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ORIGINAL ARTICLE

Colchicine for postoperative pericardial effusion: a multicentre, double-blind, randomised controlled trial

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ABSTRACT

Objectives Pericardial effusion is common after cardiac surgery. Growing evidence suggests that colchicine may be useful for acute pericarditis, but its efficacy in reducing pericardial effusion volume postoperatively has not been assessed.

Methods This randomised, double-blind, placebo-controlled study conducted in 10 centres in France included 197 patients at high risk of tamponade (ie, with moderate to large-sized persistent effusion (echocardiography grades 2, 3 or 4 on a scale of 0–4)) at 7–30 days after cardiac surgery. Patients were randomly assigned to receive colchicine, 1 mg daily (n=98), or a matching placebo (n=99). The main end point was change in pericardial effusion grade after 14-day treatment. Secondary end points included frequency of late cardiac tamponade.

Results The placebo and the colchicine groups showed a similar mean baseline pericardial effusion grade (2.9 ±0.8 vs 3.0±0.8) and similar mean decrease from baseline after treatment (−1.1±1.3 vs −1.3±1.3 grades). The mean difference in grade decrease between groups was −0.19 (95% CI −0.55 to 0.16, p=0.23). In total, 13 cases of cardiac tamponade occurred during the 14-day treatment (7 and 6 in the placebo and colchicine groups, respectively; p=0.80). At 6-month follow-up, all patients were alive and had undergone a total of 22 (11%) drainages: 14 in the placebo group and 8 in the colchicine group (p=0.20).

Conclusions In patients with pericardial effusion after cardiac surgery, colchicine administration does not reduce the effusion volume or prevent late cardiac tamponade.

Clinical trial reg No NCT01266694.

After cardiac surgery, the incidence of pericardial effusion is high (50–85%) and it peaks at the end of the first postoperative week.[1–3] Cardiac tamponade occurs in 1–2% of patients. Early tamponade (occurring during the first seven postoperative days) is due to surgical bleeding; it is usually easily diagnosed and treated because it occurs while the patient is still in the intensive care unit. However, most tamponade cases occur later than 7 days after surgery[3–5] and may develop slowly without clear-cut clinical signs in asymptomatic patients. This is a concern because, at this time, patients have often been discharged from the hospital.

Persistence of a moderate to important effusion more than 7 days after surgery is a powerful predictor of late tamponade[6] and of rehospitalisation.[7] It is sought that inflammation plays a part in these late postoperative pericardial effusion events. Indeed, the fluid of about 15% of these late effusions is lemon-yellow,[5] and late tamponade seems to occur more often in patients with postpericardiotomy syndrome (PPS).[8] Colchicine is an anti-inflammatory drug efficient for the treatment of acute pericarditis.[9] Furthermore, if it is administered before or within 3 days after surgery this drug helps prevent PPS, an inflammatory postinjury pericardial syndrome that usually mimics acute pericarditis, often involves a small pericardial effusion and whose evolution is usually spontaneously benign.[10 11] However colchicine has not been tested for actual postoperative pericardial effusions; therefore whether the drug reduces their volume and prevents late cardiac tamponade is not known. Furthermore, a high rate of gastrointestinal adverse effects and drug discontinuation limit the clinical applicability of colchicine in early perioperative care.[11] We performed a randomised, double-blinded, placebo-controlled, parallel-groups study comparing the efficacy of colchicine and placebo in reducing the volume of postoperative pericardial effusion in patients with postoperative effusion persisting more than 7 days after heart surgery.

METHODS

Patients

This randomised, double-blinded, placebo-controlled, parallel-group trial was performed in 10 centres in France. Patients were screened between 1 April 2011 and 1 March 2013. Eligible patients were of either sex, aged 18 years or older, who were hospitalised in a postoperative cardiac rehabilitation centre for <30 days after cardiac surgery and showed pericardial effusion ≥grade 2 (ie, loculated effusion >10 mm or circumferential effusion of any size (table 1)) on the first transthoracic echocardiography (TTE_1) performed more than 7 days after surgery.

