week 52. Hospitalization due to worsening HF was significantly reduced with FCM compared with placebo.

The secondary end points of self-reported Patient Global Assessment (PGA) score and NYHA class improved early and were sustained at week 52. The odds ratio for PGA was >1 at week 6 and week 52 with FCM vs placebo (P=.29 and P=.001, respectively). The odds ratio for change in NYHA class was >1 at week 6 and week 52 (P=.067 and P<.001, respectively).

Dr Ponikowski concluded that treatment of iron deficiency with FCM in symptomatic HF patients resulted in sustained improvement in functional capacity, symptoms, and quality of life and resulted in a reduction in HF hospitalizations.

POPE-2: No Benefit With Colchicine to Reduce Persistent Postoperative Pericardial Effusion

Written by Mary Mosley

Postoperative pericardial effusion (POPE) is present within the first 7 days after cardiac surgery in 50% to 80% of patients, and the risk for early cardiac tamponade ranges from 0.5% to 1%. There is no drug that can treat this local hemorrhagic complication, stated Philippe Meurin, MD, Les Grands Prés, Villeneuve Saint Denis, France. From day 8, patients with POPE are at risk for persistence of the effusion, with the risk for tamponade dependent on its size. Although nonsteroidal anti-inflammatory drugs do not reduce persistent POPE, it is unknown whether the anti-inflammatory drug colchicine (COL) might be effective. COL has been shown to be effective in treating other pericardial conditions, including acute pericarditis [Imazio M et al. *N Engl J Med.* 2013] and postpericardiotomy syndrome [Imazio M et al. *Eur Heart J.* 2010].

The Colchicine Treatment for Post-operative Pericardial Effusion [POPE-2; NCT01266694] was a double-blind, placebo-controlled study to evaluate whether COL could reduce the volume of POPE. Conducted at 10 cardiac rehabilitation centers in France, the trial randomized 197 patients with moderate to large pericardial effusion (ie, grades II, III, and IV) on admission echocardiography (8 to 30 days after surgery) to a 14-day treatment course of placebo (n=99) or COL (n=99). The dose of COL was adjusted according to patient weight; all patients received 1 mg/day, except those who weighed ≥70 kg, who received an additional 1 mg on day 1. The primary end point was the change in mean pericardial effusion grade (MPEG) in the COL arm relative to placebo.

The patients has a mean age of 65 years, and most were men, 89% and 84% of the placebo and COL groups, respectively. At baseline, both groups were similar for the proportion of patients with grade II, III, and IV effusions and for MPEG.

Table 1. Primary End Point of Decrease in Mean Pericardial Effusion Grade

	Placebo Group	Colchicine Group	Mean Change (95% CI)	*P* Value
Baseline	2.9 ± 0.8	3.0 ± 0.8	NA	NA
Final	1.8 ± 1.3	1.7 ± 1.2	NA	NA
Change	−1.1 ± 1.3	−1.3 ± 1.3	−0.19 (−0.55 to 0.16)	.23

NA, not applicable.

The difference in the reduction of MPEG between the arms was not significant (Table 1).

Development of cardiac tamponade after 14 days of treatment did not significantly differ (log-rank P=.801) between the arms; neither did the requirement for pericardial drainage within 6 months (log-rank P=.202). The proportion of patients who had a ≥1-MPEG decrease was nonsignificant between the arms (67% and 74% of the placebo and COL groups, respectively; P=.27), as was the presence of atrial fibrillation at the end of the study (12% and 15%, respectively; P=.51). The reductions in the width of the echo-free space were similar at –4.7 and –5.8 mm in the placebo and COL groups, respectively (P=.23).

Furthermore, no difference was found with COL in any of the prespecified subgroups, including C-reactive protein level ≥30 mg/L and receiving an oral anticoagulant or in the per protocol analysis.

The POPE-2 study confirmed that a moderate to large POPE persisting >7 days is a serious condition, with cardiac tamponade occurring in 13 patients (6.6%) and pericardial drainage within 6 months occurring in 22 patients (11.2%) across both arms. COL did not provide any benefit either by echocardiography or on clinical events.

COPPS-2: Colchicine Reduced PPS in Cardiac Surgery Patients

Written by Mary Mosley

Colchicine (COL) administered perioperatively in patients undergoing cardiac surgery reduced the incidence of the primary end point of postpericardiotomy syndrome (PPS) compared with placebo. Secondary end points of postoperative atrial fibrillation (POAF) and postoperative pleural and pericardial effusions were not significantly reduced in an investigator-initiated,

double-blind, randomized clinical trial conducted at 11 centers in Italy. Massimo Imazio, MD, University of Torino, Torino, Italy, presented the results of the Colchicine for Prevention of the Post-pericardiotomy Syndrome and Post-operative Atrial Fibrillation trial [COPPS-2; Imazio M et al. *JAMA*. 2014].

