

## Atrial fibrillation and hypertrophic cardiomyopathy:

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### Editorial

## Atrial fibrillation and hypertrophic cardiomyopathy: co-existing conditions with additive risks



Hypertrophic cardiomyopathy (HCM) is defined by the presence of increased left ventricular wall thickness in the absence of abnormal loading conditions and occurs in 1 in 500 of the general population. HCM is associated with an increased risk of sudden cardiac death and is probably the most common cause of sudden cardiac death in young people. The underlying pathology of HCM including disorganized myocardial architecture and replacement fibrosis represents arrhythmogenic substrate, causing lethal ventricular tachyarrhythmias such as ventricular tachycardia and ventricular fibrillation.

Atrial fibrillation (AF) is also a common arrhythmic event in patients with HCM that leads to disastrous outcomes including heart failure, stroke, and death. The prevalence of AF in patients with HCM has been reported to be 4- to 6-fold greater than that in the general population. Although the true prevalence depends on the study populations and diagnostic methods used for AF detection, AF prevalence has been reported to range from 17% to 28% (Table 1).<sup>1–5</sup> It is well recognized that AF is a major predictor of stroke, and stroke prevention is the principal priority in AF management.<sup>6</sup>

Some cohort studies demonstrate that age, left atrial enlargement, and New York Heart Association (NYHA) class are associated with an increased risk of developing AF, with heterogeneity among studies. Patients with HCM are more likely to develop AF at a younger age than the general population. In one cohort study, the prevalence of AF in patients with HCM was 25% before age 50 years, whereas in the general population, it was 0.5% at age 40–50 years.<sup>3</sup> Left atrial enlargement, assessed by echocardiography as an increase in left atrial diameter or volume, is also an independent predictor of AF in patients with HCM, and the current ESC guidelines for the management of HCM recommend that patients in sinus rhythm with left atrial diameter  $\geq 45$  mm should undergo 48-h ambulatory ECG monitoring every 6 to 12 months for AF detection (class IIA recommendation).<sup>7</sup> In particular, left atrial enlargement is one of the risk factors for thromboembolism in HCM patients even in sinus rhythm<sup>8</sup> and should be carefully assessed with other risk factors as well.

However, these predictors for developing AF may be interpreted as surrogate markers for disease progression of HCM. The underlying pathophysiology in HCM such as diastolic dysfunction and mitral regurgitation due to left ventricular outflow tract obstruction cause left atrial pressure loading. Long-term accumulation of myocardial remodeling, which represents left atrial enlargement and replacement of atrial myocardial fibrosis, results in the substrate of developing AF and thrombus formation. Consequently,

the development of AF in patients with HCM may indicate that the disease has already progressed to an end-stage phase.

In this issue of the journal, Zegkos et al sought to investigate the prevalence and clinical features of AF in patients with HCM.<sup>9</sup> In this study, a substantial number of patients (23.4%) with HCM developed AF, in line with previous studies. Female gender, NYHA class, and left atrial enlargement were independent predictors of AF (odds ratio (OR) 2.2, 95% confidence interval (CI) 1.3–3.5,  $p = 0.001$ , OR 1.9, 95% CI 1.1–3.5,  $p = 0.02$ , OR 2.2, 95% CI 1.6–3.3,  $p < 0.001$ , respectively). Moreover, they demonstrate the impact of AF on mortality in patients with HCM, whereby AF was associated with an increased risk of overall mortality (hazard ratio 3.4, 95% CI 1.7–6.5). Subgroup analysis of 126 patients who underwent cardiopulmonary exercise testing showed that AF was an independent predictor of exercise intolerance in HCM patients, resulting in reduced quality of life.

It is well recognized that thromboembolic events are also frequently associated with HCM per se. A recent systematic review reported that the prevalence and annual incidence of thromboembolic events including stroke and peripheral embolism in patients with HCM and AF were 2.4% and 5.0% per 100 patients, respectively.<sup>10</sup> Risk stratifications for thromboembolism, such as the CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASC score, in patients with non-valvular AF are well established, and oral anticoagulants are widely used for thromboembolism prophylaxis.

