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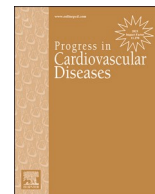
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Is it safe to use class 1C antiarrhythmic drugs in patients with coronary artery disease and/or cardiomyopathy?

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ABSTRACT

Class 1C antiarrhythmic drugs (AADs) are a key treatment option for effective rhythm control in several common arrhythmias. Here, we review the relevant background on Class 1C AADs, these drugs' indications and contraindications, and potential safe ways to use them. The safety profile of 1C AADs, and related restrictions on their use, has been largely based on the decades-old CAST trial, but more recent evidence may favor re-evaluating previously excluded populations. This review examines opportunities to reconsider certain patient populations that have previously been excluded from the use of 1C AADs. This reconsideration is made feasible due to advances in cardiac reperfusion, medical therapies for heart failure, and cardiac imaging.

Introduction

Atrial fibrillation (AF) is the most common abnormal heart rhythm in the United States, with an increasing population prevalence of approximately 6.6 million in 2015 and 10.6 million in 2019, with projections reaching as high as 12.1 million in 2030.^{1–5} The treatment tactic of rhythm control, in which patients are treated with antiarrhythmic drugs (AADs) and/or ablation (catheter-based or surgical), is increasingly preferred over the rate control strategy (i.e., accepting AF as long as the heart rate is not high).^{6–8} Rate control previously was considered non-inferior to rhythm control following major trials such as AFFIRM, but ongoing advances in rhythm-control strategies using catheter ablation or pharmacotherapy are resulting in improved safety and efficacy of rhythm control.^{6,9–11} This review summarizes the history of 1C AADs, indications for, and contraindications to, their use, and evaluates studies potentially showing safe ways in which those restrictions may be relaxed.

Mechanism of 1C AADs and indications for use

The use of the rhythm control strategy via pharmacotherapy is

limited by specific AAD contraindications and side effect profiles. For example, in the current ACC/AHA/HRS guidelines, the class 1C AAD, such as flecainide or propafenone, are first-line agents for AF, atrial flutter, PVCs, and SVT.¹² However, the guidelines caution against using these drugs in some patients: specifically, those with structural heart disease (SHD) or significant coronary artery disease (CAD). These limitations manifested in large part because of the Cardiac Arrhythmia Suppression Trial (CAST; see below), which showed that when used for PVC suppression following myocardial infarction, while indeed effective for PVC suppression, 1C AADs were associated with the very significant side effects of cardiac arrest and increased mortality.¹³ These results have been extrapolated, perhaps unfoundedly, to cause many clinicians to avoid 1C AADs completely in any patient with any amount of CAD or any cardiomyopathy.

The proarrhythmic effect of 1C AADs is likely related to their effect of decreasing myocardial conduction velocity, which predisposes to myocardial reentry around and through regions of infarcted myocardium.^{13,14} In the absence of a scar substrate, this effect could be expected to be less significant. Also, it should be recognized that CAST predates the PCI era, and timely revascularization via PCI may reduce the risk of proarrhythmic myocardial scar formation. Thus, even when CAD is

Abbreviations: AAD, Anti-arrhythmic drugs; AF, Atrial fibrillation; CAD, Coronary artery disease; CAST, Cardiac Arrhythmia Suppression Trial; CFC, Coronary flow capacity; HCM, Hypertrophic cardiomyopathy; LVEF, Left ventricular ejection fraction; PET, Positron emission tomography; PVC, Premature ventricular contraction; PVC-CM, Premature ventricular contraction induced cardiomyopathy; PVI, Pulmonary vein isolation; SHD, Structural heart disease.

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present, contemporary therapies have greatly uncoupled the existence of CAD and myocardial scar.

