

# Aggressive Treatment of Atrial Fibrillation in Hypertrophic Cardiomyopathy Patients Improve Quality of Life

Gerald Naccarelli<sup>1</sup> and Eric Popjes<sup>2</sup>

<sup>1</sup>Penn State Health Milton S Hershey Medical Center

<sup>2</sup>Penn State College of Medicine

March 10, 2024

## **Aggressive Treatment of Atrial Fibrillation in Hypertrophic Cardiomyopathy Patients Improve Quality of Life**

Gerald V. Naccarelli MD

Eric D. Popjes MD

From: Penn State University College of Medicine

Penn State Health

Penn State Heart and Vascular Institute.

The Milton S. Hershey Medical Center

Hershey, Pa, USA

Running Title: Atrial Fibrillation and Hypertrophic Cardiomyopathy

Key Words: Antiarrhythmic Drugs; Atrial Fibrillation; Hypertrophic Cardiomyopathy; Quality of Life

Total Word Count: Editorial (1276) and with references (1911)

Corresponding Author:

Gerald V. Naccarelli MD

Penn State University College of Medicine

Penn State Hershey Heart & Vascular Institute

500 University Drive, Room H1511

Hershey PA 17033

Phone: 1-717-531-3907

Fax: 1-717-531-4077

[gnaccarelli@penntatehealth.psu.edu](mailto:gnaccarelli@penntatehealth.psu.edu)

Potential Conflicts; Gerald V. Naccarelli MD (Consultant: Milestone, Sanofi, In Cardia Therapeutics, Acision, Glaxo Smith Kline); Eric Popjes MD (none)

Hypertrophic cardiomyopathy (HCM) is a common inherited disease occurring in about 1 of 500 births. Atrial fibrillation (AF) is the most commonly occurring tachyarrhythmia and often occurs in patients with structural heart disease. Thus, it is not surprising that AF occurs in about 25% of patients with HCM and is likely to occur due to changes in atrial histology including myocyte hypertrophy and disarray, interstitial fibrosis and left atrial dilatation secondary to left ventricular hypertrophy, outflow obstruction and mitral regurgitation (1,2). AF can lead to rapid rates, the loss of an atrial contribution to cardiac output and shortening of diastolic filling time that can lead to increased left ventricular filling pressures and significant hemodynamic symptoms and heart failure in HCM patients. In addition, stroke rates increase eight-fold when these two diseases co-exist independent of any risk score. The HCM guideline (3) states that a principal goal of treating patients with symptomatic HCM is to improve their symptoms and their overall function and quality of life (QOL). Based on these facts and previous research, the presence of concomitant AF with HCM are of major concern related to prognostic and QOL indicators.

In this edition of the Journal of Cardiovascular Electrophysiology, Rowin et al report on the QOL in fifty patients who had HCM and AF at one major HCM center (4). These patients came from a cohort of 218 consecutive patients with HCM who filled out patient reported outcome measures. The investigators used the Kansas City Cardiomyopathy Questionnaire (KCCCQ)(5) in all HCM patients and the Atrial Fibrillation Effect on Quality of Life (AFEQT)(6) in the AF cohort. Patients had AF for a median of 5.5 years prior to the study survey. Of note, 66% of patients were treated with a rhythm control strategy and the remainder a rate control strategy utilizing beta-blockers and calcium blockers. The AFEQT reported that 52% of patients experienced no or minimal AF-related disability with 22% describing mild to moderate and 26% severe issues. There was no difference based on HCM phenotype. After treatment, the presence of AF did not impact QOL in these patients. Using the KCCCQ-OS score heart failure symptoms were similar with 59% having no or minimal symptoms. Surprisingly, a history of concomitant AF was associated with less HF symptoms and improved QOL.

The results of this study need to be put into clinical perspective. This trial was a retrospective analysis and there was no prospective, controlled randomization of treatments. Patients were treated at a major HCM center with expertise in using guideline management, including anticoagulation and aggressive use of rhythm control strategies including antiarrhythmic drugs and catheter ablation (3,7). Of the fifty patients, 70% had obstructive HCM and seventeen patients had prior surgical myectomy and four patients had alcohol septal ablation. Two-thirds of the AF patients had rhythm control attempts including one-third with catheter ablations procedures and ten patients (20%) had MAZE procedures at the time of their myectomy and only six patients were treated with sotalol or amiodarone. The remaining AF patients were treated using just rate control drugs. From a HCM perspective the severity of baseline disease and obstructive physiology is validated by the fact that twenty-one of the patients had either a septal or alcohol myectomy. A prior study showed that 80% of patients who had septal myectomy had over a 20-point improvement in their KCCCQ score (8). Although this group of patients were sicker and referred to a major HCM center, we would caution extrapolating these findings to HCM patients with AF who may not require aggressive management. This population does not represent the bell-shaped curve of all patients with HCM cared for in a routine cardiologist's practice.

