REVIEW ARTICLE

# Management of arrhythmias in heart failure. What a practicing physician should know in the current times

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## Abstract

*Arrhythmias play a significant role in the mortality and morbidity as well as hospitalizations of patients who carry a diagnosis of congestive heart failure. With improving survival in a world of novel medications and devices, an understanding of the pathophysiology and management of these arrhythmias is crucial. Majority of the basic heart failure medications such as beta--blockers, angiotensin converting enzyme inhibitors/aldosterone receptor blockers and aldosterone antagonists play a pivotal role in prevention of sudden cardiac deaths which can be a direct/indirect result of these arrhythmias. Anti-arrhythmic drugs and implantable cardioverter--defibrillators were also beneficial in selected patients. Innovative electrophysiological techniques need to be considered in special situations.* (Cardiol J 2012; 19, 6: 567–577)

**Key words: arrhythmias, heart failure**

## Introduction

Heart failure (HF) is a progressively increasing epidemic of this century with an estimated 5.2 million American (2.5%) currently being affected by it [1–3]. One in 5 adults greater than age forty will develop HF in their lifetime with an estimated direct and indirect health care burden of $33.2 billion [3, 4]. The rate of hospitalizations due to/or involving HF is progressively increasing (tripled from 1979 to 2004), making it currently the most common reason for admission in the elderly [5, 6]. Arrhythmias play a major role in these frequent hospitalizations and office visits. Sudden cardiac death (SCD), a common result of arrhythmias contribute to more than 30–50% of all-cause mortality in patients classified as New York Heart Association (NYHA) II–III [7]. Hence, an in-depth understanding of the concepts which aide in its management is of prime importance.

Majority of the abnormal heart rhythms generally tend to occur in patients with reduced left ventricular (LV) systolic function even though their presentation in HF with preserved ejection fraction (HFpEF) is not uncommon [8]. Arrhythmias encountered in HF are diverse but ventricular fibrillation (VF) and pulseless ventricular tachycardia (VT) are responsible for SCD in this cohort [9]. Atrial fibrillation (AF) and atrial flutter (AFL) are frequently associated with worse hemodynamic compromise in HF patients. Moreover, they are generally related to factors which enhance triggered

arrhythmias, when compared to patients without HF [10].

With the advances in HF management prevention of arrhythmias is gaining greater significance. However, the currently available antiarrhythmic drugs have some limitations due to their side effects profile and proarrhythmic effect. The efficacy of implantable cardioverter-defibrillators (ICD) in preventing SCD had revolutionized the management strategies in the subgroup of patients with low left ventricular ejection fraction (LVEF) [11]. However, this therapy is not free of complications such as inappropriate shocks, advisories, and driving limitations [12–15].

Hence, we made an effort to outline the currently available studies and literature in this field with intent to guide a practicing physician in managing these complex arrhythmias in HF. All the recommendations will be grounded upon evidence-based medicine. However, therapy in any particular HF patient should be individualized, since each patient presents with unique set of challenges dictated by the particular arrhythmia, symptoms, co-morbidities, genetics and personal treatment preferences.

## Current standard heart failure medications

Standard HF medications such as beta-blockers (BB), angiotensin converting enzyme (ACE) inhibitors and aldosterone receptor blockers (ARBs) have shown significant reduction in the risk of SCD. There are numerous trials done on these medications, but only a few of these directly addressed the impact on SCD. While the treatment and prevention of SCD demands specifically targeted therapy, this background standard medical therapy must not be ignored.