Limitations on 1C AADs

Flecainide and propafenone are first-line agents for rhythm control, according to the 2023 American College of Cardiology/American Heart Association/American College of Clinical Pharmacy/Heart Rhythm Society Guidelines for the Diagnosis and Management of Atrial Fibrillation.¹⁵ However, the guidelines also state that 1C AADs should be avoided in patients with CAD, or in the presence of sinus node or atrioventricular node dysfunction, heart failure, atrial flutter, infranodal conduction disease, Brugada syndrome, or liver disease.¹⁶ Flecainide use also is cautioned against in patients with renal dysfunction, and propafenone use is relatively contraindicated in patients with asthma due to its additional beta-blocking activity.¹⁶

Since the initial publication of the CAST investigation more than three decades ago, many have considered class 1C AADs unsafe for use in patients with CAD or other SHD.^{13,14,17} The CAST trial studied the use of 1C AADs in 1500 patients with a recent MI, a depressed LVEF, and frequent PVCs. The study found 1C AADs to be effective in PVC suppression. However, there was a significantly higher rate of death from arrhythmia and death from other cardiac causes in the 1C group, which was enough to halt the trial and significantly restrict the use of 1C AADs.^{13,17} Although these results were significant, the CAST trial findings have been broadly applied well beyond the initial group studied, which specifically comprised patients with an MI and an at least mildly depressed LVEF. The CAST results have since been generalized to all patients with any degree of CAD or cardiomyopathy, labeling them as having increased risk if treated with 1C AADs, regardless of their LVEF and regardless of whether myocardial scar is present. Though CAST demonstrated that patients with a recent MI are at higher risk from 1C AADs, this likely was due to ventricular tachyarrhythmias potentiated by myocardial fibrosis or ischemia, which serves as a substrate for reentry. Patients with CAD but no MI (and therefore no scar) may not have the same risk.

Evidence of 1C safety in CAD

Given the high prevalence of arrhythmias in patients with CAD, but the signal of 1C AAD-related increased mortality in those who have suffered MI, it may be useful to reassess the safety of 1C AADs in those who are adjacent to this population.

Some evidence implies that 1C AADs may be safe as long as there is no active ischemia present. A key point is that the CAST trial had several important limitations. The study was performed prior to the use of thrombolytics or primary PCI, which is significant because subsequent evidence links adverse events with an interaction between ongoing ischemia and Class 1C AAD use.^{14,18–21} Because revascularization was not as complete in the CAST era as it typically is today, CAST patients likely were more susceptible not only to scar formation, but also to ongoing ischemia that could contribute to arrhythmic events.²² It should be noted that elderly patients with significant pre-existing cardiovascular disease, LV dysfunction, and ventricular arrhythmias were not excluded from the CAST population.^{13,22} In relation to the more frequently incomplete revascularization in CAST, some argue that the link between drug and *ischemia*, rather than drug and *scar*, was identified in the CAST trial. This concept was further supported in the European Rythmol Atrial Fibrillation Trial (ERAFT), which supported the link between ischemia and electrical instability as an increased risk for interaction with 1C AADs. The ERAFT population contained some patients with a prior MI but none with current unstable angina. Patients were treated with 1C AADs (propafenone at 325 or 425 mg twice a day) without any increase in mortality or ventricular arrhythmias compared to placebo.^{22,23} Importantly, approximately 40 % of that population had known SHD (mainly CAD), but exclusion criteria included unstable

angina and stable class III or IV angina, or recent acute MI. Thus, in this population with a significant amount of CAD but a low probability of active ischemia, propafenone treatment appeared safe.

There also exists evidence to support the safety of 1C AADs even in the proved presence of significant but subclinical CAD. Our own laboratory at Ochsner Medical Center examined the safety of 1C AAD use in an age-matched cohort study including 96 patients with AF and without a history of MI or known CAD, but with positron emission tomography (PET)-derived coronary flow capacity (CFC) indicating that they had hemodynamically significant occult CAD.^{14,24} Among these patients, no 1C-based survival difference was found (Fig. 1). Thus, in the absence of infarct, the presence of CAD may not imply increased risk from 1C AADs. Due to the retrospective nature and moderate size of this study, however, further evidence will be needed to increase confidence in 1C drugs' safety in this setting.