Exclusion criteria were patient refusal to participate, pregnancy, allergy to colchicine, known myopathy, renal failure (defined by a serum creatinine level ≥250 µmol/L and/or creatinine clearance <30 mL:min/kg as calculated by the Cockroft and

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Table 1 Echo-free space width between the pericardium and myocardium used to determine the grade of pericardial effusion

Grades	Loculated pericardial effusion (mm)	Circumferential pericardial effusion (mm)
0	–	–
1 (minimal)	1–9	–
2 (moderate)	10–14	1–9
3 (medium)	15–19	10–14
4 (large)	≥20	≥15

Gault formula[12]) chronic use of colchicine, renal or heart transplantation or correction of congenital heart anomalies, cardiac surgery >30 days before TTE_1, pure right retroauricular haematoma, and finally, compressive pericardial effusion requiring immediate pericardial drainage.

Study design

All patients underwent TTE at arrival in the postoperative cardiac rehabilitation centre. If they met the inclusion criteria, they were included and underwent a laboratory exam on the same day. An independent statistician generated a randomisation list with permuted blocks of two and four and stratified by centre using online randomisation software. Assignment to therapy, placebo or colchicine was random. After the allocation, each patient received the appropriate study dosage (colchicine, 1.0 mg twice daily for the 1st day followed by a maintenance dose of 1 mg daily for patients ≥70 kg and 1 mg per day without a loading dose for patients <70 kg, or matching placebo) for 14 days. Double-blinding was achieved by packaging the colchicine and placebo as identical pink pills in identical boxes (blister packs). Patients underwent a mandatory second TTE (TTE_2) and a laboratory test after 14 days of treatment or earlier if tamponade was suspected. Low-dose aspirin or oral anticoagulants (vitamin K antagonists) were routinely administered to patients who had undergone coronary artery bypass grafting or valvular replacement or repair, respectively.

Initiation, monitoring, close-out visits, clinical study coordination, data management and data analysis were conducted by the clinical research unit at Hôpital Européen Georges Pompidou (Assistance Publique des Hôpitaux de Paris). Colchicine pills, 1 mg, and matching placebo were provided by Laboratoires Mayoly-Spindler, marketing authorisation holder of the drug, Chatou France.

Study end points

The primary efficacy end point was the mean change from baseline in grade of echocardiography-measured size of pericardial effusion (mean pericardial effusion grade) after 14 days of treatment expressed as mean pericardial effusion grade decrease.

Secondary prespecified end points were, after 14 days of treatment, (1) frequency of cardiac tamponade, (2) number of patients in whom the individual effusion grade decreased by at least one grade, (3) evolution of mean effusion width expressed in millimetres and (4) occurrence of atrial fibrillation. In addition, the frequency of pericardial drainage after 30 days and 6 months were prespecified secondary end points.

Echocardiography variables

Patients underwent M-mode, cross-sectional and Doppler TTE. A standard echocardiographic technique with parasternal (long axis and short axis), apical (four chambers and two chambers) and subcostal projections was used. Pulsed and continuous Doppler echocardiograms of the mitral, aortic and tricuspid flows were from the apical view. Pericardial effusion was visualised, during the end diastolic phase, as an echo-free space around the heart that could be diffused (circumferential) or loculated. Pericardial effusion was classified into four grades by site and size as described in table 1. Each examination was performed jointly by two experienced operators. When the pericardial effusion was not homogeneous, its width was measured where the effusion volume was the largest. The diagnosis of tamponade was left to the investigator: it was based on findings of clinical and echographic variables. Clinical variables were[8] hypotension, pulsus paradoxus, tachycardia, dyspnoea, oliguria and signs of right heart failure. Echocardiographic signs were, in addition to large pericardial effusion, right atrial collapse, RV collapse, LV collapse, distension of the inferior vena cava with blunted inspiratory response, swinging heart aspect (swinging of the heart within the pericardial space), and large respiratory fluctuations in mitral or tricuspid flows.[8]

Heart rhythm assessment

A 12-lead ECG recording was performed at least at inclusion and at the end of the study. The rhythm was defined as atrial fibrillation when there were no consistent P waves before each QRS complex and the ventricular rate was irregular.

Statistical analysis

Sample size assessment: From published results for similar patients,[6] we determined the sample size with the assumption that spontaneous mean pericardial effusion grade decrease would be a minimum of 0.6 grades in the control group. We calculated that 172 patients (86 by group) were needed for 80% power to detect a significant difference between treatment with colchicine and placebo corresponding to a supplementary reduction of 50% of the mean pericardial effusion grade (ie, 0.9 grades) in the colchicine group, corresponding to an effect size of 0.3 units and an SD of the change score of 0.7 grade units, with a two-sided type 1 error of 5%.

