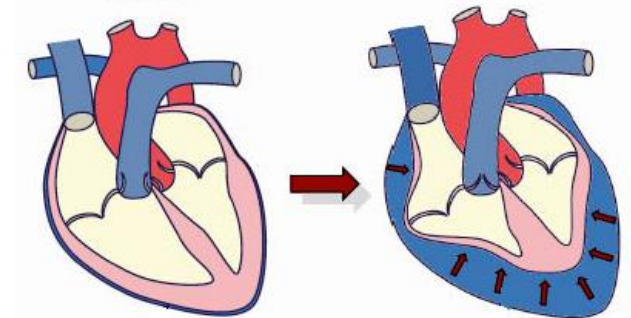




## Ημέρες Παθολογίας 2023: Διλήμματα στην Κλινική Παθολογία Ιδιοπαθής υποτροπιάζουσα περικαρδίτιδα.



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Ιπποκράτειο Γ.Ν. Αθηνών



## Disclosures

- I have received honoraria from Menarini, Bayer, Pfizer, Roche Diagnostics and Kiniksa pharmaceuticals.

# Pericardial syndromes

- Most common pericardial syndromes include acute pericarditis (either first episode or recurrences), cardiac tamponade, constrictive pericarditis (permanent, transient and effusive constrictive) and isolated pericardial effusions without evidence of inflammation.
- The estimated incidence of acute pericarditis is ~28 cases / 100,000 subjects in the general population / year respectively.

**Aetiology of pericardial diseases. The pericardium may be affected by all categories of diseases, including infectious, autoimmune, neoplastic, iatrogenic, traumatic, and metabolic**

**A. Infectious causes:**

**Viral (common):** Enteroviruses (coxsackieviruses, echoviruses), herpesviruses (EBV, CMV, HHV-6), adenoviruses, parvovirus B19 (possible overlap with aetiological viral agents of myocarditis).

**Bacterial:** *Mycobacterium tuberculosis* (common, other bacterial rare), *Coxiella burnetii*, *Borrelia burgdorferi*, rarely: *Pneumococcus* spp, *Meningococcus* spp, *Gonococcus* spp, *Streptococcus* spp, *Staphylococcus* spp, *Haemophilus* spp, *Chlamydia* spp, *Mycoplasma* spp, *Legionella* spp, *Leptospira* spp, *Listeria* spp, *Providencia stuartii*.

**Fungal (very rare):** *Histoplasma* spp (more likely in immunocompetent patients), *Aspergillus* spp, *Blastomyces* spp, *Candida* spp (more likely in immunocompromised host).

**Parasitic (very rare):** *Echinococcus* spp, *Toxoplasma* spp

**B. Non-infectious causes:**

**Autoimmune (common):**

Systemic autoimmune and auto-inflammatory diseases (systemic lupus erythematosus, Sjögren syndrome, rheumatoid arthritis, scleroderma), systemic vasculitides (i.e. eosinophilic granulomatosis with polyangiitis or allergic granulomatosis, previously named Churg-Strauss syndrome, Horton disease, Takayasu disease, Behçet syndrome), sarcoidosis, familial Mediterranean fever, inflammatory bowel diseases, Still disease.

**Neoplastic:**

Primary tumours (rare, above all pericardial mesothelioma).  
Secondary metastatic tumours (common, above all lung and breast cancer, lymphoma).