Class 1C AADs also have been tested in the post-ablation period in patients with known CAD but without infarcts. In a retrospective study of patients undergoing AF ablation (pulmonary vein isolation, or PVI), patients with mild or moderate CAD were treated with propafenone ($n = 263$) or amiodarone ($n = 499$) during the three-month post-PVI "blanking period." After 12 months of follow up, there was no statistically significant signal of any ill effect from the propafenone: 11 patients in the propafenone group and 9 patients in the amiodarone group experienced the primary outcome of NSVT (4.2 % vs. 1.8 %, $p = 0.25$).²⁵ No sustained VT, VF, SCD, or cardiovascular mortality was observed. One limitation of this study was that it is unclear what imaging or characteristics were used to stratify patients regarding their degree of CAD, which would be important for analysis of safety, and design of future trials.

A recent retrospective study examined the safety of 1C AADs in patients with varying degrees of CAD (categorized as none, non-obstructive, or obstructive). "Obstructive" CAD included patients with any history of angina, previous MI, or revascularization by PCI or CABG. Patients with prior VT, ICD, or nonrevascularized MI were excluded. Only 110 of 3445 patients in the 1C group and 263 of 2216 patients in the class III group (sotalol, dofetilide) had "obstructive" CAD.²⁶ The primary endpoint was a composite of death, VT/VF, or admission for decompensated heart failure. In the entire population, there were 365 total events, but only 36 (9.9 %) of these events occurred in the obstructive CAD group.²⁶ Overall, there were 157 (4.6 %) events in the class 1C group vs. 208 (9.4 %) events in the class III group. This retrospective study, which may have been subject to significant selection bias, concluded that in the entire population, class 1C agents were associated with *better* event-free survival than class III agents. However, analysis of interaction later showed that 1C use was associated with a numerical but not statistically significant increase in events among those with nonobstructive CAD (HR 1.5 [0.9–2.6], $p = 0.139$). Moreover, there was poorer event-free survival when those with obstructive CAD were treated with a 1C AAD (HR 3.8 [1.7–8.7], $p = 0.002$).

It should also be noted that some evidence more directly implicates 1C agents in terms of increased arrhythmic risk in acute ischemia. In the 1990s, Faber et al. randomized to propafenone or placebo 98 patients undergoing coronary angioplasty.²⁷ During PTCA-induced transient ischemia, significantly more prolongation of ventricular repolarization dispersion was seen in the propafenone group. This increase was especially pronounced during interventions on the left anterior descending artery (difference in QT dispersion: +74 % for 1C vs. +14 % for placebo, $p = 0.025$). Because repolarization dispersion is a risk factor for electrical reentry, these data indicate that the use of 1C drugs may increase arrhythmic susceptibility in the presence of acute ischemia.

1C AADs in cardiomyopathy

Patients with NICM can have significant morbidity from frequent arrhythmias such as PVCs. In addition, frequent PVCs are associated with lower LVEF, lower rates of biventricular pacing, higher rates of

