

Colchicine for the prevention of atrial fibrillation (COP-AF)

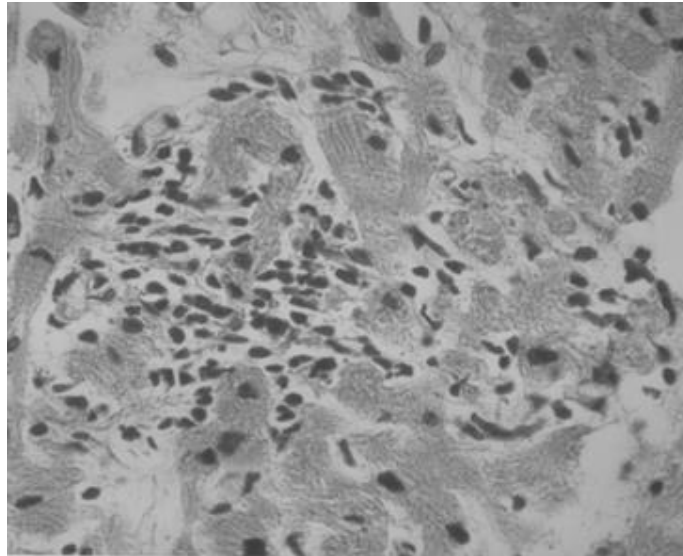
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Background

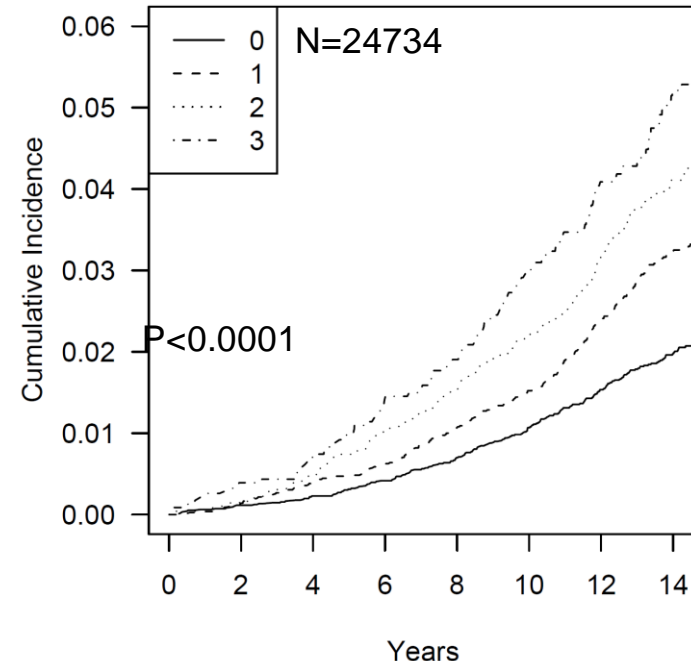
- Perioperative Atrial Fibrillation (POAF) is the most common cardiac arrhythmia after thoracic surgery.
- POAF is associated with adverse hemodynamic changes, an increased length of hospital stay, stroke, and death.
- Risk factors for POAF include age and type of surgery.
- As age of the population and that of thoracic surgery patients increases, incidence of POAF and associated complications will likely increase.

Inflammation & Atrial Fibrillation

Histological findings in lone AF patients

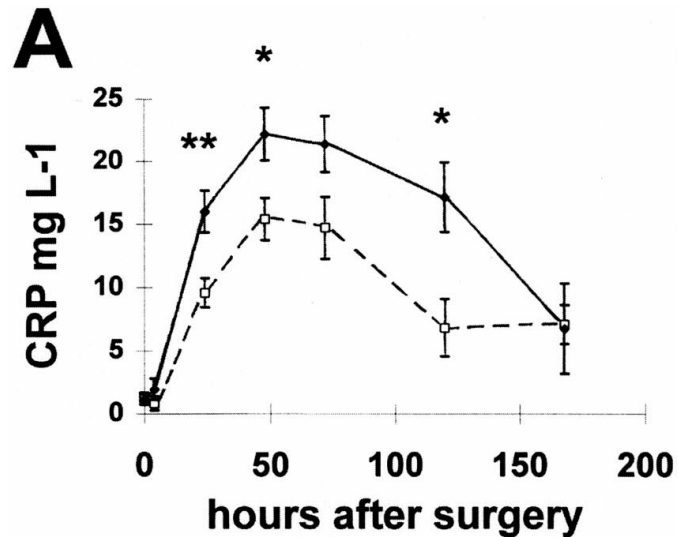


Inflammation score & incident AF



Inflammatory Response After Surgery

41 patients undergoing major thoracic surgery (VATS vs thoracotomy)