**Metabolic:** Uraemia, myxoedema, anorexia nervosa, other rare.

**Traumatic and Iatrogenic:**

Early onset (rare):

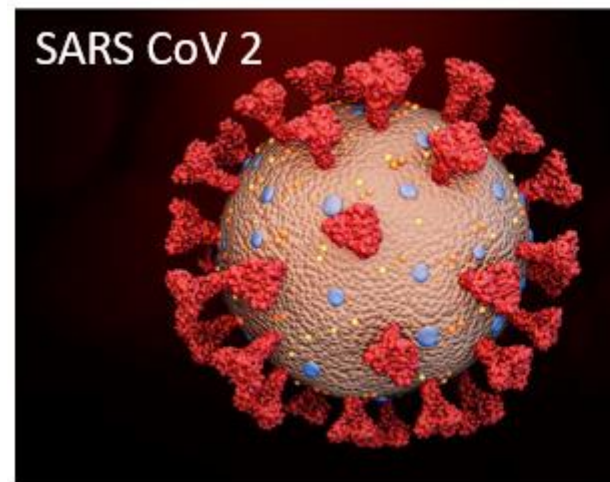
- Direct injury (penetrating thoracic injury, aesophageal perforation).
- Indirect injury (non-penetrating thoracic injury, radiation injury).

Delayed onset: Pericardial injury syndromes (common) such as postmyocardial infarction syndrome, postpericardiotomy syndrome, posttraumatic, including forms after iatrogenic trauma (e.g. coronary percutaneous intervention, pacemaker lead insertion and radiofrequency ablation).

**Drug-related (rare):** Lupus-like syndrome (procainamide, hydralazine, methyl dopa, isoniazid, phenytoin); antineoplastic drugs (often associated with a cardiomyopathy, may cause a pericardiopathy): doxorubicin, daunorubicin, cytosine arabinoside, 5-fluorouracil, cyclophosphamide; penicillins as hypersensitivity pericarditis with eosinophilia; amiodarone, methysergide, mesalazine, clozapine, minoxidil, dantrolene, praxolol, phenylbutazone, thiazides, streptomycin, thiouracils, streptokinase, p-aminosalicylic acid, sulfa-drugs, cyclosporine, bromocriptine, several vaccines, GM-CSF, anti-TNF agents.

**Other (common):** Amyloidosis, aortic dissection, pulmonary arterial hypertension and chronic heart failure.

**Other (uncommon):** congenital partial and complete absence of the pericardium.



In 0.3-1.5% of cases in the setting of SARS-CoV-2 infection develops pericarditis

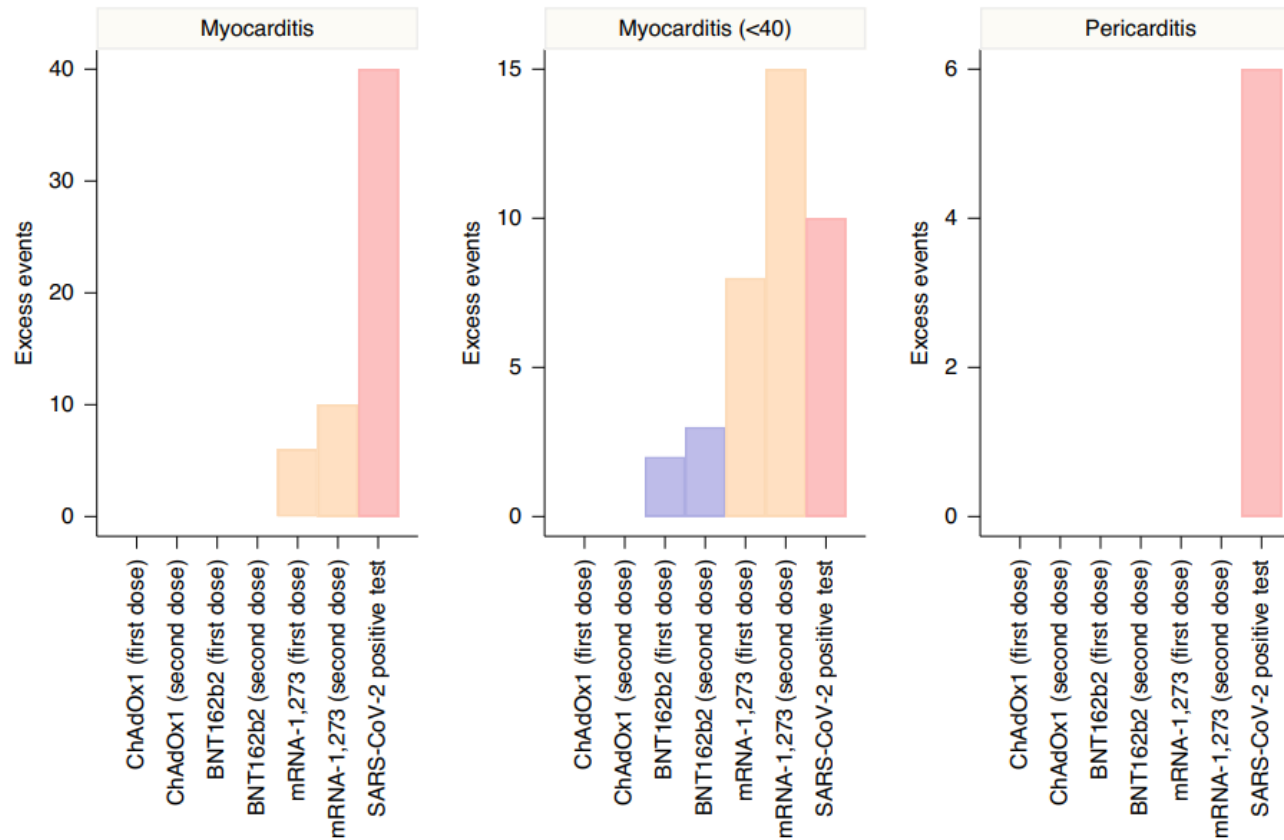
Adler Y, et al. Eur Heart J. 2015;36:2921-2964.  
LIP GYP, et al. Eur J Clin Invest 2021;51:e13679.  
J Am Coll Cardiol 2023;81:557-569.