Analysis set: prespecified analyses involved the intent-to-treat principle. Patients who were randomised were included in the analysis. Continuous data (normally and non-normally distributed) are presented as mean±SD. The primary end point was analysed as the difference between treatment groups in mean pericardial effusion grade decrease from baseline and compared by the Mann-Whitney U test as for other non-normally distributed continuous variables (change from baseline in pericardial width, change from baseline in pericardial effusion grade in prespecified subgroups). Normally continuous distributed variables were compared by Student's t test, and categorical variables were compared by χ^2 test. A two-sided $p<0.05$ was considered statistically significant. We used the Kaplan-Meier method to estimate time-to-event distributions, which were compared by log-rank test. Analyses involved use of SAS V.9.3 (SAS Institute, Cary, North Carolina, USA).

Subgroup analyses: The evolution of pericardial effusion in prespecified subgroups was evaluated for patients with inflammatory syndrome (C reactive protein (CRP) level >30 mg/L (285.60 nmol/L)) and patients receiving a vitamin K antagonist.

A per protocol analysis was planned after exclusion of the patients (1) who had received the experimental treatment for <80% of the observation time or (2) in whom TTE_2 was not performed in due time (ie, before 10 days after inclusion or after 18 days after inclusion).

Role of the funding source
The French Society of Cardiology and the French Federation of Cardiology provided funding for this study and Laboratoires Mayoly-Spindler provided colchicine and the matched placebo. The funding sources had no role in the design, conduct and analysis of the study or decision to submit the manuscript for publication.

RESULTS
Study population
In total, 8140 consecutive patients who underwent cardiac surgery were assessed (figure 1); 252 met the inclusion criteria. We excluded 55 patients and enrolled 197: 98 were randomly assigned to receive colchicine and 99 placebo. Patients were included at the time of the TTE_1 at a mean of 16.2±5.3 days after surgery. The mean treatment duration was 13.7±2.8 days. Patients were followed up until 6 months after inclusion. The two groups did not differ in clinical characteristics, type of surgery or background treatment (see table 2 for baseline characteristics).

Data were analysed on an intent-to-treat basis, for all the 197 patients. Ten patients in the colchicine group and three in the placebo group stopped therapy before the end of the study because of new symptoms or late withdrawal of consent (see tolerance paragraph below). However, we obtained baseline and follow-up echocardiographies and clinical follow-up for all of them. Among these latest patients, 11 had a <80% compliance (see figure 1) and were therefore excluded of the per protocol analysis.

Study efficacy end points and events
Mean pericardial effusion grade at inclusion was 2.9±0.8 and 3.0±0.8 for the placebo and colchicine groups, respectively (p=0.46), which confirms the quite large mean pericardial effusion volume at inclusion. A total of 62 patients had grade 2 effusion, 79 grade 3 and 56 grade 4. The main end point, mean