However, these simple risk scores are not well validated in patients with HCM and AF. Guttman et al reported that the CHA<sub>2</sub>DS<sub>2</sub>-VASC score did not adequately risk stratify for thromboembolism in HCM patients with AF who were not treated with vitamin K antagonists (VKAs).<sup>11</sup> Perhaps HCM patients with AF tend to be younger and do not more frequently present with vascular disease compared to other high-risk populations; however, this study categorized some HCM patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASC score of 0, despite HCM patients essentially having diastolic dysfunction, as such patients (with so-called heart failure with preserved ejection fraction) would score 1 point for the C criterion on the CHA<sub>2</sub>DS<sub>2</sub>-VASC score.<sup>6</sup> Indeed, heart failure can be a powerful driver of stroke risk even amongst young AF patients.<sup>12</sup>

In addition, non-vitamin K antagonist oral anticoagulants are being increasingly established as alternatives to the VKAs for effective stroke prevention<sup>13,14</sup>; however, there are limited data to support the efficacy and safety in patients with HCM and AF (as these patients were excluded from the randomized trials), although some small observational series of HCM have been reported.<sup>15</sup>

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**Table 1**  
Prevalence and predictors of AF and annual incidence rate of thromboembolism in patients with HCM

Year	Study	Number of patients, n	Follow-up period, years	Prevalence of AF, n	Predictors of AF	Incidence rate of thromboembolism in AF patients, %
2001	Olivotto I, et al <sup>1</sup>	480	9.1 ± 6.4	107 (22%)	age, LA enlargement, NYHA ≥II	21.5
2002	Maron BJ, et al <sup>2</sup>	900	7 ± 7	192 (21%)	n/a	23.4
2004	Losi MA, et al <sup>3</sup>	150	5.2 ± 2.9	20 (13%)	age, LA enlargement, MR, LVOT obstruction	n/a
2009	Kubo T, et al <sup>4</sup>	261	n/a	74 (28%)	age, NYHA ≥III, prior embolism/HF, LA/LV enlargement	20.2
2014	Siontis KC, et al <sup>5</sup>	3673	4.1 (median)	650 (18%)	age, prior CAD/stroke, high BNP, LA enlargement, non-obstructive LVOT, MR, LVEF<50%	n/a

AF; atrial fibrillation, HCM; hypertrophic cardiomyopathy, LA; left atrial, NYHA; New York Heart Association, MR; mitral regurgitation, LVOT; left ventricular outflow tract, HF; heart failure, LV; left ventricular, CAD; coronary artery disease, BNP; brain natriuretic peptide, LVEF; left ventricular ejection fraction, HT; hypertension.

Given the specific clinical features and high incidence of thromboembolism in HCM patients, these risk schemes are not directly applicable to the HCM population. Current ESC guidelines for the management of HCM patients also advocate that all patients with AF should receive treatment with VKAs, irrespective of their risk scores.<sup>7</sup> Japanese cohort studies demonstrated that cardiomyopathy (including both dilated and hypertrophic cardiomyopathy) is independently associated with an increased risk of thromboembolic events,<sup>16</sup> and the coagulation system is activated in patients with cardiomyopathy.<sup>17</sup> Therefore, Japanese guidelines recommend that anticoagulation should be considered in AF patients with cardiomyopathy (class IIA recommendation).

In conclusion, AF has crucial impacts on morbidity and mortality in patients with HCM. Many cohort studies demonstrate an intimate relationship between AF and HCM, and AF in the HCM population has some specific features that predispose to thromboembolism. To prevent adverse outcomes in these patients, further efforts to optimize clinical assessment and management pathways for patients with AF are needed in an integrated and holistic manner.