Even though prior to treatment this group may have had more advanced HCM disease, 75% had mild to moderate QOL scores. This paper only reports on QOL measure from the most recent clinic visit. Patients did not have baseline QOL measures that obviously improved at the time of these QOL surveys post aggressive treatment. In addition, all QOL measures are limited and using two different QOL surveys in the same group of patients may limit the findings of this study. In addition, QOL data was collected at a single point in time and thus treatment effect size could not be determined. This limitation could have been minimized by collecting data over a longer time. Clinically meaningful treatment effects have been controversial using QOL survey tools; although, Holmes et al, using the ORBIT-AF registry, defined a plus or minus 5-point change as clinically meaningful for AF patients (9). AF history averaged 5.5 years prior to the QOL surveys, and most patients did not have AF recurrence in the month before the survey.

The authors are major experts in the care of such patients and the results may not be extrapolated to other caretakers with less experience. Patients were offered anticoagulation in this trial consistent with guideline recommendations (3,7) independent of CHA2Ds2-VASc score given the fact that HCM patients with AF have an embolic risk like those with a CHA2Ds2-VASc score of 3. This is a practice we follow at our own center.

The data suggests that minimizing AF recurrences improves and reverses heart failure symptoms in these patients given most patients in this study had paroxysmal AF and only four patients had permanent AF. To no surprise the patients with the most frequent AF recurrences had more symptoms and worse QOL scores. Younger patients with a high number of AF recurrences had worse reported AF disability and patients with less episodes reported less disability. This finding supports the aggressive rhythm strategies used by these investigators including the fact that HF symptoms improve upon controlling AF in such patients. The CABANA trial, in a patient population without HCM, previously reported the benefits of catheter ablation over antiarrhythmic drugs in a large AF population in improving QOL using the AFEQT score (10). The high use of ablation for the AF patients may have affected the results but also suggests aggressive management of HCM with AF should be instituted earlier given the concerns of the safety and less efficacy of antiarrhythmic drugs in this patient population. Using catheter ablation for AF in such patients is supported by the recent data from Castagno et al (11) who reported that catheter ablation was effective in controlling AF in 61% of 111 patients with 6 years follow-up; although on average, patients required 1.6 ablations to achieve this efficacy.

This report represents a small population that limits sub-analyses although the authors did their best given this major limitation. There are cohorts of HCM patients that may have QOL issues such as those with pulmonary hypertension (12) who might benefit from specific forms of therapy that could not be analyzed given the small sample size. Further large prospective studies in patients with HCM and AF should be performed measuring QOL measure before and after treatments in a longitudinal fashion so that the best management of these patients can be determined. New treatments for HCM and AF will continue to be a moving target. Mavacamten, a new cardiac myosin inhibitor treatment for HCM, improved KCCQ overall scores compared to placebo in patients with symptomatic, obstructive HCM and this difference returned to baseline after discontinuation of the active treatment (13). Data from the present trial was collected before large scale use of this treatment was available. Obviously, similar studies cannot be performed for irreversible treatments such as catheter ablation of AF or septal myectomy. In the meantime, data from this study suggests that current treatment strategies are effective and aggressive management of both their HCM and AF is useful in making these patients happy and enjoying their QOL.