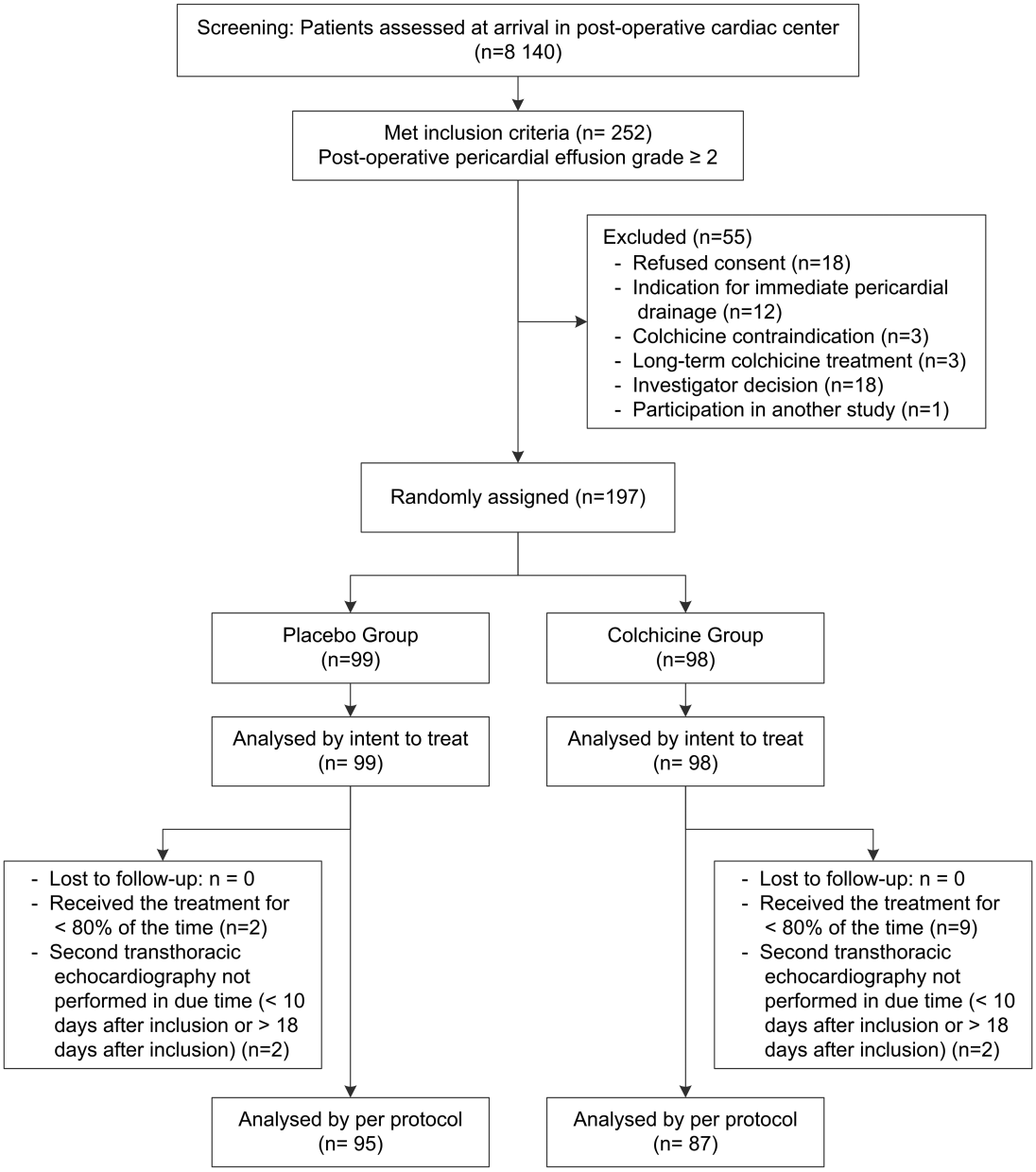

Figure 1 Study flow diagram.

pericardial effusion change in grade from baseline, was −1.1 ±1.3 vs −1.3±1.3 grades for the placebo versus the colchicine group (mean difference between groups, −0.19; 95% CI −0.55 to 0.16; p=0.23) (table 3).

The initial mean pericardial effusion width was of 14.2 ±4.3 mm. None of the secondary end points differed between placebo and colchicine administration: frequency of tamponade at 14 days, 7 (7)% vs 6 (6)%, p=0.80 (figure 2); mean effusion width change from baseline, −4.7±6.9 mm vs −5.8±6.6 mm, CI 95% −1.13 (−3.03 to 0.77), p=0.27, proportion of patients with echocardiographic grade decrease ≥1, 66.7% vs 74.5%, p=0.23 (table 4); and proportion of patients with atrial fibrillation at the end of the study, 12.1% vs 15.3% (p=0.52) in the placebo and colchicine groups, respectively.

Finally, the treatment did not modify pericardial effusion evolution for the prespecified subgroups of patients with an inflammatory syndrome (CRP level ≥30 mg/L) or those receiving an oral anticoagulant (table 5).

Per protocol analysis findings agreed with intent-to-treat findings: in these 182 patients, the mean pericardial effusion grade change from baseline was −1.1±1.3 and −1.3±1.3 grades for the placebo group (n=95) and colchicine group (n=87); 95% CI −0.18 (−0.56 to 0.20), p=0.28.

At 6-month follow-up, all patients were alive and had undergone a total of 22 surgical pericardiotomies (11% of the 197 patients): 14 in the placebo group and 8 in the colchicine group (p=0.20). None of the nine pericardial drainages performed after the 14 days of the study was due to a tamponade: they were all elective operations for large persisting asymptomatic pericardial effusion. No patient died.

