population has brought about an increase in cardiovascular morbidity and rising healthcare costs.^{1,2} More than 50 % of patients with permanent AF have a concurrent diagnosis of HF and this proportion is expected to rise.³ It is well established that the detrimental impact of AF in patients with HF results in a greater number of hospital admissions, longer hospital stays and an overall increase in mortality in HF patients with AF.^{4,5}

Pathophysiology of AF and HF: A Brief Overview

The pathophysiology of AF and HF are closely interlinked. Patients with HF develop an increase in left ventricular filling pressure secondary to either systolic or diastolic dysfunction.⁶ Such changes lead to a remodelling of the left atrium, which in turn can act as a substrate for AF. HF patients also demonstrate altered calcium handling leading to calcium overload, which in turn can alter depolarisation patterns, resulting in arrhythmias. AF itself can alter the efficiency by which systole and diastole take place, the end result being a shortened left ventricular filling time. This, along with suboptimal rate control, reduces myocardial contractility resulting in systolic HF.

With regards to the complications of thromboembolism, both AF and HF confer a prothrombotic state, by fulfilment of Virchow's triad for thrombogenesis.^{7,8} Hence, the risk of stroke and thromboembolism is increased with either AF or HF, and accentuated when both conditions are present concomitantly.

What Should We Do?

Whilst AF and HF are intimately related, which develops first? The Framingham Study suggested that patients were more likely to develop HF first rather than AF (41 % versus 38 %), while in 21 % of patients, both conditions occurred simultaneously.⁹ Asymptomatic AF is common, and would often be first diagnosed when the onset of AF leads to decompensated HF. Conversely, prolonged AF with poorly controlled ventricular rates may lead to presentation with HF, sometimes related to progressive left ventricular impairment and dilatation (the so-called tachycardia-induced cardiomyopathy).¹⁰

Treatment with HF therapies may modulate the onset of AF. The use of angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptor inhibitors (ARBs) reduces the risk of developing AF by nearly 30 % overall, with an even greater risk reduction in HF patients.¹¹ The Candesartan in Heart Failure Assessment of Reduction in Morbidity and Mortality Program (CHARM) suggests a benefit for ARBs in the primary prevention of AF, whether with left ventricular systolic or diastolic dysfunction.¹²

The benefit of beta-blockers (BBs) in patients with HF and AF versus those with sinus rhythm is less well established. Both European and US guidelines recommend the use of BBs in patients with HF and concomitant AF.^{13,14} This is in keeping with a meta-analysis of registry data including over 200,000 patients showing that patients with AF and concomitant HF had lower all-cause mortality when treated with BBs.¹⁵ Nonetheless, an individual patient analysis of trial data showed less prognostic benefit of BBs in HF with associated AF,¹⁶ but this may be due in part to the fact that ventricular rates <70 beats/min have been associated with poorer outcomes in these patients leading to no prognostic benefit.¹⁷

Conflicting evidence is also apparent for the use of mineralocorticoid receptor antagonists (MRAs) in patients with left ventricular systolic dysfunction and AF. Sub-analyses from the Atrial Fibrillation and Congestive Heart Failure trial (AF-CHF) showed an increase in mortality in such patient cohorts (HR 1.4; 95 % CI 1.1–1.8); however, patients receiving MRA therapy were probably more unwell and this may have been a confounding factor in this analysis.¹⁸ In the Eplerenone in Mild Patients Hospitalization and Survival Study

in Heart Failure (EMPHASIS-HF) study, the use of eplerenone reduced new-onset AF and improved prognosis in HF due to systolic impairment, whether or not AF was present.¹⁹

In summary, there are some data suggesting a beneficial effect of ACEIs, ARBs, BBs and MRAs in patients with HF with reduced ejection fraction (HFrEF) and AF compared with sinus rhythm (SR). Such therapy has the potential to aid favourable left ventricular remodelling and limiting cardiac fibrosis, leading to a reduction in new onset AF and improved prognosis.¹³

Role of Anticoagulation With NOACs versus Warfarin

All patients with HF and AF are at increased risk of stroke and thromboembolism, and should be considered for stroke prevention with oral anticoagulation (OAC). Such patients should be assessed using the CHA₂DS₂-VASc score (congestive heart failure, hypertension with blood pressure [BP] >140/90, age 65–74 or age ≥75, diabetes mellitus, previous stroke/transient ischaemic attack or thromboembolism, vascular disease) and the HAS-BLED score (hypertension [systolic BP >160 mmHg], abnormal liver/renal function [with creatinine ≥200 µmol/L], stroke, bleeding history or predisposition, labile international normalised ratio [INR] in range <60 % of the time, elderly [>65], concomitant drugs/alcohol) to help decision making when balancing the benefits and risks of stroke prevention against bleeding.²⁰

The non-vitamin K oral anticoagulants (NOACs) have gained preferential use over warfarin in patients with HF and AF in guidelines, and a recent meta-analysis points to the superiority of NOACs in AF patients with associated HF.^{13,21} The vitamin K antagonists (VKAs), eg. warfarin, are alternative OACs, but attention to quality of anticoagulation control with a high (>70 %) time in therapeutic range (TTR) between 2.0 and 3.0 is needed.

Conclusion

New-onset HF in patients with established AF is often benign,²² but AF in a patient with established HF is associated with a worse outcome.^{23,24} The management of HF with concomitant AF requires optimisation of HF medical therapy as per evidence-based guidelines. Appropriate thromboprophylaxis is also needed, whether with a NOAC or VKA with well-managed anticoagulation control.

Farhan Shahid¹ and Gregory Y H Lip^{1,2}

1. University of Birmingham Institute of Cardiovascular Sciences, City Hospital, Birmingham, UK;

2. Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

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DOI: 10.15420/AER.2016.5.3.ED3