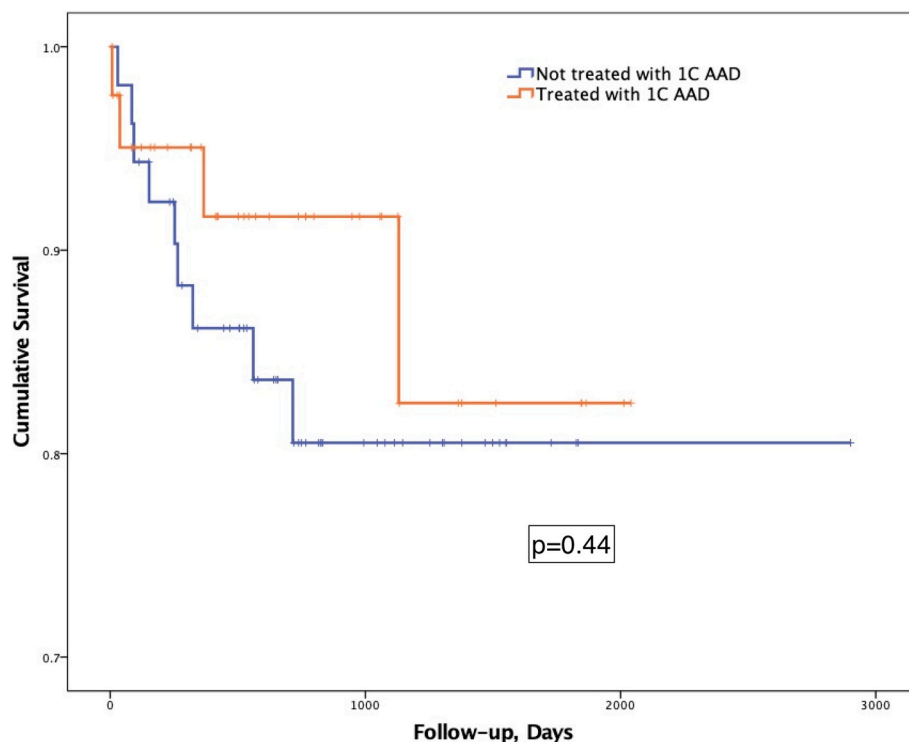


Fig. 1. Kaplan-Meier survival analysis of patients with >50 % of myocardium showing reduced coronary flow capacity by PET scan, stratified by 1C AAD use. (Figure adapted from original data presented in Pantlin et al.).

sustained ventricular arrhythmias, more heart failure exacerbations, and death. PVC suppression can be an important treatment in this patient population. Catheter ablation can be successful, but often there are limitations due to multiple foci or anatomically challenging sites of origin. Some medicines frequently used for PVC suppression among patients with LV dysfunction are Class III AADs, including amiodarone, sotalol, and dofetilide. These medications can be effective, but can be limited by potential toxicity to other organs, acute heart failure, renal dysfunction, and need for inpatient initiation due to the potential for QT prolongation.²⁸ Thus, the use of 1C drugs in this population could fill an unmet need.

An important study by Hyman et al., *Class 1C antiarrhythmic drugs for suspected premature ventricular contraction-induced cardiomyopathy*, studied the safety of 1C AADs when used to suppress PVCs in twenty patients with suspected PVC-induced cardiomyopathy (PVC-CM).²⁸ In their cohort, patients had either failed prior treatment with other AADs and/or had undergone unsuccessful PVC ablation, and then were treated with flecainide or propafenone for suspected PVC-CM. Patients were assessed with cardiac magnetic resonance imaging prior to initiation of 1C AADs, in order to exclude any myocardial scar that could serve as a possible substrate for VT. Although this was a small cohort, the 1C AADs effectively suppressed PVCs and led to LVEF recovery in the majority of patients.

In a continuation of Hyman's work, Raad et al. recently examined the safety of 1C AADs for patients with various nonischemic etiologies of cardiomyopathy (LVEF all <50 %; 76 % of cases idiopathic, with representation also from sarcoidosis, filamin-C, peripartum, and viral cardiomyopathies).¹⁹ Their study demonstrated considerable PVC suppression with 1C AADs (20 ± 13 % to 6 ± 7 %, $p < 0.001$), as well as increases in biventricular pacing percentage among those with CRT-D (85 ± 9 % vs. 93 ± 7 %, $p = 0.005$), which individually or together led to some LVEF improvement in the majority of patients (Fig. 2). No adverse events were observed during treatment.¹⁹ This study specifically examined the safety of 1C AADs in various forms of NICM with the added protection of an ICD in case of proarrhythmia, which is a rather