Study safety end points and events

The mean increase in serum creatinine level was negligible and similar between the placebo and colchicine groups: 0.5±15.5 µmol/L vs 1.4±13.1 µmol/L (p=0.68).

A total of 13 patients did not complete the study: 10 in the colchicine group because of diarrhoea (n=7), digestive haemorrhage (n=1) leucopenia (n=1), and constipation (n=1) and 3 in the placebo group because of constipation (n=1), cerebral infarction (n=1), and consent withdrawal (n=1).

DISCUSSION

This trial assessing the effectiveness of colchicine to treat asymptomatic postoperative pericardial effusion found that use of the drug did not significantly reduce the volume of pericardial effusion or risk of late cardiac tamponade.

Among the multiple causal mechanisms of postoperative pericardial effusion persisting after postoperative day 7, inflammation plays a part. Because of this 'inflammatory theory', non-steroidal anti-inflammatory drugs (NSAIDs) have been widely prescribed in this setting (up to 77% of patients in a large study[3]), and European guidelines published in 2005[8] suggested their use. However, the hypothesis that NSAIDs could be useful for treating postoperative pericardial effusion was invalidated in 2010 in a prospective double-blinded randomised study.[13]

Colchicine is effective (given in addition to usual anti-inflammatory therapy) to prevent recurrent pericarditis[14–19] and even to treat a first episode of acute pericarditis.[9]

Furthermore, the COPPS double-blind placebo-controlled study[10] found the use of colchicine, administered for 1 month from the 3rd day after heart surgery, efficient in preventing—not treating—a pericardial postoperative disease: PPS. However PPS is a clinical syndrome that has little in common with asymptomatic postoperative pericardial effusion (on which our study focused): it is an inflammatory disease that occurs in 5–20% of patients after cardiac surgery[20] and may include

Table 2 Baseline patient characteristics

Characteristic	Placebo (n=99)	Colchicine (n=98)
Clinical and demographical characteristics		
Age, years	64.7±10.6	64.2±11.8
Male	88 (88.9%)	82 (83.7%)
BMI, kg/m^2	27.6±4.3	26.7±3.8
History of hypertension	62 (62.6%)	59 (60.2%)
History of diabetes	21 (21.2%)	23 (23.5%)
Atrial fibrillation	17 (17.2%)	19 (19.4%)
Surgery performed*		
CABG	52 (52.5%)	58 (59.2%)
No. of grafts	2.6±1.1	2.8±1.1
No. of internal thoracic artery implants	1.6±0.6	1.7±0.6
AV replacement	48 (48.5%)	34 (34.7%)
Mechanical	16 (16.2%)	14 (14.3%)
Bioprosthesis	32 (32.3%)	20 (20.4%)
MV replacement	5 (5.1%)	7 (7.1%)
Mechanical	2 (2.0%)	3 (3.1%)
Bioprosthesis	3 (3.0%)	4 (4.1%)
MV repair	7 (7.1%)	7 (7.1%)
AA replacement	15 (15.2%)	15 (15.3%)
Delay surgery-inclusion days	16.2±5.1	16.1±5.5
Baseline echocardiographic characteristics (TTE$_1$)		
LVEF %	57.4±8.1	60.5±8.9
PE mean grade	2.9±0.8	3.0±0.8
Grade 2	35 (35.4%)	27 (27.6%)
Grade 3	36 (36.4%)	43 (43.9%)
Grade 4	28 (28.3%)	28 (28.6%)
PE localisation		
Loculated	36 (36.4%)	42 (42.9%)
Circumferential	63 (63.6%)	56 (57.1%)
PE width, mm	14.1±4.3	14.3±4.2
Baseline biological parameters		
Haemoglobin level, g/dL	10.9±1.3	10.8±1.1
Creatine level		
µmol/L	85.8±22.8	87.0±22.0
mg/L	9.7±2.6	9.8±2.5
Mean INR in VKA-treated patients	2.4±0.7	2.4±0.9
CRP level		
mg/L	33.6±29.5	33.9±29.4
nmol/L	319.4±281.2	323.1±280.0
Drug therapy		
VKA	45 (45.5%)	41 (41.8%)
Other anticoagulant	5 (5.1%)	11 (11.2%)
Aspirin	74 (74.7%)	67 (68.4%)
Mean dose, mg/day	94.7±35.7	93.0±33.7
Clopidogrel	6 (6.1%)	7 (7.1%)
Statin	66 (66.7%)	67 (68.4%)
β blocker	65 (65.7%)	76 (77.6%)
Corticosteroids	4 (4.0%)	6 (6.1%)
NSAIDs	0 (0.0%)	2 (2.0%)
ACE-I	46 (46.5%)	32 (32.7%)