OPEN

## Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection

Martina Patone<sup>1</sup>, Xue W. Mei<sup>1</sup>, Lahiru Handunnetthi<sup>2</sup>, Sharon Dixon<sup>1</sup>, Francesco Zaccardi<sup>3</sup>, Manu Shankar-Hari<sup>4,5,6</sup>, Peter Watkinson<sup>7,8</sup>, Kamlesh Khunti<sup>3</sup>, Anthony Harnden<sup>1</sup>, Carol A. C. Coupland<sup>1,9</sup>, Keith M. Channon<sup>10</sup>, Nicholas L. Mills<sup>4,11</sup>, Aziz Sheikh<sup>4</sup> and Julia Hippisley-Cox<sup>1</sup>✉

Number of excess events in the 1–28 days postvaccination/SARS-CoV-2 positive test per 1 million vaccinated/infected



Number of excess events due to exposure per 1 million exposed



## 2015 ESC Guidelines for the diagnosis and management of pericardial diseases

The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC)

Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS)

**Authors/Task Force Members:** Yehuda Adler\* (Chairperson) (Israel), Philippe Charron\* (Chairperson) (France), Massimo Imazio† (Italy), Luigi Badano (Italy), Gonzalo Barón-Esquivias (Spain), Jan Bogaert (Belgium), Antonio Brucato (Italy), Pascal Gueret (France), Karin Klingel (Germany), Christos Lionis (Greece), Bernhard Maisch (Germany), Bongani Mayosi (South Africa), Alain Pavie (France), Arsen D. Ristić (Serbia), Manel Sabaté Tenas (Spain), Petar Seferovic (Serbia), Karl Swedberg (Sweden), and Witold Tomkowski (Poland)