#### Declarations of Interest

The authors declare no conflicts of interest.

#### Reference

- Olivotto I, Cecchi F, Casey SA, Dolara A, Traverse JH, Maron BJ. Impact of atrial fibrillation on the clinical course of hypertrophic cardiomyopathy. *Circulation*. 2001;104(21):2517–2524.
- Maron BJ, Olivotto I, Bellone P, et al. Clinical profile of stroke in 900 patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2002;39(2):301–307.
- Losi MA, Betocchi S, Aversa M, et al. Determinants of atrial fibrillation development in patients with hypertrophic cardiomyopathy. *Am J Cardiol*. 2004;94(7):895–900.
- Kubo T, Kitaoka H, Okawa M, et al. Clinical impact of atrial fibrillation in patients with hypertrophic cardiomyopathy. Results from Kochi RYOMA study. *Circ J*. 2009;73(9):1599–1605.
- Siontis KC, Geske JB, Ong K, Nishimura RA, Ommen SR, Gersh BJ. Atrial fibrillation in hypertrophic cardiomyopathy: prevalence, clinical correlations, and mortality in a large high-risk population. *J Am Heart Assoc*. 2014;3(3), e001002.
- Lip GYH, Freedman B, De Caterina R, Potpara TS. Stroke prevention in atrial fibrillation: Past, present and future. Comparing the guidelines and practical decision-making. *Thromb Haemost*. 2017;117(7):1230–1239.
- Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J*. 2016;37(38):2893–2962.

- Overvad TF, Nielsen PB, Larsen TB, Sogaard P. Left atrial size and risk of stroke in patients in sinus rhythm. A systematic review. *Thromb Haemost*. 2016;116(2):206–219.
- Zegkos T, Efthimiadis GK, Parcharidou DG, et al. Atrial fibrillation in hypertrophic cardiomyopathy: A turning point towards increased morbidity and mortality. *Hellenic J Cardiol*. 2017;58:331–339.
- Guttmann OP, Rahman MS, O'Mahony C, Anastasakis A, Elliott PM. Atrial fibrillation and thromboembolism in patients with hypertrophic cardiomyopathy: systematic review. *Heart*. 2014;100(6):465–472.
- Guttmann OP, Pavlou M, O'Mahony C, et al. Prediction of thrombo-embolic risk in patients with hypertrophic cardiomyopathy (HCM Risk-CVA). *Eur J Heart Fail*. 2015;17(8):837–845.
- Chan YH, Wu LS, Chang SH, et al. Young male patients with atrial fibrillation and CHA2DS2-VASc score of 1 may not need anticoagulants: A nationwide population-based study. *PLoS One*. 2016;11(3), e0151485.
- Carmo J, Moscoso Costa F, Ferreira J, Mendes M. Dabigatran in real-world atrial fibrillation. Meta-analysis of observational comparison studies with vitamin K antagonists. *Thromb Haemost*. 2016;116(3).
- Beyer-Westendorf J, Camm AJ, Coleman CI, Tamayo S. Rivaroxaban real-world evidence: Validating safety and effectiveness in clinical practice. *Thromb Haemost*. 2016;116(suppl. 2):S13–S23.
- Noseworthy PA, Yao X, Shah ND, Gersh BJ. Stroke and bleeding risks in NOAC- and warfarin-treated patients with hypertrophic cardiomyopathy and atrial fibrillation. *J Am Coll Cardiol*. 2016;67(25):3020–3021.
- Tomita F, Kohya T, Sakurai M, et al. Prevalence and clinical characteristics of patients with atrial fibrillation: analysis of 20,000 cases in Japan. *Jpn Circ J*. 2000;64(9):653–658.
- Yamamoto K, Ikeda U, Furuhashi K, Irokawa M, Nakayama T, Shimada K. The coagulation system is activated in idiopathic cardiomyopathy. *J Am Coll Cardiol*. 1995;25(7):1634–1640.

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