## Preventing Postpericardiotomy Syndrome with Colchicine: Results from the COPPS Study

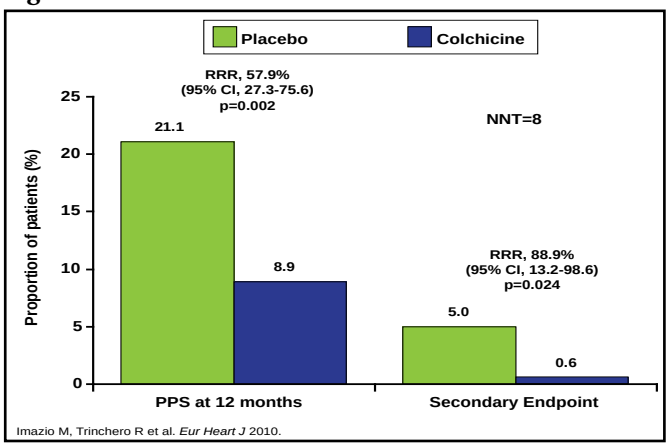
Colchicine therapy is safe and effective for the prevention of postpericardiotomy syndrome (PPS) and may decrease the risk of postsurgical PPS development by >50%. PPS, a complication that often follows cardiac surgery, occurs in 10% to 45% of patients, and though some treatment approaches, such as NSAIDs, colchicine, and corticosteroids, may be used, optimal treatment for PPS prevention has yet to be established [Finkelstein Y et al. *Herz* 2002]. Massimo Imazio, MD, Maria Vittoria Hospital, Torino, Italy, discussed results from the COlchicine for the Prevention of the Postpericardiotomy Syndrome (COPPS; NCT00128427).

COPPS was a multicenter, double-blind study that included 360 patients who were randomized to colchicine (n=180; 1.0 mg twice daily for 1 day followed by 0.5 mg twice daily for 1 month for patients ≥70 kg or 0.5 mg twice daily for 1 day followed by 0.5 mg for 1 month for patients <70 kg) or placebo (n=180) on the third postoperative day. PPS was defined as the presence of at least two of the following criteria: fever that lasted beyond the first postoperative week without evidence of systemic or focal infection, pleuritic chest pain, friction rub, pleural effusion, and new or worsening pericardial effusion. The primary efficacy endpoint was the incidence of PPS at 12 months, and the secondary endpoint was the combined rate of disease-related hospitalization, cardiac tamponade, constrictive pericarditis, and relapses. The groups were well matched at baseline.

At 12 months, there was a significant reduction in the incidence of PPS among patients who were treated with colchicine compared with placebo (RRR, 57.9%; 95% CI, 27.3 to 75.6; p=0.002; NNT=8; Figure 1). The rate of the composite secondary endpoint was also lower in the colchicine group compared with placebo (0.6% vs 5.0%, respectively; p=0.024). The adverse event profiles were similar for both groups, with no severe side effects reported across the study population. The most common side effects were gastrointestinal in nature for both groups.

This study demonstrated that colchicine halves the risk of PPS following cardiac surgery compared with placebo. This therapeutic strategy appears to be safe and effective for the prevention of postsurgical PPS. It is important to note that the diagnostic criteria for PPS were nonspecific and allowed for the detection of milder forms of pleuropericardial involvement following cardiac surgery, because at present, there are no guidelines or consensus documents on the diagnosis of PPS. Therefore, further study is warranted to determine the strength of these data.

**Figure 1. COPPS Trial: Main Results.**

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Further reading: Imazio M et al. *European Heart J* 2010.

## DANPACE: Dual-Chamber Pacing Preferred in Sick Sinus Syndrome

Dual-chamber pacing improved long-term outcomes compared with single-chamber pacing in patients with sick sinus syndrome (SSS) in the long-term Danish Multicenter Randomized Study on AAIR Versus DDDR Pacing in Sick Sinus Syndrome (DANPACE; NCT00236158) study and should be the preferred pacing mode in these patients, according to investigators from the DANPACE study.

Bradycardia can be treated with several types of pacing, including rate-adaptive single-lead atrial pacing (AAIR), rate-adaptive ventricular (VVIR) pacing, and rate-adaptive dual-chamber pacing (DDDR). However, after VVIR pacing was shown to increase the risk of atrial fibrillation (AF) compared with physiological pacing in patients with SSS [Andersen HR, Nielsen JC, Thomsen PE et al. *Lancet*. 1997], AAIR and DDDR became the standard options for controlling bradycardia in SSS, said Jens Cosedis Nielsen, MD, PhD, Aarhus University Hospital, Skejby, Denmark. The Danish trial is the first large, multicenter, randomized trial that is designed to compare long-term outcomes that are associated with AAIR and DDDR pacing in patients with SSS.