## References

1. Rowin EJ, Link MS, Maron MM, Maron BJ. Evolving contemporary management of atrial fibrillation in hypertrophic cardiomyopathy. *Circulation* 2023;148:1797–1811.
2. Masri A, Kanj M, Thamilarasan M, Wazni O, Smedira NG, Lever HM, Desai MY. Outcomes in hypertrophic cardiomyopathy patients with and without atrial fibrillation: A survival meta-analysis. *Cardiovasc Diagn Ther* 2017;7:36–44.
3. Ommen SR, Mital S, Burke MA, Day SM, Deswal A, Elliott P, Evanovich LL, Hung J, Joglar JA, Kantor P, Kimmelstiel C, Kittleson M, Link MS, Maron MS, Martinez MW, Miyake CY, Schaff H V., Semsarian C, Sorajja P. 2020 AHA/ACC Guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy: A report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *J Am Coll Cardiol* 2020;76:e159–e240.
4. Rowin EJ, Wadid M, Maron MS, White M, Hook B, Harnish P, Silver J, Reynolds M, Maron B. Assessing the impact of atrial fibrillation on symptoms and quality of life in hypertrophic cardiomyopathy. *J Cardiovasc Electrophysiol* 2024 (final reference to be provided by editor on publication).
5. Spertus JA, Jones PG, Sandhu AT, Arnold S V. Interpreting the Kansas City Cardiomyopathy Questionnaire in clinical trials and clinical care: JACC State-of-the-Art Review. *J Am Coll Cardiol* 2020;76:2379–2390.

6. Spertus J, Dorian P, Bubien R, Lewis S, Godejohn D, Reynolds MR, Lakkireddy DR, Wimmer AP, Bhandari A, Burk C. Development and validation of the Atrial Fibrillation Effect on Quality-of-life (AFEQT) questionnaire in patients with atrial fibrillation. *Circ Arrhythm Electrophysiol* 2011;4:15–25.
7. Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM, Deswal A, Eckhardt LL, Goldberger ZD, Gopinathannair R, Gorenek B, Hess PL, Hlatky M, Hogan G, Ibeh C, Indik JH, Kido K, Kusumoto F, Link MS, Linta KT, Marcus GM, McCarthy PM, Patel N, Patton KK, Perez MV, Piccini JP, Russo AM, Sanders P, Streur MM, Thomas KL, Times S, Tisdale JE, Valente AM, Van Wagoner DR. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2024; 149: e1-e156.
8. Desai MY, Tower-Rader A, Szpakowski N, Mentias A, Popovic ZB, Smedira NG. Association of Septal Myectomy with Quality of Life in Patients with Left Ventricular Outflow Tract Obstruction from Hypertrophic Cardiomyopathy. *JAMA Netw Open* 2022;5(4):e227293. doi:10.1001/jamanetworkopen.2022.7293
9. Holmes DN, Piccini JP, Allen LA, Fonarow GC, Gersh BJ, Kowey PR, O'Brien EC, Reiffel JA, Naccarelli GV, Chan PS, Spertus JA, Peterson ED, Thomas L, on behalf of the ORBIT AF Investigators and Patients. Defining Clinically Important Difference in the Atrial Fibrillation Effect on Quality-of-Life (AFEQT) Score: Results from the ORBIT-AF Registry. *Circ Cardiovasc Clin Outcomes* 2019;12:e005358. DOI: 10.1161/CIRCOUTCOMES.118.005358
10. Mark DB, Anstrom K, Sheng S, Piccini JP, Baloch KN, Monahan KH, Daniels MR, Bahnson TD, Poole JE, Rosenberg Y, Lee KL, Packer DL, for the CABANA Investigators. Effect of Catheter Ablation vs. Medical Therapy on Quality of Life Among Patients with Atrial Fibrillation. The Cabana Randomized Clinical Trial. *JAMA* 2019;321(13):1275-1285.
11. Castagno D, Donna P Di, Olivotto I, Frontera A, Calò L, Scaglione M, Arretini A, Anselmino M, Giustetto C, Ferrari GM De, Cecchi F, Haissaguerre M, Gaita F. Transcatheter ablation for atrial fibrillation in patients with hypertrophic cardiomyopathy: Long-term results and clinical outcomes. *J Cardiovasc Electrophysiol* 2021;32:657–666.
12. Capota R, Militaru S, Ionescu AA, Rosca M, Baicus C, Bogdan AP, Jurcut R: Quality of life status determinants in hypertrophic cardiomyopathy as evaluated by the Kansas City Cardiomyopathy Questionnaire. *Health Qual Life Outcomes* 2020;18,351. doi.org/10.1186/s12955-020-01604-9
13. Spertus JA, Fine JT, Elliott P, Ho CY, Olivotto I, Saberi S, Li W, Dolan C, Reaney M, Sehnert AJ, Jacoby D. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): health status analysis of a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2021;397: 2467-2475.