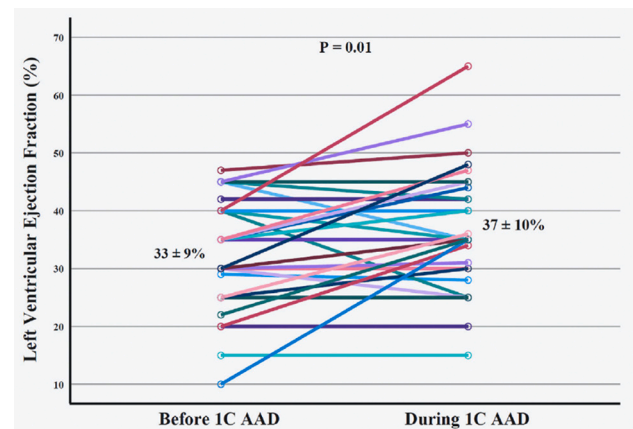


Fig. 2. The effect of PVC suppression using 1C antiarrhythmic drugs in patients with nonischemic cardiomyopathy. The mean left ventricular ejection fraction improved from 33 ± 9 % to 37 ± 10 %. With permission from Rand et al. AAD = antiarrhythmic drug.

novel concept that may enable larger prospective study. Further study is needed to determine the safety of 1C AADs in the broad population of idiopathic and PVC-induced nonischemic cardiomyopathy. Given the higher chance for LVEF recovery with effective PVC suppression, such patients without an ICD potentially could be prescribed a wearable defibrillator vest during treatment with a 1C AAD, in hopes of allowing LVEF recovery and avoidance of permanent ICD implantation.

Antiarrhythmic therapy in SHD is frequently limited to amiodarone. Due to clinical and therapeutic advancements across cardiovascular medicine, it is worth re-evaluating whether should still be the case. A recent study by Zylla et al. re-assessed the safety of 1C AAD as treatment for ventricular or atrial arrhythmias in patients with structural heart disease and a protective ICD in place.²⁹ Fifty patients at four tertiary

centers in Germany were enrolled, and SHD was represented mostly by dilated cardiomyopathy (42 %), or ischemic cardiomyopathy (26 %), though other significant pathology (e.g., congenital heart disease, hypertrophic cardiomyopathy, sarcoidosis, or arrhythmogenic cardiomyopathy) was included. During the 27-month follow up, there was an overall reduction in VA burden, and pro-arrhythmia was suspected in 3 (6 %) patients. Thus, class 1C AAD use showed a low but not insignificant rate of pro-arrhythmic effects or cardiovascular mortality.²⁹ A particular strength of this study was its continuous monitoring for significant arrhythmia, by virtue of the presence of an ICD in all patients. Further trials with a larger enrollment of both ischemic and nonischemic patients with an ICD already in place could provide further data, including longer follow up and examining a more diverse population.

Although formal guidelines regarding use of 1C agents are not available for all varieties of SHD without ischemia, some data support the notion that they may be safer than previously thought, as shown in the *central illustration*. While 1C agents often are thought to be contraindicated in the presence of significant LV hypertrophy, Chung et al. showed in an observational cohort study that 1C treatment of AF in patients with significant LVH (i.e., wall thickness ≥ 1.4 cm) was in fact not associated with increased mortality compared to treatment with amiodarone, even after propensity-score matching.³⁰ The 2020 AHA/ACC guidelines for hypertrophic cardiomyopathy caution against the use of 1C AADs in patients with HCM and AF due to risk of proarrhythmia.³¹ However, in a small study of symptomatic HCM patients treated with flecainide for its potential to decrease the left ventricular pressure gradient (LVPG), there indeed was a decrease in LVPG similar to that seen with disopyramide, without the vagolytic side effects and also without any signal of arrhythmic risk.³² In the same vein, patients with arrhythmogenic cardiomyopathy (ARC) are predisposed to ventricular arrhythmia that may be challenging to suppress.³³ There have been reports of adding flecainide to a baseline of sotalol and/or metoprolol in these patients, with anecdotal results of greatly decreased VA thereafter.³⁴ Prospective controlled studies are required to verify these suggestive findings.

