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# Adverse Effects of Intravenous Diltiazem for Control of Atrial Fibrillation in Patients with Heart Failure

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## Abstract

**Background:** Atrial fibrillation (AF) is the most common cardia arrhythmia requiring acute management. Calcium channel blockers should not be used in decompensated heart failure as it leads to hemodynamic compromise.

**Case Presentation:** We present 5 cases at high volume cardiac centers where patients had no history of heart failure but presented with clinical signs of heart failure and had treatment of AF with diltiazem which led to severe hemodynamic compromise. Case 1 is a 45-year-old female requiring Abiomed Impella® support after receiving diltiazem for AF. Case 2 is a 75-year-old male who developed PEA cardiac arrest and cardiogenic shock requiring inotropic therapy after AV nodal blockade to treat AF. Case 3 is a 32-year-old male requiring VA ECMO after receiving diltiazem for AF. Case 4 is a 40-year-old male who developed cardiac arrest and subsequent cardiogenic shock requiring inotropic therapy after receiving diltiazem for AF. Lastly, Case 5 is a 52-year-old male requiring VA ECMO then LVAD placement after receiving diltiazem for AF.

**Conclusions:** It is important to screen for heart failure and ventricular dysfunction prior to treatment of AF as calcium channel blockers are often first line therapy but can lead to significant hemodynamic compromise in patients with heart failure.

## Introduction

Atrial fibrillation (AF) is the most common arrhythmia requiring acute management by physicians [1-3]. AF frequently complicates heart failure. This may be particularly important in the acute care setting, where up to one-third of patients admitted with decompensated HF will be in AF at the time of presentation [4-6]. Atrial fibrillation with rapid ventricular response is also a common cause of new onset heart failure that is often reversible.

The 2014 AHA/ACC/HRS Guidelines for the Management of AF mandate rate control for symptomatic AF with rapid ventricular response (RVR) using atrioventricular nodal blockers (Class I recommendation) shown in **Figure 1** [7]. A Class III recommendation indicates that calcium channel blockers should not be used in the setting of decompensated heart failure. Recognition of acute decompensated HF is thus a critical component of the initial evaluation of AF. However, patients presenting with AF frequently receive inappropriate treatment that worsens hemodynamic decompensation. We describe five illustrative cases from high volume cardiac centres (**Table 1**).

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**Abbreviations**

AF: Atrial fibrillation; ED: Emergency department; EF: Ejection fraction; HF: Heart failure; LV: Left ventricular; OSH: Outside hospital; RVR: Rapid ventricular response; TTE: Transthoracic echocardiogram; VA ECMO: Veno-arterial extracorporeal membrane oxygenation.

| | Age (years) | Pre-existing LV dysfunction | AV nodal blocker | LVEF at Presentation | Mechanical Support for Cardiogenic Shock | Outcome |
|---|---|---|---|---|---|---|
| Case 1 | 45 | No | Diltiazem | 0.10 | Abiomed Impella® | Death |
| Case 2 | 75 | No | Diltiazem/Metoprolol | 0.35 | None | Recovery of LV function |
| Case 3 | 32 | No | Diltiazem | 0.15 | VA ECMO | Recovery of biventricular function |
| Case 4 | 40 | No | Diltiazem | 0.25 | None | Recovery of LV function |
| Case 5 | 52 | No | Diltiazem | 0.25 | VA ECMO | Death |