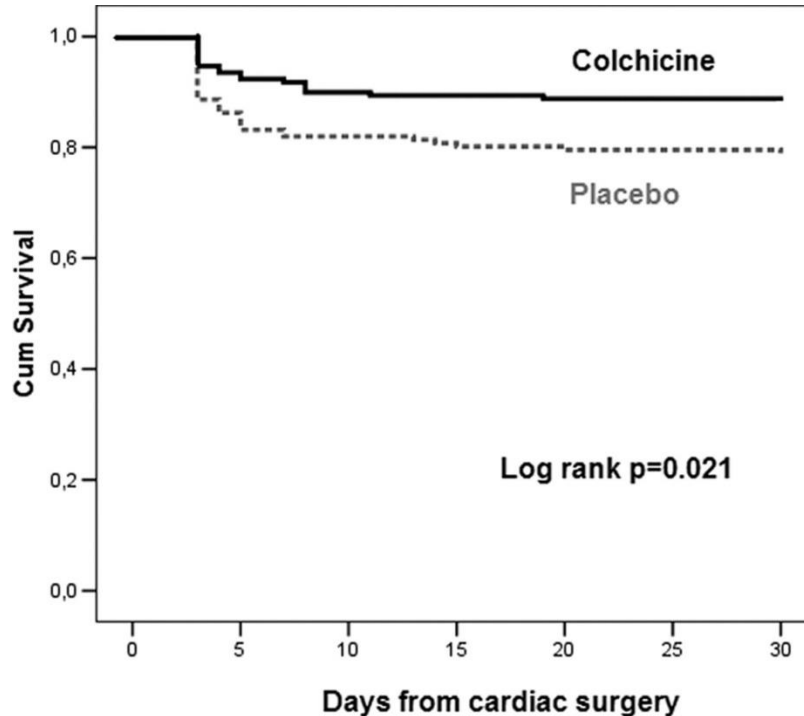


Incidence of perioperative AF after thoracic surgery: 10-20%

Colchicine

- Colchicine is a potent anti-inflammatory agent. It inhibits leukocyte migration, interferes with kinin formation and prevents beta tubulin binding.
- It also impairs the assembly of the inflammasome, thereby reducing the release of IL-1 β .
- Colchicine is effective in treating many inflammatory disorders, such as gout or pericarditis.
- It may prevent the post-pericardiotomy syndrome and POAF in patients undergoing cardiac surgery.

Colchicine in Cardiac Surgery



- N = 336 patients undergoing cardiac surgery and in SR at randomization
- Colchicine vs. placebo starting on postoperative day 3
- This secondary analysis showed an incidence of perioperative AF of 12% vs. 22% in favor of colchicine
- A follow-up study starting colchicine 48-72 hours before surgery showed similar results

Trial Design & Intervention

- 2,800 patients undergoing thoracic surgery
- Blinded, placebo-controlled trial
- Colchicine 0.5mg BID vs. matching placebo for 10 days
- 14 day follow up period

Patient Population

Inclusion Criteria:

- Undergoing thoracic surgery with general anesthesia
- ≥ 55 years of age at the time of randomization
- Expected to require at least an overnight hospital admission after surgery

Patient Population

Exclusion Criteria:

- Patients with a prior history of documented atrial fibrillation
- Patients currently taking anti-arrhythmic medication other than β -blockers, calcium channels blockers or digoxin
- Patients undergoing minor thoracic interventions
- Patients with contraindications to colchicine
- Patients not expected to take oral medications for >24 hours after surgery
- Patients scheduled for lung transplantation
- Patients taking non-study colchicine before surgery



Patient Population

Exclusion Criteria Continued:

- Patients with severe hepatic dysfunction
- Patients with aplastic anemia
- Women of childbearing potential who are not taking effective contraception, pregnant or breast-feeding
- Patients who took within the last 14 days or scheduled to take clarithromycin, erythromycin, telithromycin, cyclosporine, ketoconazole, or itraconazole during the first 10 days after surgery
- HIV patients treated with antiretroviral therapy

Outcomes

Primary Outcome

To determine whether the administration of colchicine compared with placebo reduces the occurrence of clinically important POAF within 14 days of randomization.

Secondary Outcomes

1. First occurrence of the composite of all-cause mortality, nonfatal myocardial infarction, or nonfatal stroke within 14 days of randomization
2. Occurrence of myocardial injury after noncardiac surgery (MINS);
3. Number of days alive and at home
4. Time to chest tube removal within 14 days of randomization
5. Duration of stay in ICU, step-down, and in hospital
6. All-cause mortality within 14 days of randomization
7. Occurrence of myocardial infarction within 14 days of randomization



Follow-Up

- Patients followed daily during their hospitalization until discharge
- Troponin measurements and ECGs taken POD 1-3
- Final follow up occurs 14 days after randomization in clinic or via telephone