In DANPACE, 1415 patients with SSS were randomly assigned to receive AAIR devices (n=707) or DDDR devices (n=708). The primary endpoint was all-cause mortality. Secondary endpoints included AF, stroke, heart failure hospitalization, and pacemaker reoperation.

After a mean follow-up of 5.4 years, the all-cause mortality rates were similar in the AAIR and DDDR groups (p=0.53). Patients in the AAIR and DDDR groups also had similar rates of stroke (p=0.56), diuretic use (p=0.89), and heart failure hospitalization (p=0.90).

Patients in the DDDR group had a lower rate of paroxysmal AF than those in the AAIR group (p=0.024) and were less likely to require pacemaker reoperation (p<0.001). As illustrated by Kaplan-Meier survival curves, these benefits, favoring dual-chamber pacing, were apparent within 12 months of randomization.

In a multivariate analysis, AAIR was associated with a 24% higher rate of paroxysmal AF (HR, 1.24; 95% CI, 1.01 to 1.52; p=0.042) and a 2-fold increase in the risk of pacemaker reoperation (HR, 2.00; 95% CI, 1.54 to 2.61; p<0.001) compared with DDDR.

A similar percentage of atrial beats were paced in the AAIR and DDDR groups (58% vs 59%; p=0.52). In the DDDR group, 65% of the ventricular beats were paced. DDDR pacing with an AV interval ≤220 milliseconds was the preferred pacing mode for patients with SSS.

DANPACE investigators concluded that AAIR pacing should no longer be used in patients with SSS, but other experts disagreed. DANPACE discussant Carina Blomström-Lundqvist, MD, Uppsala University, Uppsala, Sweden, said that AAIR pacing may have an important role in some patients with SSS, such as those with sinus dysfunction and no suspected abnormality of AV conduction. Additional studies with long-term efficacy and safety outcomes may help to determine the optimal pacing mode for different subgroups of patients with SSS.

## ARB Therapy in the Setting of Paroxysmal AF: Results from the ANTIPAF Trial

Olmesartan does not reduce the incidence of atrial fibrillation (AF) episodes among patients with paroxysmal AF without structural heart disease. Andreas Goette, MD, Department of Cardiology, St. Vincenz-Hospital, Paderborn, Germany, discussed findings from the Angiotensin II Antagonist in Paroxysmal Atrial Fibrillation (ANTIPAF; NCT0098137) trial. ANTIPAF was conducted by the German Competence Network on Atrial Fibrillation (AFNET), an interdisciplinary national research network that is funded by the German Federal Ministry of Education and Research.

AF, the most common cardiac arrhythmia, is a progressive illness that is characterized by increased episodes over time. While angiotensin II antagonists (ARBs) may potentially reduce the incidence of AF without the side effects that are often seen with other antiarrhythmic therapies, this suggestion is based on numerous meta-analyses and has not yet been supported by focused prospective trial data. ANTIPAF was designed to evaluate the impact of the ARB olmesartan on episodes of paroxysmal AF in a prospective, randomized, double-blind, placebo-controlled trial.

ANTIPAF included 425 patients with documented paroxysmal AF (≤6 months), stratified by β-adrenoceptor antagonist use, who were randomized to receive either olmesartan 40 mg daily (n=214) or placebo (n=211) over the course of 12 months. The groups were well matched at baseline. Those who took ARBs and ACE inhibitors, or Class I and III antiarrhythmic drugs prior to randomization and those who initiated β-blocker therapy after randomization were excluded from participation in this study. The primary endpoint was percentage of days with documented episodes of paroxysmal AF during 12 months of follow-up (defined as the number of days with PAF/number of days with at least one readable Tele-ECG recording). A total of 207 Tele-ECGs per patient were performed, amounting to 1.12 Tele-ECGs per patient and follow-up day. Secondary endpoints included time to first recurrence of documented AF, time to persistent AF, time to prescription of "recovery medication" (amiodarone), quality of life measures, percentage of days with documented paroxysmal episodes or suspected persistent AF after 90 days of therapy, number of hospitalizations for cardiovascular (CV) reasons, number of unscheduled outpatient visits for CV reasons, and number of cerebrovascular events.

There was no significant difference between olmesartan and placebo for AF burden, as determined by the primary endpoint. The cumulative incidence of AF recurrence and persistent AF was also similar between the two groups. The cumulative event rates at 12 months, as measured by the secondary outcomes, were comparable for both groups. However, time to prescription of "recovery medication" favored olmesartan (HR, 0.41; 95% CI, 0.186 to 0.904; p=0.0224). The rate of serious adverse events was similar for both groups.

Olmesartan did not reduce the number of AF episodes in this cohort compared with placebo. Therefore, ARB therapy may not be appropriate as first-line treatment for paroxysmal AF in the absence of other indications. The only intergroup difference that was noted within ANTIPAF was the time to prescription of amiodarone for recovery treatment. All other measures were comparable between olmesartan and placebo, suggesting that previous meta-analysis findings may have been due to variables that were independent of ARB treatment.