**Table 1:**

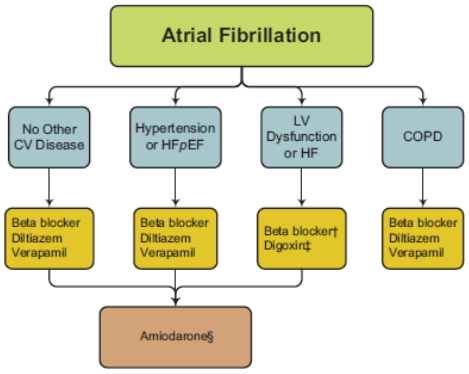


**Figure 1:**

**Case 1**

A 45-year-old Caucasian female presented to outside hospital (OSH) emergency department (ED) with shortness of breath and a near syncopal episode. She presented in AF with RVR and was treated with intravenous diltiazem leading to systolic blood pressure of 56 mmHg. Her left heart catheterization demonstrated normal coronaries and left ventricular ejection fraction (EF) 0.10-0.15. She was transferred to Vanderbilt University Medical Center Cardiac Care Unit after biventricular mechanical support with Abiomed Impella® was established. During her hospital course, her LVEF improved to 0.4-0.45 and biventricular support was weaned and removed. Endomyocardial biopsy was negative for inflammatory or infiltrative processes. Unfortunately, despite improvement in cardiac function, she developed acute hemorrhagic shock secondary to Impella® access site bleeding and died.

**Case 2**

A 75-year-old Caucasian male presented to OSH ED with lightheadedness, dyspnea with exertion, orthopnea, and chest pain. He had a medical history that included heart failure with preserved ejection fraction (LVEF 0.65) and prior coronary artery bypass surgery. On presentation, he was in atrial flutter 2:1 AV block with a heart rate of 150 bpm and an elevated troponin. He was treated with aspirin, clopidogrel, intravenous heparin, and intravenous diltiazem. He was transferred after becoming hypotensive and progressively dyspneic. After arrival with an initial blood pressure of 115/76, he was given intravenous metoprolol for rate control then subsequently became hypotensive and went into PEA cardiac arrest. After successful resuscitation, he was transferred to the cardiac intensive care unit where a pulmonary artery catheter placed demonstrated elevated right and left sided filling pressures and cardiogenic shock with cardiac index 1.4 L/min/$m^2$. He received intravenous inotropic therapy and diuretics then cardioversion to sinus rhythm. Transthoracic echocardiogram (TTE) showed LVEF of 0.35 that subsequently normalized to 0.55 one week later.

**Case 3**

A 32-year-old Caucasian male presented to the OSH ED with 3 days of progressive dyspnea. Medical history was notable for Grave's disease, paroxysmal AF with prior normal LV systolic function, and methamphetamine use. At presentation, he was in AF with RVR and received intravenous diltiazem. He was transferred to Vanderbilt University Medical Center Emergency Department where he was again given intravenous diltiazem for persistent AF with RVR. He subsequently became dyspneic, diaphoretic, and hypotensive requiring emergent intubation and vasopressor support. Initial labs were notable for elevated BNP. Cardiac catheterization showed normal coronary arteries. TTE showed LVEF of 0.15 and moderately depressed right ventricular function. He required veno-arterial extracorporeal membrane oxygenation (VA ECMO). He was successfully weaned from ECMO and had recovery of biventricular systolic function (LVEF 0.50). He was discharged home after 31 hospital days.

**Case 4**

A 40-year-old Caucasian male presented to his primary care physician with two weeks of progressive dyspnea, cough, and palpitations. He had a history of heavy alcohol consumption but no prior history of heart failure. During the visit, he was in AF with RVR and transferred to the OSH ED where he received subcutaneous enoxaparin and intravenous diltiazem. He subsequently developed ventricular fibrillation cardiac arrest and was quickly defibrillated with return of spontaneous circulation and sinus rhythm. He was intubated and placed on vasopressors, milrinone, and amiodarone then transferred to Hospital of University of Pennsylvania for management of his cardiogenic shock. TTE showed LVEF 0.25 with global hypokinesis. Subsequent evaluation showed normal coronary arteries, and endomyocardial biopsy was negative for acute inflammatory or infiltrative process. After a few days, inotropic therapy was weaned, and oral heart failure medications initiated. He was discharged home. Repeat TTE demonstrated recovery of LV function (LVEF 0.50). He was started on dofetilide for AF rhythm control then had subsequent pulmonary vein isolation for refractory AF.