**Document Reviewers:** Stephan Achenbach (CPG Review Coordinator) (Germany), Stefan Agewall (CPG Review Coordinator) (Norway), Nawwar Al-Attar (UK), Juan Angel Ferrer (Spain), Michael Arad (Israel), Riccardo Asteggiano (Italy), Héctor Bueno (Spain), Alida L. P. Caforio (Italy), Scipione Carerj (Italy), Claudio Ceconi (Italy), Arturo Evangelista (Spain), Frank Flachskampf (Sweden), George Giannakoulas (Greece), Stephan Gielen (Germany), Gilbert Habib (France), Philippe Kolh (Belgium), Ekaterini Lambrinou (Cyprus), Patrizio Lancellotti (Belgium), George Lazaros (Greece), Ales Linhart (Czech Republic), Philippe Meurin (France), Koen Nieman (The Netherlands), Massimo F. Piepoli (Italy), Susanna Price (UK), Jolien Roos-Hesselink (The Netherlands),

# Diagnostic criteria for acute and recurrent pericarditis

## 2015 ESC Guidelines for the diagnosis and management of pericardial diseases

Recurrent pericarditis in a patient with a first episode of acute pericarditis is diagnosed when at least 2 of the following criteria are present:

- Typical chest pain
- Pericardial friction rub
- Suggestive ECG changes (typically widespread ST-segment elevation, PR depression)
- New or worsening pericardial effusion

-Elevation of CRP is a confirmatory finding and evidence of pericardial inflammation by an imaging technique (CT or CMR) are considered supporting findings.

-CRP in approximately 22% of cases is found within normal limits at the time of presentation. This is due to CRP synthesis rate kinetics, as CRP levels start rising beyond normal values approximately 6 hours after an inflammatory process. However, CRP values have been found to be elevated in 96% of patients with acute pericarditis if measured at least 12 hours after symptoms onset

<b>Incessant</b>	Pericarditis lasting for >4–6 weeks but <3 months without remission.
<b>Recurrent</b>	Recurrence of pericarditis after a documented first episode of acute pericarditis and a symptom-free interval of 4–6 weeks or longer <sup>a</sup> .
<b>Chronic</b>	Pericarditis lasting for >3 months.

**Hospital admission is required in the following cases:**

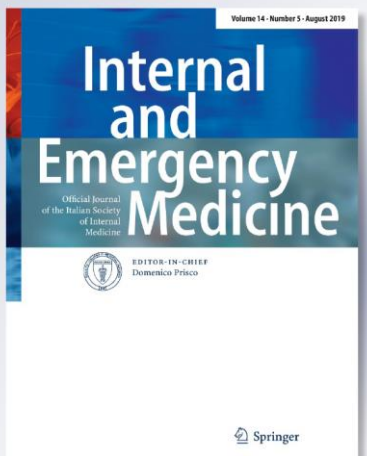
### Predictors of poor prognosis:

#### Major

- Fever >38°C
- Subacute onset
- Large pericardial effusion
- Cardiac tamponade
- Lack of response to aspirin or NSAIDs after at least 1 week of therapy

#### Minor

- Myopericarditis
- Immunosuppression
- Trauma
- Oral anticoagulant therapy



## Clinical significance of pleural effusions and association with outcome in patients hospitalized with a first episode of acute pericarditis

George Lazaros<sup>1</sup> · Alexios S. Antonopoulos<sup>1</sup> · Massimo Imazio<sup>2,3</sup> · Eirini Solomou<sup>1</sup> · Emilia Lazarou<sup>1</sup> · Dimitrios Vassilopoulos<sup>4</sup> · Yehuda Adler<sup>5,6</sup> · Christodoulos Stefanadis<sup>1,7</sup> · Dimitris Tousoulis<sup>1</sup>

177 patients, median follow-up 12 months

Pleural effusion, <i>n</i> (%)	94 (53.1)*
Localization, <i>n</i> (%)	
Right	17 (9.6)
Left	27 (15.3)
Bilateral	50 (28.2)

\* (52.2% in idiopathic and 56.1% in secondary ones,  $p=NS$ ).