Data are mean±SD or number (%).
*Patients could have more than one type of surgery.
AA, ascending aorta; AV, aortic valve; BMI, body mass index; CABG, coronary artery bypass grafting; CRP C reactive protein; INR, international normalised ratio; MV, mitral valve; NSAID, non-steroidal anti-inflammatory drug; PE, pericardial effusion; TTE$_1$, transthoracic echocardiography 1, performed a mean of 16.2±5.3 days after surgery; VKA, vitamin k antagonist.

Table 3 Pericardial effusion grade evolution in the two groups

Grade	Placebo (n=99) Mean±SD	Colchicine (n=98) Mean±SD	Difference Mean (95% CI)	p Value
Initial	2.9±0.8	3.0±0.8		0.46
Final	1.8±1.3	1.7±1.2		0.47
Change	−1.1±1.3	−1.3±1.3	−0.19 (−0.55 to 0.16)	0.23

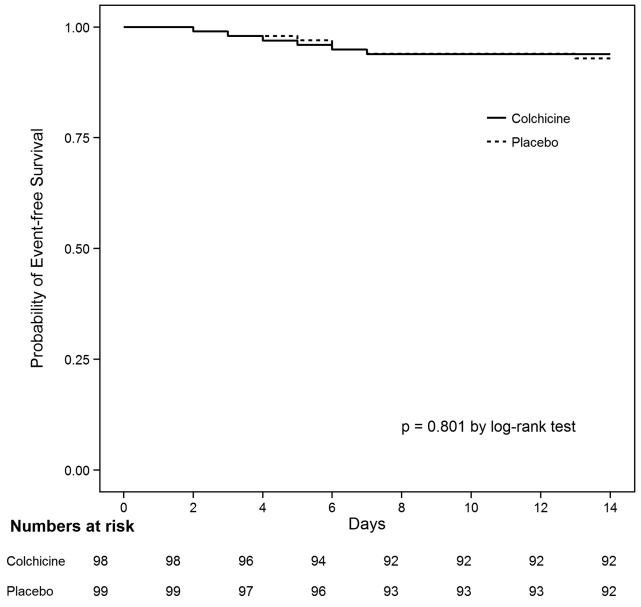

Figure 2 Pericardial drainage cases during 14-day treatment.

fever, friction rub, chest pain, pleuritis and pericardial effusion. Its evolution to cardiac tamponade is rare: among the 360 patients included in the COPPS study, 54 cases of PPS were diagnosed, with only 9 cases of moderate to large pericardial effusion and 1 case of tamponade. Thus, the goal of the COPPS study was not to predict whether colchicine could help reduce the volume of postoperative pericardial effusion or prevent the occurrence of tamponade which is in contrast to our study in which a much higher number of patients (n=197) with significant pericardial effusion and therefore a much higher number (n=22) of cases of pericardial drainages were observed. In the same way, in the COPPS-2 study, colchicine administration starting between 48 h and 72 h before surgery and continued for

Table 4 Baseline and end-of-treatment pericardial effusion (PE) grade

	End-of-treatment PE grade					
Baseline PE grade	0	1	2	3	4	Total
Placebo						
2	7	11	12	2	3	35
3	5	12	14	3	2	36
4	2	6	6	3	11	28
Total	14	29	32	8	16	99
Colchicine						
2	4	12	6	3	2	27
3	9	16	11	3	4	43
4	2	7	7	5	7	28
Total	15	35	24	11	13	98

Shaded areas represent decrease in at least one grade.

1 month after surgery reduced the incidence of PPS but not of postoperative pericardial/pleural effusion.[11]

Therefore, acute pericarditis and PPS (both clinical syndromes) should not be confused with persistent postoperative pericardial effusion, which is usually asymptomatic but of concern because it frequently evolves to cardiac tamponade. This confusion is why NSAIDs and colchicine have been frequently and incorrectly prescribed without any proof of efficacy in this latest setting.