### Beta-blockers

The use of BB in patients with chronic HF had been associated with improved morbidity and LV function in multiple trials some of which also reported their specific impact on SCD. The MERIT-HF study showed that metoprolol succinate reduced the all-cause mortality by 34%, mortality due to sudden death by 41% and mortality due to progression of HF by 49% (Fig. 1) [7, 16]. Similarly, it was evident from the Cardiac Insufficiency Bisoprolol Study II (CIBIS–II) trial (which included equal number of ICM or NICM patients as well as NYHA III–IV) that bisoprolol reduced the risk of SCD by 41% (34% reduction total mortality) [17]. The US Carvedilol Heart Failure Study Group have shown that use of
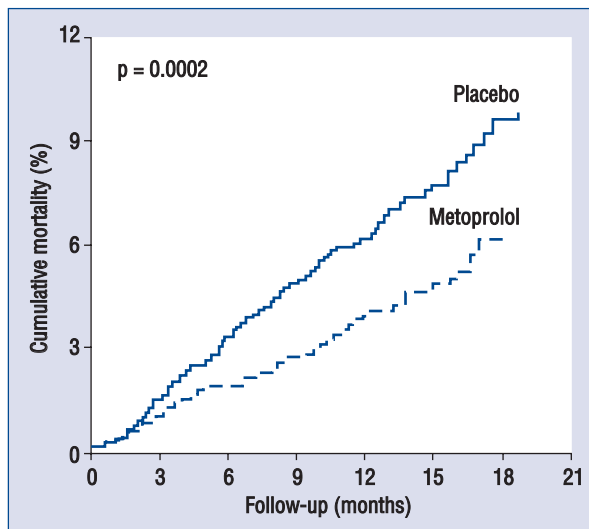


**Figure 1.** Effect of metoprolol in preventing sudden cardiac death (MERIT-HF study)

carvedilol (a non-selective blocker of beta-1 and alpha-1 receptors) for HF resulted in a 56% reduction in SCD [18]. The COMET study demonstrated a further 3% absolute reduction of SCD in carvedilol group compared to metoprolol tartrate (14% vs. 17%) [19]. Overall, there is 40–50% relative risk reduction or 4.4% absolute reduction in SCD with the use of BB.
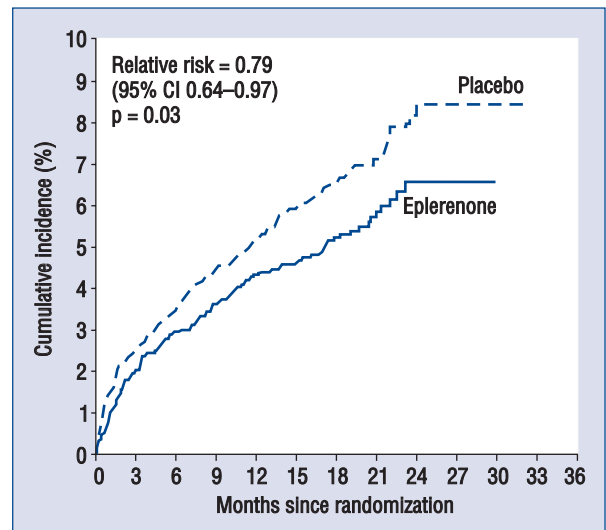
### ACE inhibitors

The importance of the effect of ACE inhibitors is very clear in light of trials highlighting their significant benefit in preventing SCD. The Vasodilator Heart Failure trial II (V-HEFT II) showed that the use of enalapril was associated with 39% reduction in SCD compared to the use of a combination of hydralazine/isosorbide dinitrate [20]. The AIRE Trial (Acute Infarction Ramipril Efficacy) showed that use of ramipril resulted in 27% reduction in SCD at 15 months vs. placebo [21]. Use of ramipril in the HOPE (Heart Outcomes Protection Evaluation) trial demonstrated a 21% reduction in SCD in patients classified as HF Stage A [22]. The TRACE (Trandolapril Cardiac Evaluation) (post AMI, EF < 35% vs. placebo at 24–50 months) showed that trandolapril did reduce SCD by 24% (Fig. 2) [23]. Overall there is 20–40% relative risk reduction of SCD with the use of ACE inhibitors.

