

# Suppression of Non-Sustained Ventricular Tachycardia with Ranolazine: A Case Report

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## ABSTRACT

**Background:** Ranolazine is a new anti-anginal agent that inhibits abnormal late sodium currents, indirectly causing a decrease in diastolic cardiomyocyte calcium levels. This produces an energy-sparing effect and stabilizes cardiac membranes. Ranolazine has been shown to be a potent inhibitor of triggered activity in the experimental setting.

**Methods:** This case report describes the dramatic anti-arrhythmic effects of ranolazine in a patient with highly symptomatic complex ventricular ectopy, including non-sustained ventricular tachycardia (NSVT). Cardiac ischemia and left ventricular systolic dysfunction were ruled out by cardiac catheterization. After failing standard treatment, we initiated ranolazine therapy.

**Results:** Ranolazine was effective in suppressing ectopic ventricular activity and completely suppressed NSVT.

**Conclusions:** Further research on the anti-arrhythmic properties of ranolazine in the clinical setting is needed.

## INTRODUCTION

Malignant arrhythmias are a leading cause of sudden cardiac death in patients with ischemic heart disease, as well as those without it.<sup>1</sup> The mechanisms of arrhythmias are varied and include enhanced automaticity, reentry, and triggered activity from after depolarizations.<sup>2-6</sup> Triggered activity may be the most important arrhythmia mechanism in patients without cardiac ischemia.<sup>3,5-6</sup> Ranolazine is a novel anti-anginal agent that inhibits the abnormal late inward sodium (Na<sup>+</sup>) current in ventricular cardiomyocytes.<sup>7</sup> This produces an energy-sparing effect and indirectly decreases diastolic

intracellular cardiomyocyte calcium (Ca<sup>++</sup>) levels. This effect also improves membrane stability.<sup>7</sup> Ranolazine has also been shown to be a potent inhibitor of afterdepolarizations produced by a number of mechanisms.<sup>8-10</sup> As such, it could prove to have anti-arrhythmic properties in some arrhythmic situations, particularly those mediated by after depolarizations. In this case report, we describe the dramatic anti-arrhythmic effects of ranolazine in a patient with symptomatic non-sustained ventricular tachycardia (NSVT).

## CASE

A previously healthy 79-year-old woman presented to our emergency department (ED) with a 2-week history of heart palpitations and episodes of lightheadedness, with mild intermittent chest heaviness during her palpitations. Her medical history included a history of paroxysmal supra-ventricular tachycardia (PSVT) due to AV nodal re-entrant tachycardia, which had responded well to catheter-based radio frequency ablation several years earlier. She was concerned about a possible recurrence of PSVT given her recurrent palpitations and lightheadedness. Concomitant medications included omeprazole on an as-needed basis for intermittent dyspepsia, and a few over-the-counter supplements: coenzyme Q10, multiple vitamins and fish oil.

The patient's physical exam was unremarkable except for an irregular cardiac rhythm. All routine laboratory studies, including those for electrolytes, cardiac enzymes, and thyroid function, were normal. Her electrocardiogram (ECG) (Figure 1) showed very frequent unipolar premature ventricular contractions (PVCs). Other than frequent PVCs, her ECG, as well as her 2-dimensional echocardiogram (echo) and Doppler study were normal. Because she had normal left ventricular function by echo and no evidence of an acute coronary syndrome, she was discharged from the ED after a 48-hour Holter monitor was placed.

Two days later, the patient was called back to the hospital for an urgent direct admission immediately

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after the Holter monitor technician processed the study. This monitor demonstrated very frequent PVCs accounting for 12% of all QRS complexes. More importantly, frequent runs (86 runs) of NSVT (3-38 beats in duration) were observed, which included a 38-beat episode (Figure 2).

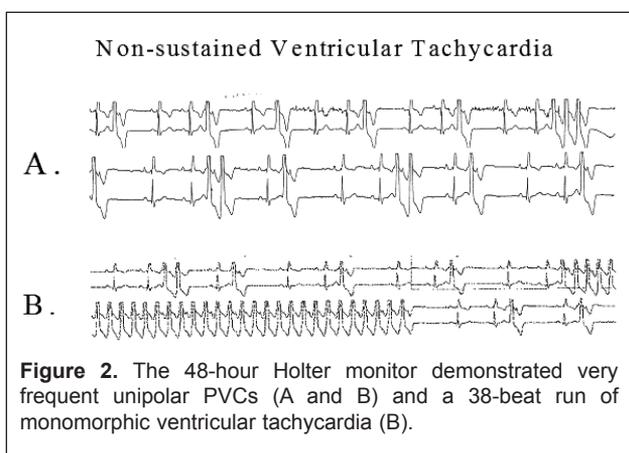
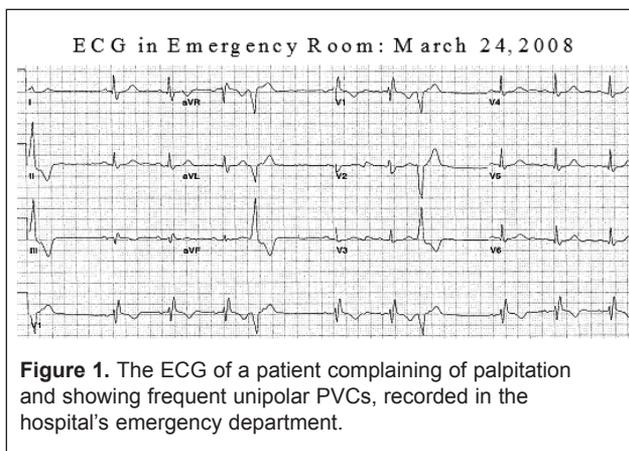
### Hospital Course

As before, the patient presented with symptoms of intermittent lightheadedness, palpitations, and mild chest pressure. Her exam was significant only for frequent PVCs. The patient was given 50 mg metoprolol twice a day and scheduled for cardiac catheterization to exclude an ischemic cause for her NSVT. The metoprolol had no apparent effect on the ventricular ectopy after approximately 24 hours. The following day, her catheterization revealed normal coronary arteries and normal left ventricular function.