Our findings of no efficacy of colchicine as compared with placebo could be explained by the inflammatory component not being the predominant mechanism for most cases of postoperative pericardial effusion. Indeed, these patients constitute a mixed groups of those individuals having (1) postoperative haemorrhagic effusions, (2) pericardial effusion due to postoperative heart failure, (3) patients with a true PPS, population in which colchicine could actually be efficient as shown in the ICAP study.[9] As in clinical practice, distinguishing these three mechanisms is difficult, so the only possible path would be to treat or not to treat all of them indiscriminately. Indeed, the absence of efficacy of colchicine for patients with CRP level >30 mg/L (285.6 nmol/L) suggests that no usual non-invasive test can separate inflammatory and haemorrhagic effusions.

Our study has several limitations. First, because its objective was to evaluate the efficacy of colchicine for treating persistent postoperative pericardial effusion, we began treatment at day 8 after surgery in patients with actual pericardial effusion. Therefore, the potential efficacy of colchicine given systematically preoperatively as preventive treatment of clinically

Table 5 Change in pericardial effusion grade in prespecified subgroups

Subgroup	Placebo (n=99) N, mean±SD	Colchicine (n=98) N, mean±SD	Difference mean (95% CI)	p Value*
CRP level				
≥30 mg/L (≥285.6 nmol/L)	(42) −1.3±1.4	(40) −1.4±1.4	−0.11 (−0.72 to 0.49)	0.81
<30 mg/L (<285.6 nmol/L)	(54) −1.0±1.2	(56) −1.3±1.2	−0.27 (−0.72 to 0.18)	0.12
VKA+other AC				
Yes	(50) −0.9±1.3	(52) −1.4±1.2	−0.48 (−0.99 to 0.02)	0.06
No	(49) −1.3±1.2	(46) −1.2±1.3	0.11 (−0.40 to 0.63)	0.81

*By non-parametrical Mann–Whitney test.
AC, anticoagulants; CRP, C reactive protein; VKA, vitamin K antagonist.

significant pericardial effusion is beyond the scope of our study. However, in the COPPS-2 study, perioperative administration of colchicine did not reduce the incidence of pericardial effusions or drainages.[11] Second, this study was underpowered to evaluate adverse clinical events, because only 98 patients received the drug. Finally, even if it is a secondary end point, a 12-lead ECG recording at inclusion and at the end of the study is insufficient to assess the effect of a drug on the incidence of atrial fibrillation and a 24 h Holter monitoring should have been conducted. However, regarding atrial fibrillation prevention, our results confirm the results of the COPPS-2 study.[11]

In conclusion, among patients with moderate to severe pericardial effusion persisting more than 7 days after cardiac surgery, colchicine administration did not have a significant impact on the evolution of the effusion.

Key messages

What is already known on this subject?

- Pericardial effusion persisting more than 1 week after cardiac surgery is usually asymptomatic, but worrying because it can evolve to cardiac tamponade after discharge from the hospital.
- Colchicine is efficient for the treatment of acute pericarditis and for the prevention of postpericardiotomy syndrome: an inflammatory postinjury pericardial syndrome which usually mimics acute pericarditis, but it has not been tested for treatment of actual postoperative pericardial effusion.

What might this study add?

- Among patients with moderate to severe pericardial effusion persisting more than 7 days after cardiac surgery, 9.1% required pericardial drainage within 1 month after inclusion. Moreover, Colchicine administration did not have a significant impact on the evolution of the effusion.

How might this impact on clinical practice?

- In patients with moderate to severe pericardial effusion persisting more than 7 days after cardiac surgery regular echographic follow-up is mandatory until effusion disparition or significant volume decreases.

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Contributors PM planned, designed and conducted the study. He analysed the data and has written the draft of the article. All the authors have codesigned the study during several meetings. All the authors have coconducted the study. All the authors had full access to the data. All the authors have participated in the final writing of the paper. HP and JYT paid special attention to statistical analysis.

Competing interests None declared.

Patient consent Obtained.

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Data sharing statement PM and HP have full access to all the data and take responsibility for the integrity of the data and the accuracy of the data analysis. The database can be obtained by asking at the following email address philippemeurin@hotmail.com.