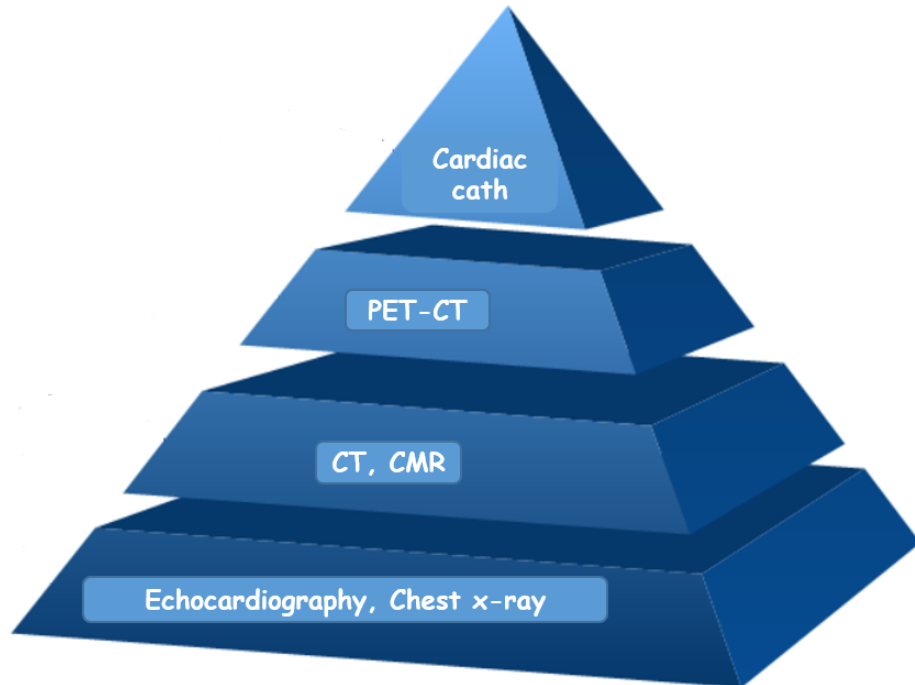
-Pleural effusions were strongly associated with CRP levels at admission but no association with secondary forms (including systemic autoimmune diseases).  
-Pleural effusions were found in 9 patients in the absence of pericardial effusion.  
-Bilateral PLEs were associated with increased risk for in-hospital cardiac tamponade (OR = 7.52, 95% CI 2.16-26.21).

There was no association of PLEs with new onset atrial fibrillation or pericarditis recurrence during long-term follow-up.

**-PLEs are common in patients hospitalized with acute pericarditis. They are related to the intensity of inflammatory reaction, and they should not be considered necessarily as a marker of secondary etiology.**



# Multimodality imaging in pericardial syndromes offer valuable information on diagnosis, risk stratification, prognosis and treatment guidance



**Anatomy:** Echo, CT, CMR  
**Function:** Echo, CMR  
**Inflammation:** CMR, PET-CT  
**Tissue characterization:** CMR  
**Comorbidities:** CT

J Cardiovasc Med (Hagerstown). 2016;774-782.

- The recurrence rate after an initial episode of pericarditis ranges from 15-30% within 18-24 months of the first episode.



- A second recurrence after the first occur in 25 to 50%.
- A third after a second in 20-40%.
- Multiple recurrences occur in ~6% (the range in percentages depends on colchicine and corticosteroids administration) → mean duration of disease 2.8-4.7 years.



Letter to the Editor

## The landscape of acute pericarditis in Greece: Experience from a tertiary referral center

Lazaros G, Solomou E, Antonopoulos AS, et al.  
Hellenic J Cardiol. 2019 Mar-Apr;60(2):139-140.