### Angiotensin receptor blockers

Major trials involving ARBs including the Val-HeFT, CHARM and VALIANT had mixed results on mortality benefits when compared to the ACE
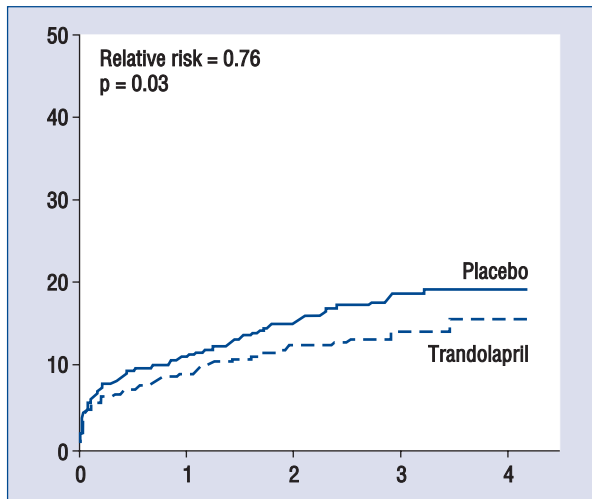
**Figure 2.** Effect of trandolapril in preventing sudden cardiac death (TRACE trail)



**Figure 3.** Sudden cardiac death in EPHESUS trial, comparing patients randomized to the selective aldosterone antagonist eplerenone versus placebo.

inhibitors and none of them specifically addressed their impact on SCD [24–26].

### Aldosterone antagonists

The RALES (Randomized Aldactone Evaluation Study) revealed that spironolactone was associated with a 29% risk reduction of SCD (overall 30% reduction at 2 years) [27]. Preventing cellular efflux and overall loss of magnesium has been proposed as the potential mechanism [28]. In addition, the EPHESUS (Eplerenone Post AMI Heart failure Efficacy trial) proved that eplerenone also carried a similar benefit with an overall reduction of SCD by 21% (Fig. 3). Necessity of aldosterone antagonism in chronic severe systolic HF as well as HF after myocardial infarction has been proven beyond doubt [29]. Of late, there is growing evidence supporting the use of aldosterone antagonists even in mild systolic HF in an effort to prevent SCD [30]. Overall, there is a 20–30% risk reduction of SCD by using aldosterone antagonists.

### Antiarrhythmic drugs

All antiarrhythmic drugs possess potential proarrhythmic toxicity and in general class IA and IC drugs are contraindicated in HF patients. Class III agents such as amiodarone, dofetilide and azimilide have a low incidence of ventricular proarrhythmias (Table 1) [31]. A recent meta-analysis showed that amiodarone reduces the risk of SCD by 29% and cardiovascular disease by 18%, and

therefore, represents a viable alternative in patients who are not eligible for or who do not have access to ICD therapy for the prevention of SCD. This drug can be considered as adjuvant therapy to ICD in preventing recurrent shocks [32]. However, amiodarone therapy is neutral with respect to all-cause mortality and is associated with a 2 and 5 fold increased risk of pulmonary and thyroid toxicity respectively [33]. Dofetilide and azimilide did not demonstrate a mortality benefit either [34–36]. In summary, there is little role for prophylactic antiarrhythmic medications for the primary prevention of SCD in patients with HF except amiodarone. The benefits of the ICDs demonstrated to be superior to the effect of antiarrhythmic drugs for primary prevention of SCD.

### Implantable cardioverter-defibrillator

ICDs have gained a lot of popularity in the management of SCD replacing the use of antiarrhythmic drugs in primary prevention and relegated their role as co-adjuvant treatment for reducing the incidence of appropriate (or inappropriate incase of AF) shocks in patients with pre-existing ICDs [32]. It uses antitachycardia pacing (ATP), cardioversion, defibrillation and pacing for bradycardia to achieve its goal. Trials that looked at primary prevention using ICDs mainly included patients with EF < 35% and NYHA class II–IV. From all these trials, it was evident that patients who have EF < 35% and experiencing NYHA class II–III symp-