Conclusion

Class 1C AADs are an important treatment option for multiple arrhythmias. However, primarily due to the results of one >30 year old trial, in certain populations these drugs are commonly avoided. More recent studies suggest that 1C AADs may be safe to use in some groups that previously were excluded, such as those with ectopy-induced cardiomyopathy without CAD, or cardiomyopathy in the presence of an ICD, but further study is needed. Whether patients with nonobstructive CAD without ischemia, prior MI, or myocardial scar can be safely treated with 1C agents remains controversial. Given advances in acute reperfusion, medical therapy for HF, and stress imaging modalities, it is reasonable to continue to evaluate populations for whom the use of 1C AADs may be safe. The use of an ICD as an additional level of protection in such patients is a safer way to continue studying those patients previously deemed to be at higher 1C-related risk, while having the reassurance of device-based monitoring and device therapies available.

Take home points

1. Class 1C anti-arrhythmic drugs are an important treatment option in many arrhythmias and their safety profile needs to be re-examined in previously excluded patient populations.
2. Advances in reperfusion, heart failure medical treatment, and advanced imaging provides the opportunity to assess patients with non-obstructive CAD without ischemia or myocardial scar for safe use of 1C AADs.
3. Patients with an ICD offer an additional protection for further study in patients previously excluded from use of 1C AADs.

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Peter G. Pantlin: Writing – original draft. **Sahil Bharwani:** Writing – original draft, Writing – review & editing. **Mina K. Chung:** Writing – review & editing. **Daniel P. Morin:** Conceptualization, Writing – review & editing, Supervision.

Declaration of competing interest

None.