The COPPS-1 trial showed that COL started 3 days after cardiac surgery, compared with placebo, reduced the primary end point of PPS at 12 months ($P = .002$ vs placebo) and reduced secondary end points of POAF, disease-related hospitalizations, cardiac tamponade, constrictive pericarditis, and recurrent pericarditis [Imazio M et al. *Eur Heart J* 2010]. Because most POAF events occur in the first postoperative days (days 1 to 3), the authors supposed that an early administration of COL before surgery could improve its efficacy. The COPPS-2 trial was conducted to confirm the findings of COPPS-1 as well as determine whether oral COL might be even more effective at reducing PPS, POAF, and pleural and pericardial effusions if started prior to surgery.

Patients aged >18 years undergoing cardiac surgery were randomized to placebo (n=180) or COL (n=180; 0.5 mg BID for patients ≥70 kg or 0.5 mg once daily for patients <70 kg). COL was started 48 to 72 hours before surgery and continued until 1 month after surgery. Adherence to study medication was assessed by pill counts; unconscious patients were administered medication via a nasogastric tube. Follow-up continued for 3 months after surgery. Key exclusion criteria were current atrial fibrillation, being a candidate for cardiac transplantation, serum creatinine >2.5 mg/dL, and a contraindication to COL.

The mean age of the patients was 67.5 years, and most were men (68.9%). Surgery was valvular alone in 36.4%, coronary artery bypass grafting alone in 33.9%, aortic surgery alone in 6.1%, and combinations of these in 23.6% of patients.

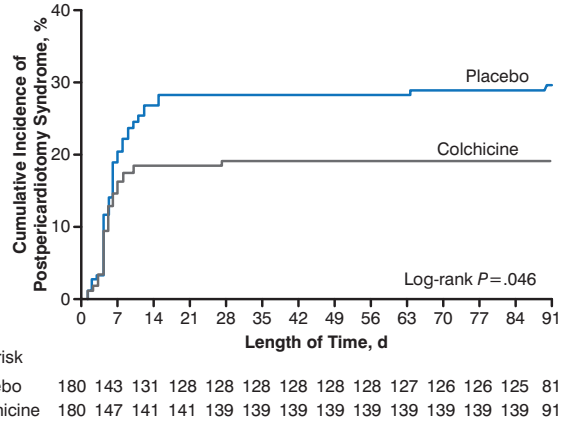
The primary end point of PPS occurred in 35 patients (19.4%) in the COL group and 53 patients (29.4%) in the placebo group (Figure 1). The absolute difference between the groups was 10% (95% CI, 1.1% to 18.7%), with a number needed to treat (NNT) of 10 to prevent 1 occurrence of PPS.

The secondary end point of POAF occurred in 33.9% of the COL group and 41.7% of the placebo group (absolute difference, 7.8%; 95% CI, –2.2% to 17.6%). Postoperative pericardial or pleural effusion occurred in 57.2% and 58.9% of the COL and placebo groups, respectively, in the intention-to-treat analysis.

Drug discontinuation was high at 21.7% and 17.8% of the COL and placebo groups, respectively. The difference between the groups was due largely to gastrointestinal intolerance (Table 1). Because of an expectation of significant discontinuation rates, a prespecified on-treatment analysis was performed, which demonstrated a reduction in POAF with COL compared with placebo (27% of 141 patients vs 41.2% of 148 patients, respectively); the absolute difference was 14.2% (95% CI, 3.3% to 24.7%) with an NNT of 7. It is likely that a lower drug discontinuation rate would have demonstrated a significant impact of COL on POAF in the intention-to-treat analysis.

In light of COL-induced gastrointestinal effects and strict trial exclusion criteria, careful consideration must be taken to select appropriate patients if COL is to be used as treatment for the prevention of PPS.

Figure 1. Kaplan-Meier Rate of PPS in Patients Receiving COL Versus Placebo



COL, colchicine; PPS, postpericardiotomy syndrome.

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Table 1. Safety Profile of COL in the COPPS-2 Trial

Feature	Placebo (n = 180)	COL (n = 180)	Absolute Difference (95% CI)
Adverse events	21 (11.7%)	36 (20.0%)	8.3 (0.76 to 15.9)
Gastrointestinal intolerance[a]	12 (6.7%)	26 (14.4%)	7.7 (1.4 to 14.3)
Hepatotoxicity[b]	2 (1.1%)	1 (0.6%)	0.50 (–2.1 to 3.4)
Drug discontinuation	32 (17.8%)	39 (21.7%)	3.9 (–4.4 to 12.5)

COL, colchicine.

[a]Diarrhea, nausea, cramping, abdominal pain, or vomiting.

[b]Any elevation of aminotransferase levels above the normal reference range.