**Table 1.** Summary of outcomes in major clinical trials involving antiarrhythmic drugs usage with heart failure.

| Trial | Agent studied | Enrollment criteria | Trial size/mean follow up | Results | Clinical implications | Caveats |
|---|---|---|---|---|---|---|
| CAST (1989) | Flecainide, encainide vs. placebo | Post MI (6 days–2 years) > 5 PVCs/h No EF cutoff | 1,727 pts 10 months | Increase in mortality 7.7% vs. 3.0% | Recognition of proarrhythmias | |
| CAST II (1992) | Moricizine vs. placebo | Post MI < 90 days LVEF < 40% | 1,325 pts | Terminated prematurely due to increase in mortality in the initial 14 days (RR 5.6) | Recognition of proarrhythmias | |
| SWORD (1996) | D-sotalol | LVEF < 40% Recent MI (6–42 days) or HF with remote MI NYHA II–III 93% | 3,121 pts 148 days | Terminated prematurely due to increase in mortality 5% vs. 3.1% (p = 0.006) Arrhythmic death increased by 77% | Empiric d-sotalol increases mortality in ICM | |
| GESICA (1994) | Amiodarone vs. placebo | NYHA II–IV (NYHA III 48%) Systolic dysfunction by CXR, EF, or LVEDD (mean EF 20%), NSVT | 516 pts (40% ICM) 13 months | Mortality decreased by 28% 33.5% vs. 41.4% (p = 0.02) Reduced both SCD (27%) and HF death (23%) | Amiodarone may improve survival in mixed CMP. Poor overall survival | |
| CHF-STAT (1995) | Amiodarone vs. placebo | NYHA II–IV LVEF < 40% 10 PVC/h symptomatic | 674 pts (71% ICM) 45 months | No mortality difference (30% at 2 years) No effect on SCD Trend to improved mortality in NICM (p = 0.07) | Amiodarone may improve mortality in NICM | |
| EMIAT (1997) | Amiodarone vs. placebo | LVEF < 40 (mean 30%) Recent MI NYHA I 47% | 1,486 pts 1.7 years | No mortality difference SCD reduced by 35%, 4% vs. 2.6% (p = 0.05) | Amiodarone may ↓SCD in recent MI and ICM. Possible synergy with BB | High discontinuation rates 40% vs. 21% |
| CAMIAT (1997) | Amiodarone vs. placebo | Recent MI (6–45 days) > 10 PVCs or NSVT | 1,202 pts 1.8 years | 38% decrease in SCD 18% decrease in total mortality (NS) | Amiodarone may ↓SCD and mortality in recent MI with ectopies | High discontinuation rates 36.4% vs. 25.5% |
| DIAMOND-HF (1999) | Dofetilide vs. placebo | EF < 35% Recent hospitalization NYHA II–III > 90% QTC < 460 ms (< 500 ms if BBB) Creatinine clearance > 20 CC/mL | 1,518 pts (67% ICM) 18 months | No mortality difference 41% HF admissions decreased 30% vs. 38% (p = 0.001) Dofetilide converted and maintained SR in pts with baseline AF TdP↓with ↓in dose 2.9% (75% in first 3 days) | Dofetilide is safe in HF May decrease HF admissions by preventing AF | Only 10% on BB High overall mortality Dosing protocol altered during study |
| ALIVE (2004) | Azimilide vs. placebo | Recent MI (5–21 days) EF 15–35% (mean: 29%) NYHA I 48% | 3,717 pts 1 year | No mortality difference 12% AF decreased by 50% 0.5 vs. 1.2% (p < 0.04) < 1% TdP and neutropenia | Azimilide is safe in ICM and may ↓incidence of AF | |

MI — myocardial infarction; PVC — premature ventricular contractions; EF — ejection fraction; RR — relative risk; pts — patients; LVEF — left ventricular ejection fraction; HF — heart failure; ICM — ischemic cardiomyopathy; NYHA — New York Heart Association; CXR — chest X-ray; LVEDD — left ventricular end-diastolic dimension; SCD — sudden cardiac death; BB — beta-blockers; SR — sinus rhythm; CMP — cardiomyopathy; NICM — non-ischemic cardiomyopathy; AF — atrial fibrillation; NSVT — non sustained ventricular tachycardia; BBB — bundle branch block; TdP — torsades de pointes

toms despite optimal medical therapy are at high risk of SCD and thus this population will benefit with the use of an ICD (Table 2) [37–40].

Given the significant increase in use of ICDs, a clear understanding of scenarios when they deliver therapy and management of arrhythmias in these situations is crucial.