References

1. Flecainide Versus Amiodarone in the Cardioversion of Paroxysmal Atrial Fibrillation at the Emergency Department, in Patients With Coronary Artery Disease Without Residual Ischemia (FLECA-ED). <https://clinicaltrials.gov/study/NCT05549752?cond=Arrhythmia&term=1cantiarrhythmic&rank=5>; 2025.
2. Turakhia MP, Guo JD, Keshishian A, et al. Contemporary prevalence estimates of undiagnosed and diagnosed atrial fibrillation in the United States. *Clin Cardiol.* 2023;46(5):484–493. <https://doi.org/10.1002/clc.23983>.
3. Noubiap JJ, Tang JJ, Teraoka JT, Dewland TA, Marcus GM. Minimum national prevalence of diagnosed atrial fibrillation inferred from California acute care facilities. *J Am Coll Cardiol.* 2024;84(16):1501–1508. <https://doi.org/10.1016/j.jacc.2024.07.014>.
4. Tsao CW, Aday AW, Almarazooq ZI, et al. *Heart Disease and Stroke Statistics - 2023 Update: A Report from the American Heart Association.* 147. 2023. <https://doi.org/10.1161/CIR.0000000000001123>.
5. Rogers PA, Bernard ML, Madias C, Thihalolipavan S, Mark Estes NA, Morin DP. Current evidence-based understanding of the epidemiology, prevention, and treatment of atrial fibrillation. *Curr Probl Cardiol.* 2018;43(6):241–283. <https://doi.org/10.1016/j.cpcardiol.2017.06.001>.
6. Kirchhof P, Camm AJ, Goette A, et al. Early rhythm-control therapy in patients with atrial fibrillation. *N Engl J Med.* 2020;383(14):1305–1316. <https://doi.org/10.1056/nejmoa2019422>.
7. Camm AJ, Naccarelli GV, Mittal S, et al. The increasing role of rhythm control in patients with atrial fibrillation: JACC state-of-the-art review. *J Am Coll Cardiol.* 2022;79(19):1932–1948. <https://doi.org/10.1016/j.jacc.2022.03.337>.
8. Kelly JP, Devore AD, Wu JJ, et al. Rhythm control versus rate control in patients with atrial fibrillation and heart failure with preserved ejection fraction: insights from get with the guidelines—heart failure. *J Am Heart Assoc.* 2019;8(24):1–9. <https://doi.org/10.1161/JAHA.118.011560>.
9. Asad ZUA, Yousif A, Khan MS, Al-Khatib SM, Stavrakis S. Catheter ablation versus medical therapy for atrial fibrillation: a systematic review and Meta-analysis of randomized controlled trials. *Circ Arrhythmia Electrophysiol.* 2019;12(9):1–13. <https://doi.org/10.1161/CIRCEP.119.007414>.
10. Andrade JG, Wazni OM, Kuniss M, et al. Cryoballoon ablation as initial treatment for atrial fibrillation: JACC state-of-the-art review. *J Am Coll Cardiol.* 2021;78(9):914–930. <https://doi.org/10.1016/j.jacc.2021.06.038>.
11. Andrade JG, Deyell MW, Macle L, et al. Progression of atrial fibrillation after cryoablation or drug therapy. *N Engl J Med.* 2023;388(2):105–116. <https://doi.org/10.1056/nejmoa2212540>.
12. Haque H. *Guideline for the Management of Patients with Atrial Fibrillation (AFib).* 9. 2014. <https://doi.org/10.3329/uhj.v9i1.19429>.
13. Akhtar M, Breithardt G, Camm AJ, et al. Preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. The cardiac arrhythmia suppression trial (CAST) investigators. *N Engl J Med.* 1989;321(6):406–412. <https://doi.org/10.1056/NEJM198908103210629>.
14. Pantlin PG, Bober RM, Bernard ML, Polin GM, Rogers PA, Morin DP. Class 1C antiarrhythmic drugs in atrial fibrillation and coronary artery disease. *J Cardiovasc Electrophysiol.* 2020;31(3):607–611. <https://doi.org/10.1111/jce.14335>.
15. Joglar JA, Chung MK, Armbruster AL, et al. 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. 149. 2023. <https://doi.org/10.1161/CIR.0000000000001193>.
16. January CT, Wann LS, Alpert JS, et al. AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive Summary. 130. 2014. <https://doi.org/10.1161/cir.0000000000000040>.
17. Epstein AE, Hallstrom AP, Rogers WJ, et al. Mortality following ventricular arrhythmia suppression by Encainide, flecainide, and Moricizine after myocardial infarction: the original design concept of the cardiac arrhythmia suppression trial (CAST). *JAMA.* 1993;270(20):2451–2455. <https://doi.org/10.1001/jama.1993.03510200057032>.
18. Anderson JL, Platia EV, Hallstrom A, et al. Interaction of baseline characteristics with the hazard of encainide, flecainide, and moricizine therapy in patients with myocardial infarction. A possible explanation for increased mortality in the cardiac