REFERENCES

1 Weitzman LB, Tinker WP, Kronzon I, *et al*. The incidence and natural history of pericardial effusion after cardiac surgery: an echocardiography study. *Circulation* 1984;69:506–11.
2 Pepi M, Muratori M, Barbier P, *et al*. Pericardial effusion after cardiac surgery: incidence, site, size and hemodynamic consequences. *Br Heart J* 1994;72:327–31.
3 Tsang TS, Barnes ME, Hayes SN, *et al*. Clinical and echocardiographic characteristics of significant pericardial effusions following cardiothoracic surgery and outcomes of echo-guided pericardiocentesis for management. Mayo Clinic Experience 1979–1998. *Chest* 1999;116:322–31.
4 Kuvin JT, Harati NA, Pandian NG, *et al*. Post operative cardiac tamponade in the modern surgical era. *Ann Thorac Surg* 2002;74:1148–53.
5 Palmer SL, Kelly PD, Schenkel FA, *et al*. CT-guided tube pericardiostomy: a safe and effective technique in the management of postsurgical pericardial effusion. *Am J Roentgenol* 2009;193:W314–20.
6 Meurin P, Weber H, Renaud N, *et al*. Evolution of the post operative pericardial effusion after day 15. The problem of the late tamponade. *Chest* 2004;125:2182–7.
7 Redžek A, Mironicki M, Gvozdenović A, *et al*. Predictors for hospital readmission after cardiac surgery. *J Card Surg* 2015;30:1–6.
8 Maisch B, Seferović PM, Ristić AD, *et al*. Task Force on the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology. Guidelines on the diagnosis and management of pericardial diseases. Full text. The task force on the diagnosis and management of pericardial diseases of the European Society of Cardiology. *Eur Heart J* 2004;25:587–610.
9 Imazio M, Brucato A, Cemin R, *et al*. ICAP A randomized trial of colchicine for acute pericarditis. *N Engl J Med* 2013;369:1522–8.
10 Imazio M, Trinchero R, Brucato A, *et al*. COPPS Investigators. COlchicine for the Prevention of the Post-pericardiotomy Syndrome (COPPS): a multicentre, randomized, double-blind, placebo-controlled trial. *Eur Heart J* 2010;31:2749–54.
11 Imazio M, Brucato A, Ferrazzi P, *et al*. COPPS-2 Investigators. Colchicine for prevention of postpericardiotomy syndrome and postoperative atrial fibrillation: the COPPS-2 randomized clinical trial. *JAMA* 2014;312:1016–23.
12 Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1971;16:31–41.
13 Meurin P, Tabet JY, Thabut G, *et al*. Non-steroidal anti-inflammatory drug treatment for postoperative pericardial effusion. *Ann Intern Med* 2010;152:137–43.
14 Rodríguez de la Serna A, Guindo Soldevila J, Martí Claramunt V, *et al*. Colchicine for recurrent pericarditis. *Lancet* 1987;2:1517.
15 Imazio M, Brucato A, Trinchero R, *et al*. Colchicine for pericarditis: hype or hope? *Eur Heart J* 2009;30:532–9.
16 Imazio M, Bobbio M, Cecchi E, *et al*. Colchicine as first-choice therapy for recurrent pericarditis:results of the CORE (COlchicine for REcurrent pericarditis) trial. *Arch Intern Med* 2005;165:1987–91.
17 Imazio M, Bobbio M, Cecchi E, *et al*. Colchicine in addition to conventional therapy for acute pericarditis: results of the COlchicine for acute PEricarditis (COPE) trial. *Circulation* 2005;112:2012–6.
18 Imazio M, Brucato A, Cemin R, *et al*., CORP (COlchicine for Recurrent Pericarditis) Investigators. Colchicine for recurrent pericarditis (CORP): a randomized trial. *Ann Intern Med* 2011;155:409–14.
19 Imazio M, Belli R, Brucato A, *et al*. Efficacy and safety of colchicine for treatment of multiple recurrences of pericarditis (CORP-2): a multicentre, double-blind, placebo-controlled, randomised trial. *Lancet* 2014;383:2232–7.
20 Imazio M, Cecchi E, Trinchero R., on behalf of the COPPS Investigators. Colchicine for the prevention of the postpericardiotomy syndrome: the COPPS trial. *Int J Cardiol* 2007;12:198–9.