## ICD shocks

Patients implanted with ICDs will experience shocks occasionally, which can be distressful. Attention needs to be paid to psychological and emotional consequences of ICD therapies. Some of the patients may refer a shock when in fact the device did not deliver therapy. Interrogation of the device is mandatory, not only to confirm the type of delivered therapy, but also to reassure the patient on how to react when a shock occurs. Initial evaluation of the patient who has received ICD discharges should focus upon any possible precipitants for arrhythmias, including electrolyte disturbances, myocardial ischemia/infarction, worsening HF or drug toxicities. Device interrogation will allow proper classification of the shock (appropriate vs. inappropriate).

**Appropriate shocks** is the one delivered for VT/VF. Recurrent appropriate shocks (also known as "electrical storm") need immediate medical attention, since it can lead to reduced survival [41, 42]. These patients are also at increased risk for non-SCD due to progression of ventricular dysfunction. Efforts to decrease device therapies should include programming ATP to terminate VT and the use of drugs to prevent VT in addition to the ICD [32]. ATP is a painless technique which involves detection of VT and timely delivery of rapid sequential ventricular pacing at rates, thereby overriding the underlying arrhythmia [43]. Patients who receive appropriate shocks were noted to have substantially higher ventricular arrhythmia burden and poor survival compared to patients treated with ATP-alone [44]. Adjunctive pharmacotherapy, in addition to ATP, was shown to reduce the incidence of shocks. Amiodarone along with BB reduced the incidence of shocks from 41% to 29% compared to BB alone [32]. However, celivarone a new noniodinated benzofuran derivative with an action similar to amiodarone failed to show similar benefit of reducing appropriate ICD therapies or SCD [45]. Use of sotalol was noted to decrease shock free survival by 49% compared to placebo. Azimilide was also shown to decrease the number of symptomatic arrhythmias treated by ATP/shock therapy in addition to reducing Emergency Room visits and hospitalizations [46, 47]. Recurrent arrhythmias lead-

ing to appropriate shocks should prompt adequate evaluation for undiagnosed ischemia as the culprit with a possibility of revascularization as needed. Finally, VT ablation should also be considered in order to modify the anatomical substrate, reducing the number of ICD discharges [48].

**Inappropriate shocks/atrial fibrillation/ /atrial flutter.** Sometimes ICD can misread other rhythms as VT/VF especially when the rate of the on-going arrhythmia is greater than the pre-set detection rate of the ICD. In this scenario, the ICD can deliver a shock, which is labelled as inappropriate. Inappropriate ICD shocks were associated with increased risk of all-cause mortality [42, 49]. The most common cause for these shocks are AF/ /AFL [49]. AF and HF are commonly encountered together, either condition predisposing to the other. The presence of each condition increases the morbidity and mortality associated with the other and their coexistence complicates patient management [50]. Of the 2 principal therapeutic strategies in managing AF, rate control and rhythm control, neither has been shown to be superior to the other in terms of survival, despite better quality of life and LV function in patients with sinus rhythm compared to those in AF (Table 3) [51, 52]. Patients with ICD are preferred to be in sinus rhythm, to prevent inappropriate shocks and readmissions. If a cardioversion is planned, it is recommended that all patients undergo transesophageal echocardiogram to rule out left atrial thrombus and preferred to be fully anticoagulated for at least 3 weeks prior the planned procedure. Anticoagulation has to be continued for at least 4–6 weeks after cardioversion despite restoring a normal rhythm. The use of antiarrhythmic agents after cardioversion can help maintain sinus rhythm and prevent inappropriate shocks [53]. Amiodarone along with BB reduces the incidence of inappropriate shocks from 41% to 29% compared to BB alone [54]. Digoxin can be used in patients with permanent and persistent AF as a rate control strategy in order to prevent inappropriate shocks [55].