**Table 1**  
Features of patients hospitalized with first episode of acute pericarditis in Greece.

### Demographics

Total cases	175
Age (years)	59.7 ± 20.7
Gender (male)	104 (59.5%)

### Etiology

1. Idiopathic forms (%)	76%
2. Secondary forms (%)	24% (28.5% de novo diagnosis)

### Clinical presentation: epidemiology

Chest pain (%)	78.7
Dyspnea (%)	51.1
Pericardial friction rub (%)	19
Fever (°C) (%)	46
Hospital stay (days)	6.5 ± 2.8
Peak incidence (month)	October

### Laboratory findings: interventions

ST-elevation in ECG (%)	19.8
Admission CRP (mg/L, normal values <5)	95.8
CRP max (mg/L)	106.7
Pericardial effusion (%)	83.3
Pericardiocentesis/pericardial window (%)	23.6/4.1

### Treatment

1. NSAIDs % (IB/AS) (%)	72 (IB 90%/AS 10%)
2. Colchicine (%)	85.1
3. Steroids (%)	26.3

### Complications

1. Sustained arrhythmias (AF) (%)	8.2
2. Recurrence (%)	38.9
3. Cardiac tamponade (%)	13.7
4. Constrictive pericarditis (%)	2.3



# Possible pathogenetic mechanisms underlying recurrent pericarditis

- Infectious etiology
- Autoimmune mechanism
- **Autoinflammatory mechanism**

Autoinflammatory diseases include those genetic disorders characterized by primary dysfunction of the innate immune system and interleukin-1 is involved in their pathogenesis (example is the Familial Mediterranean Fever).


Brucato A, et al. *Autoimmun Rev* 2008;8:44–47.

Imazio M. *Expert Rev Cardiovasc Ther* 2012;10: 1165–1172.

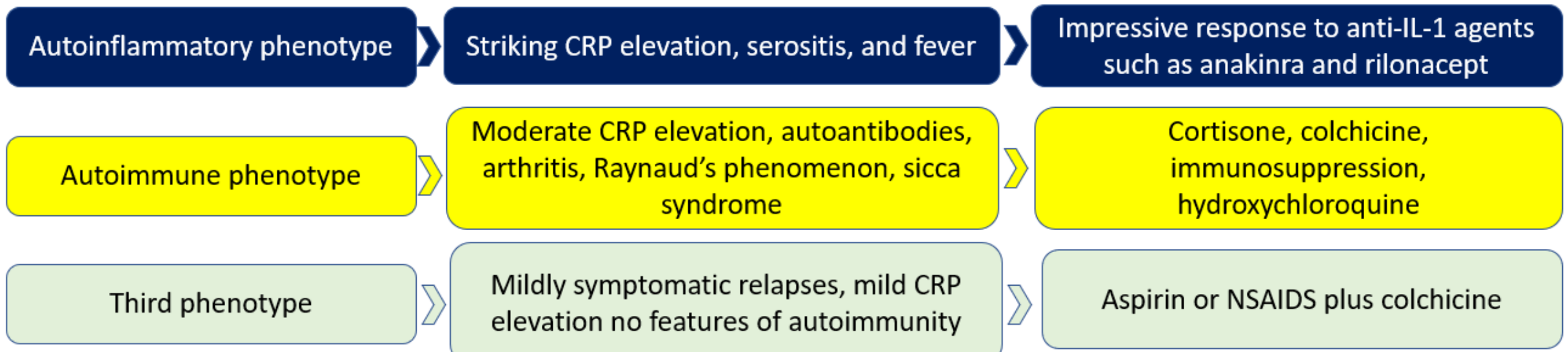
Lazaros G, et al. *Front Med (Lausanne)*. 2017 Jun 12;4:78.