In the setting of normal left ventricular function, normal coronary arteries, and lack of response to beta blockade, triggered activity was suspected as the mechanism for the patient's ventricular arrhythmias. Thus, metoprolol was discontinued, and ranolazine was initiated at 1000 mg twice daily. An ECG was recorded immediately prior (Figure 3 A) and 24 hours later (Figure 3 B). Within 24 hours of ranolazine initiation, there was near complete suppression of all ventricular ectopy (<1 PVC/hour) and complete suppression of all repetitive beats. The patient had complained about constipation, so the dose of ranolazine was decreased to 500 mg twice a day before she was discharged. A follow-up 48-hour Holter monitor performed 3 days after discharge confirmed the dramatic suppression of the ventricular ectopy, with PVCs accounting for less than 1% of all the QRS complexes. The patient's NSVT was completely suppressed. The patient continues to take ranolazine without side effects for this arrhythmia and has remained asymptomatic for more than 15 months. Because of this therapy's marked efficacy and tolerability, both the physician and the patient are reluctant to discontinue it.

### DISCUSSION

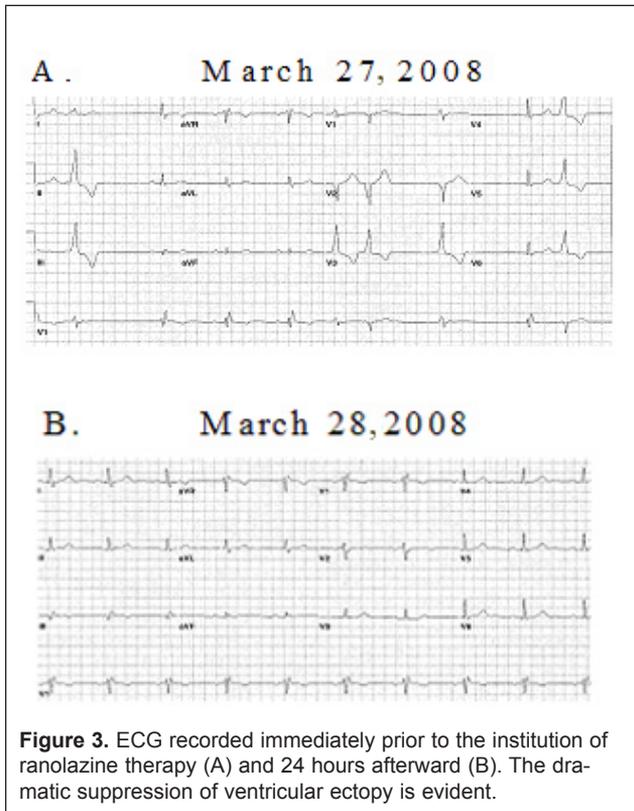
This case report demonstrates that ranolazine may have very potent anti-arrhythmic properties and may prove to be a very useful agent in treating certain arrhythmias, depending on the mechanism involved. The fact that ventricular ectopy was so prevalent before initiation of ranolazine and abated so rapidly after ranolazine was instituted (Figure 3) strongly suggests that ranolazine was the reason for suppression of the patient's ventricu-



lar arrhythmias. The time course of this effect is consistent with the pharmacokinetics of this agent.<sup>11</sup>

Although the present case report does not allow us to prove the mechanism of this anti-arrhythmic effect, it is likely due to the ability of this agent to markedly decrease triggered activity. In tissue-bath preparations, ranolazine reduces the repetitive extra systoles produced by triggered activity from a number of different causes.<sup>8-10</sup> Additionally, we have previously shown that ranolazine was effective in abolishing sustained ventricular tachycardia in a patient with cardiomyopathy and normal coronary arteries.<sup>12</sup> Triggered activity due to Na<sup>++</sup> and Ca<sup>++</sup> overload is believed to be a major cause of the malignant arrhythmias in patients with nonischemic cardiomyopathy.<sup>3,5-6</sup>

The anti-arrhythmic effects of ranolazine were recently confirmed clinically in patients with ischemic heart disease. In a study of 6560 patients surviving an acute coronary syndrome, the MERLIN Trial investigators noted that ranolazine was associated with a significant reduction in a variety of atrial and ventricular arrhythmias as recorded on prolonged Holter monitoring.<sup>13</sup> This case report, as well as our prior report about



**Figure 3.** ECG recorded immediately prior to the institution of ranolazine therapy (A) and 24 hours afterward (B). The dramatic suppression of ventricular ectopy is evident.

a patient with cardiomyopathy,<sup>2</sup> suggests that ranolazine can have potent anti-arrhythmic effects and prove useful in treating symptomatic arrhythmias in nonischemic patients as well. Furthermore, these effects occur at the same doses that are used to treat angina.

In summary, we describe the second patient in which ranolazine was used specifically for its anti-arrhythmic properties to treat symptomatic ventricular arrhythmias. In both cases, coronary artery disease was not present, indicating that this anti-arrhythmic effect occurs independent of its anti-ischemic affect. Finally, it should be noted that this is an unusual and off-label use of ranolazine. Further studies are necessary before the safety and efficacy of ranolazine as a useful anti-arrhythmic agent may be established.

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