Catheter ablation of AF is a newer technique that should be considered in a selected population of patients with HF. Atrio Ventricular Junction Ablation (AVJA) and pulmonary vein isolation are the two predominant ablation strategies used to treat AF patients who are refractory to drugs. In patients with congestive HF refractory to drugs, AVJA with biventricular pacing (BiV) for cardiac resynchronization has shown an improvement in exercise capacity and quality of life [56]. Overuse of right ventricular (RV) pacing alone in scenarios such as AVJA has a tendency to increase threshold for

**Table 2.** Summary of outcomes in major clinical trials involving devices with heart failure.

| Trial | Agent studied | Enrollment criteria | Trial size/ follow up | Results | Clinical implications | Caveats |
|---|---|---|---|---|---|---|
| MADIT I (1996) | AICD vs. standard medical treatment. Amiodaron, most frequently used antiarrhythmic | Mean EF: 26% Prior MI > 3 weeks NSVT, inducible VT not suppressed by procainamide | 196 pts 27 months | AICD reduced mortality by 54% (16% vs. 39%); p = 0.009 | AICD improves survival in pts with ICM with NSVT, EF < 35% and inducible VT | Amiodarone was discontinued in 40% |
| MUSTT (1999) | EP guided therapy (antiarrhythmic drugs with AICD if VT not suppressed or hemodynamically stable) vs. none | Mean EF: 29%, NYHA II–III 65%, CAD, NSVT (> 4 days after MI or revascularization, inducible VT | 704 pts 39 months | AICD reduced mortality by 48% vs. antiarrhythmic drugs + AICD and by 51% vs. none | EP guided antiarrhythmic drugs therapy does not ↓ mortality in ICM pts with NSVT, AICD improves survival | Protocol changed mid study. Fewer antiarrhythmic drugs needed before empiric AICD implanted |
| MADIT II (2002) | AICD vs. OPT | EF < 30% (mean: 23%) MI > 1 month NYHA evenly distributed I to III | 1232 pts 20 months | Mortality decreased by 31% (14.2% vs. 19.8%); p = 0.016 | Empiric AICD reduces mortality in ICM | No revascularization within 3 months |
| CABG/ PATCH (1997) | ICD epicardial vs. OPT in pts undergoing CABG | LVEF < 35% (mean 27%) Indication for CABG Abnormal SAECG NYHA II–III 73% | 32 months | No mortality benefit at 4 years 24% OPT vs. 27% ICD | ICD do not improve mortality in patients undergoing CABG | |
| DEFINITE (2004) | ICD vs. OPT | Mean EF 21%, NICM (mean duration 2.8 years) NYHA II–III 78% | 458 pts 29 months | Mortality decreased by 33% (12% vs. 17%); p = 0.08 SCD decreased by 79% | ICDs decrease SCD mortality in NICM with PVCs | 10% of control arm had ICD (for syncope) |
| SCD-HeFT (2005) | OPT vs. ICD vs. amiodarone | LVEF < 35%, Any CMP, NYHA II–III No ectopy specified (1/4 had NSVT) | 2521 pts 45 months | Amiodarone: no mortality benefit (HR 1.06 vs. placebo) ICD ↓ mortality by 23% Total mortality: placebo 29%, amiodarone 28%, ICD 22% | ICDs, not amiodarone, improve mortality in pts with symptomatic LV dysfunction. Similar results in ICM and NICM | |
| COMPANION (2004) | CRT-D vs. CRT-P vs. OPT | NYHA III–IV CMP (56% ICM) LVEF < 35% (mean 21%) QRS > 120 (mean 160) HF hospitalization last 12 months | 1,520 pts 12 months | Reduced mortality over OPT (19%) (CRT-P 15%, CRT-D 12%) | CRT-P improves HF morbidity in selected pts | CRT-P showed trend toward improved survival. Addition of ICD to CRT improves survival |
| DINAMIT (2005) | ICD vs. OPT | LVEF < 35% Recent MI (6–40 days) Impaired autonomic function. No NYHA IV | 30 months | Trend to increase mortality with ICDs ICDs reduced death due to arrhythmias 58% | | |

SR — sinus rhythm; AICD — automated implantable cardioverter-defibrillator; AVT — ventricular tachycardia; EP — electrophysiological study; SAECG — signal averaged electrocardiogram; CAD — coronary artery disease; OPT — optimal therapy; CABG — coronary artery bypass grafting; CTR — cardiac resynchronization therapy; HR — hazard ratio; LV — left ventricular; ICD — implantable cardioverter-defibrillator; rest abbreviations as in Table 1