**Case 5**

A 52-year-old Caucasian male presented to OSH ED with 7 days progressive dyspnea. Medical history was notable for post-operative AF after esophageal cancer resection. Upon presentation, he was in AF with RVR (heart rate 150 bpm). He was placed on an intravenous infusion of diltiazem and transferred to TriStar Centennial Hospital. On arrival, he had a blood pressure of 70/30. The diltiazem was stopped, and norepinephrine was started. He subsequently had PEA cardiac arrest and successful resuscitation. TTE demonstrated LVEF of 0.25. He was placed on VA ECMO given rapid escalation of vasopressor and inotropic doses. Subsequently, he had a left ventricular assist device placed with postoperative course complicated by right ventricular failure and interventricular cerebral haemorrhage. He transitioned to comfort care and died.

## Discussion

We present several cases managed at high volume medical centers in which the acute treatment to control ventricular rate in AF led to major morbidity and mortality. In all cases, the use of intravenous diltiazem was temporally associated with severe hemodynamic compromise. Non-dihydropyridine calcium channel blockers and/or beta blockers are recommended as first line treatment to rate control AF, but only in patients with normal biventricular systolic function. Often, measures to control heart rate are implemented before formal assessment of cardiac function is available. Thus, failure to recognize acute LV systolic dysfunction can lead to inappropriate treatment with medications that further depress systolic function leading to cardiogenic shock. As outlined in these cases, many patients with AF may have pre-existing cardiac dysfunction or manifest acute LV dysfunction with hemodynamic instability when presenting with AF and RVR. Vasodilation and acute negative inotropic effect of calcium channel blockade can precipitate acute hypotension with inadequate compensatory mechanisms to augment cardiac output.

The recognition and diagnosis of HF often rely on symptoms, physical exam, and imaging studies. Patients with acute decompensated HF often report new or worsening dyspnea with exertion, orthopnea, paroxysmal nocturnal dyspnea, fatigue, and/or lower extremity edema. However, symptoms alone cannot distinguish between presence of atrial fibrillation and true LV dysfunction. Signs of hypervolemia on physical exam include elevated jugular venous distention, presence of third heart sound, pulmonary rales, and/or lower extremity pitting edema. Chest radiograph can be helpful by demonstrating cardiomegaly, pulmonary venous congestion, and pulmonary edema. Elevated natriuretic peptide levels or worsening renal and liver function are common abnormalities seen in patients with HF [8]. However, most of these lab results are available only after urgent management interventions are implemented.

The use of point of care ultrasound has become widely used in emergency departments and hospitals and should be considered early in the evaluation process prior to treatment of AF, as it would allow for at least a crude estimate of biventricular function [9]. While limitations exist in evaluating biventricular function with tachycardia, severe dysfunction should be sufficiently evident to deter consideration of AV nodal blockers that further decrease systolic function. In cases where ventricular dysfunction is marked, other strategies for rhythm and rate control of AF should be initially considered. In the presence of hemodynamic compromise, cardioversion should be considered as first line strategy. Digoxin can be used to lower ventricular rates acutely although its rate controlling effects are often overridden by hyperadrenergic status at presentation. Intravenous amiodarone has less negative inotropic effect and can be effective in rate control. However, the polysorbate used as carrier in the intravenous preparation can cause acute vasodilation and hypotension [7,10].

These cases demonstrate the importance of evaluating for heart failure and LV systolic dysfunction in patients presenting with AF. Particularly poignant is the possibility that some patients who would otherwise recover good systolic function without chronic heart failure may instead suffer death or serious complications from the acute effects and resuscitative therapies precipitated by injudicious use of

intravenous diltiazem in the emergency setting.

## Conclusion

Patients presenting with acute symptoms and AF may have depressed ventricular systolic function that can potentially worsened using non-dihydropyridine calcium channel blockers. It is important to screen for severe cardiac dysfunction before addressing rapid ventricular response with therapies that could precipitate hemodynamic collapse.

## Declarations

**Ethics approval and consent to participate:** Not applicable

**Consent for publication:** Not applicable

**Availability of data and material:** Not applicable

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