- arrhythmia suppression trial (CAST). *Circulation*. 2012;90(6):2843–2852. <https://doi.org/10.1161/01.cir.90.6.2843>.
19. Raad M, Yogasundaram H, Oranefo J, et al. Class 1C Antiarrhythmics for premature ventricular complex suppression in nonischemic cardiomyopathy with implantable cardioverter-defibrillators. *JACC Clin Electrophysiol*. 2024;10(5):846–853. <https://doi.org/10.1016/j.jacep.2024.01.021>.
 20. Akhtar M, Breithardt G, Camm AJ, et al. CAST and beyond: implications of the cardiac arrhythmia suppression trial. *Circulation*. 1990;81(3):1123–1127. <https://doi.org/10.1161/01.CIR.81.3.1123>.
 21. Turturiello D, Cappato R. The many NOs to the use of Class IC antiarrhythmics: weren't the guidelines too strict? *Eur Hear J Suppl*. 2022;24(Si):I47–I53. <https://doi.org/10.1093/eurheartjsupp/suac073>.
 22. Lavalle C, Trivigno S, Vetta G, et al. Flecainide in ventricular arrhythmias: from old myths to new perspectives. *J Clin Med*. 2021;10(16). <https://doi.org/10.3390/jcm10163696>.
 23. Meinertz T, Lip GYH, Lombardi F, et al. Efficacy and safety of propafenone sustained release in the prophylaxis of symptomatic paroxysmal atrial fibrillation (the European Rythmol/Rytmonorm atrial fibrillation trial [ERAFT] study). *Am J Cardiol*. 2002;90(12):1300–1306. [https://doi.org/10.1016/S0002-9149\(02\)02867-9](https://doi.org/10.1016/S0002-9149(02)02867-9).
 24. Pantlin PG, Bober RM, Abi-Samra FM, et al. *A Reassessment of the Safety of 1C Antiarrhythmics in Coronary Artery Disease*. 2018.
 25. Cay Serkan, Kara Meryem, Ozcan Firat, Ozeke Ozcan, Aksu Tolga, DA& ST.. Propafenone use in coronary artery disease patients undergoing atrial fibrillation ablation. *J Interv Card Electrophysiology*. 2022;65:381–389.
 26. Kiani S, Sayegh MN, Ibrahim R, et al. The feasibility and safety of flecainide use among patients with varying degrees of coronary disease. *JACC Clin Electrophysiol*. 2023;9(7):1172–1180. <https://doi.org/10.1016/j.jacep.2022.12.021>.
 27. Faber TS, Zehender M, Krahnefeld O, Daisenberger K, Meinertz T, Just H. Propafenone during acute myocardial ischemia in patients: a double-blind, randomized, placebo-controlled study. *J Am Coll Cardiol*. 1997;29(3):561–567. [https://doi.org/10.1016/S0735-1097\(96\)00555-4](https://doi.org/10.1016/S0735-1097(96)00555-4).
 28. Hyman MC, Mustin D, Supple G, et al. Class IC antiarrhythmic drugs for suspected premature ventricular contraction-induced cardiomyopathy. *Heart Rhythm*. 2018;15(2):159–163. <https://doi.org/10.1016/j.hrthm.2017.12.018>.
 29. Zylla MM, Wolfes J, Schleberger R, et al. Use of class IC antiarrhythmic drugs in patients with structural heart disease and implantable cardioverter defibrillator. *Clin Res Cardiol*. 2024. <https://doi.org/10.1007/s00392-024-02394-6> (0123456789).
 30. Chung R, Houghtaling PL, Tchou M, et al. Left ventricular hypertrophy and antiarrhythmic drugs in atrial fibrillation: impact on mortality. *PACE - Pacing Clin Electrophysiol*. 2014;37(10):1338–1348. <https://doi.org/10.1111/pace.12426>.
 31. Leggit JC, Whitaker D. *Diagnosis and Management of Hypertrophic Cardiomyopathy: Updated Guidelines From the ACC/AHA*. 105. 2022. <https://doi.org/10.1161/CIR.0000000000000937>.
 32. Haruki S, Minami Y, Suzuki AHN. Effects of flecainide on left ventricular pressure gradient and symptoms in obstructive hypertrophic cardiomyopathy: a comparison of flecainide and disopyramide. *Heart Vessels*. 2015;30:604–610. <https://doi.org/10.1007/s00380-014-0534-3>.
 33. Towbin JA, McKenna WJ, Abrams DJ, et al. 2019 HRS expert consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. *Heart Rhythm*. 2019;16(11):e301–e372. <https://doi.org/10.1016/j.hrthm.2019.05.007>.
 34. Ermakov S, Hoffmayer KS, Gerstenfeld EP, Scheinman MM. Combination drug therapy for patients with intractable ventricular tachycardia associated with right ventricular cardiomyopathy. *PACE - Pacing Clin Electrophysiol*. 2014;37(1):90–94. <https://doi.org/10.1111/pace.12250>.