**Table 3.** Summary of outcomes in trials comparing rate vs. rhythm control strategy for atrial fibrillation in patients with heart failure.

| Study | No. | NYHA | LVEF | Mortality | NYHA | Exercise tolerance | LV function | Quality of life | Rate of hospitalization | Adverse drug effects |
|---|---|---|---|---|---|---|---|---|---|---|
| PIAF | 252 | Class IV excluded | N/A | N/A | N/A | Rhythm control better | N/A | No difference | Rate control better | Rate control better |
| AFFIRM | 4060 | N/A | EF: 55% ± 14% | No difference | N/A | N/A | N/A | N/A | Rate control better | Rate control better |
| RACE | 522 | I: 49/51% II: 48/46% III: 3/3% | EF: 30% ± 10% | No difference | N/A | N/A | N/A | N/A | N/A | Rate control better |
| STAF | 209 | II: 55% | EF < 45% | No difference | No difference | N/A | No difference | N/A | Rate control better | N/A |
| HOT CAFE | 205 | I: 48/20% II: 48/57% III: 5/14% | EF: 33% ± 7% | No difference | No difference | Rhythm control better | Rhythm control better | N/A | Rate control better | N/A |
| AF-CHF | 1376 | III: 31% | EF: 27% ± 6% | No difference | N/A | N/A | N/A | N/A | Rate control better | N/A |
| CAFÉ-II | 61 | II: 80% III: 20% | Moderate systolic impairment | N/A | No difference | No difference | Rhythm control better | Rhythm control better | N/A | N/A |

Abbreviations as in Table 1

shocks as well as cause HF exacerbation [57, 58]. When compared to RV apical pacing alone, BiV pacing resulted in improvement in LVEF [59]. However, in a head-to-head comparison, pulmonary vein antrum ablation was shown to be superior to AVJA [60]. Cure of AF in patients with congestive HF resulted in more significant morphological and functional improvements than AVJA [60]. Restoration and maintenance of sinus rhythm by catheter ablation without the use of drugs in patients with congestive HF and AF significantly improve cardiac function, symptoms, exercise capacity, and quality of life (Table 4) [50, 61, 62].

## Cardiac resynchronization therapy

Patients with NYHA class III–IV who has QRS prolongation more than 120 s and EF < 35%, were noted to benefit from cardiac resynchronization therapy (CRT) when used in conjunction with ICD (CRT-D) (recent data suggest that the benefit is more pronounced when the QRS duration is longer than 150 ms) [63–65]. CRT-D in COMPANION trial showed reduction of SCD by 56% compared to CRT alone. These benefits were not reflected in NYHA class I–II patients in the RAFT trial [66]. However, a specific subgroup of patients with NYHA class I–II (LVEF ≤ 30%) and a left bundle branch block (LBBB) were noted to derive significant benefit from CRT-D with reduction in HF progression as well as a reduction in the risk of ventricular tachyarrhythmias [67]. Patients with CRT also seem to have less recurrence of AF, which is attributed to atrial reverse-remodeling and a shorter AF duration [68].

## Non-ICD population

Patients diagnosed of HFpEF and advanced HF (NYHA IV) patients where ICD is not indicated can be considered under this category. Previous studies have indicated that this cohort constitutes 1.2% of all the patients with HFpEF and are at eight times greater risk of death [69]. These patients have preserved systolic function without known scar or fibrotic tissue burden, which is considered a potential substrate for arrhythmias in the systolic HF group. They have an annual death rate of 5.6% per the observations in I-PRESERVE HFpEF cohort of which 26% are due to sudden death [70]. Multiple hypotheses have been proposed to explain this pathological process [71], however consensus has not been reached so far making treatment plans complex. The management of arrhythmias in this cohort can be divided into ventricular and supraventricular arrhythmias.

**Table 4.** Summary of outcomes in trials involving catheter ablation strategy for atrial fibrillation in patients with heart failure.

| Study | No. | Baseline NYHA class | Mean follow up (months) | Success (%) | Change in LVEF (%) | Exercise capacity | Quality of life |
|---|---|---|---|---|---|---|---|
| HSU | 58 | 2.3 ± 0.5 | 12 | 78 | 35–56 | Improved | Improved |
| Chen | 94 | Class II: 30% Class III: 68% Class IV: 2% | 14 | 73 | 36–41 | N/A | Improved |
| Tondo | 40 | 2.8 ± 0.1 | 14 | 87 | 33–47 | Improved | Improved |
| Gentlesk | 67 | N/A | 20 | 86 | 42–56 | N/A | N/A |

Abbreviations as in Table 1

## Ventricular arrhythmias

Optimization of medical treatment should include BB, ACE inhibitor/ARBs and aldosterone antagonists in order to prevent SCD. Amiodarone is a useful addition in preventing SCD in patients with advanced HF. However, its side effect profile needs to be closely monitored. Atorvastatin therapy was associated with decreased incidence of SCD in patients with advanced chronic HF [72]. However, larger on-going studies are needed to confirm this hypothesis.

## Supraventricular arrhythmias

Atrial fibrillation is by far the most frequent arrhythmia in this clinical scenario. Major progress has been made in the management of AF in the last few years with multiple new medications joining the currently existing armamentarium of amiodarone, digoxin, BB and calcium channel blockers. The ADONIS (American-Australian-African study) and European Trial EURIDIS, both controlled trials with over 600 patients each, showed that dronedarone is significantly more effective than placebo in maintaining sinus rhythm and in reducing the ventricular rate during recurrence of AF [73, 74]. Dronedarone also reduced the incidence of hospitalization due to cardiovascular events or death in patients with AF [75]. However, in patients with severe HF and LV systolic dysfunction (NYHA III–IV), treatment with dronedarone was associated with increased early mortality related to the worsening of HF [76] and hence is contraindicated. A recent study also showed increase in major cardiac events with its use in patients with permanent AF [77]. Azimilide in the ALIVE study also showed a decrease in the incidence of AF by 50% [78]. Dofetilide in DIAMOND HF was shown to be safe along with decrease in HF readmissions by 21%, which was speculated to be through decrease in the incidence of AF [79].

GISSI-HF study revealed a beneficial effect of rosuvastatin in reducing the incidence of AF in patients with HF. Larger studies are needed to provide a definitive answer to this question [80]. An ovine HF study showed chronic n-3 PUFAs use protected against adverse atrial remodeling by preventing atrial enlargement, fibrosis and conduction abnormalities leading to shorter AF episodes [81].

## Newer management strategies

A resting heart rate above 70 bpm is an independent risk factor in systolic HF [82]. If this high heart rate persists despite the maximal tolerated BB dose, isolated heart rate reduction by ivabradine may lower the rate of hospital admissions due to worsening HF [83]. Iron deficiency should be corrected independently of the presence of anemia to improve symptoms and exercise capacity. Since sodium overload play an important role in the pathophysiology of HF, the use of ranolazine which blocks late sodium current is currently being studied for reduction of cardiac arrhythmias [84].

## Arrhythmias and mechanical circulatory support

There is growing cohort of patients with advanced HF currently being managed on mechanical circulatory support. These patients are at greater risk of arrhythmias of both atrial and ventricular origin especially post surgery [85, 86]. Increase in filling pressures, mitral and tricuspid regurgitations leading to chamber remodeling and the presence of inflow cannula in the LV are some of the inciting pathophysiological mechanisms proposed to explain this surge in events. Management of atrial arrhythmias remain the same as with other HF patients.

Ventricular tachycardias in this setting are generally managed by lowering the left ventricular assist device speeds along with BB and antiarrhythmic drugs such as amiodarone, dofetilide or mexilitine [87]. However, the rates of arrhythmias usually come down farther from the implant allowing scaling down the use of antiarrhythmic drugs. In very rare situations mechanical circulatory support is considered in management of patients with refractory ventricular arrhythmias who failed multiple attempts of medical therapy and ablations.

## Conclusions

Management of arrhythmias in patients with HF remains a challenge. This field is constantly evolving and the addition of newer techniques and medications do not stop growing. This brief review was intended to provide a guide to the practicing physicians based on currently available evidence.

**Conflict of interest:** none declared

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