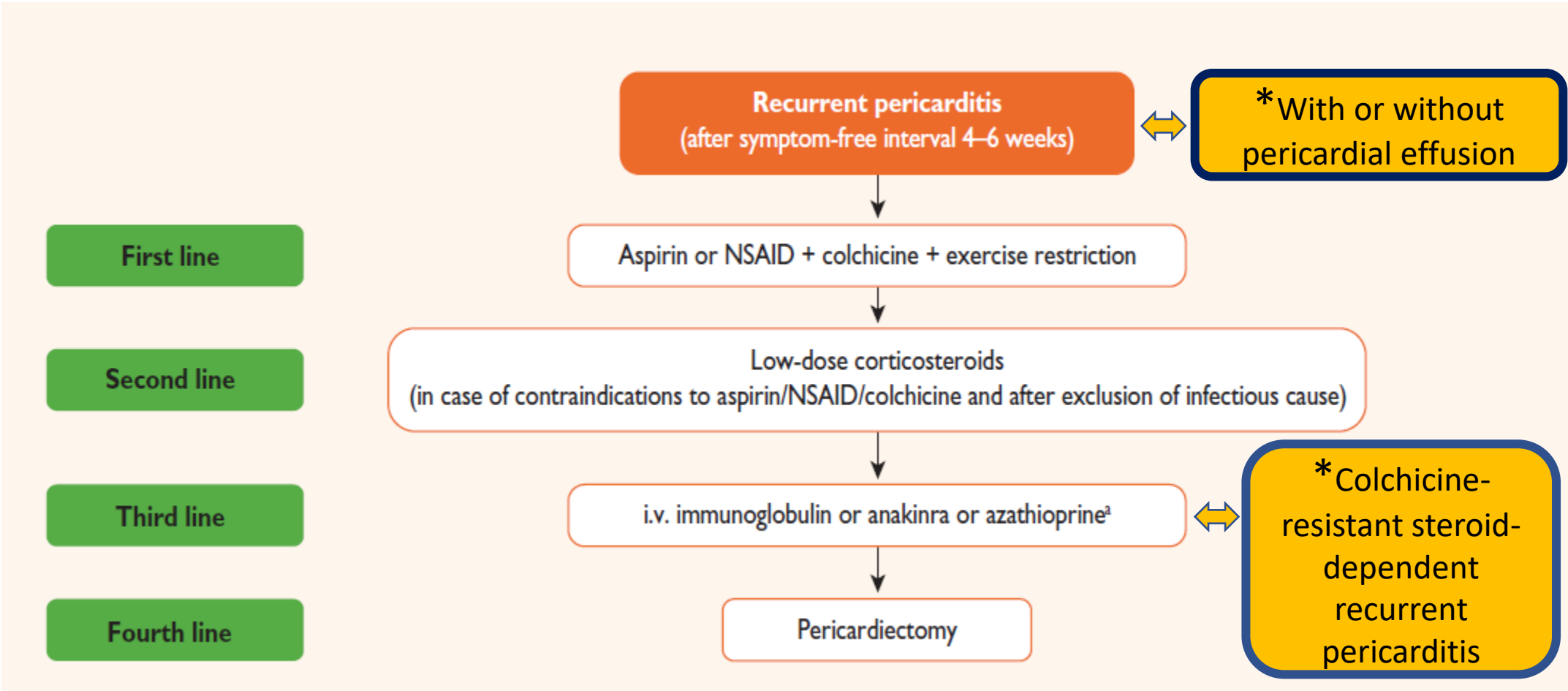
## Recurrent pericarditis: still idiopathic? The pros and cons of a well-honoured term

Antonio Brucato<sup>1</sup> · Massimo Imazio<sup>2</sup> · Paul C. Cremer<sup>3</sup> · Yehuda Adler<sup>4</sup> · Bernhard Maisch<sup>5</sup> · George Lazaros<sup>6</sup> · Marco Gattorno<sup>7</sup> · Alida L. P. Caforio<sup>8</sup> · Renzo Marcolongo<sup>9</sup> · Giacomo Emmi<sup>10</sup>  · Alberto Martini<sup>7,11</sup> · Allan L. Klein<sup>3</sup>

The goal (and our proposal) for the near future is to gradually abandon the term ‘idiopathic’ acute/recurrent pericarditis and to adopt new terms attributed to the pathophysiology of the disease such as ‘autoinflammatory’ or ‘autoimmune’ as soon as we are able to identify such mechanisms in specific patient subsets.



2015 ESC Guidelines for the diagnosis and management of pericardial diseases



**First line**

**Aspirin or NSAID + colchicine + exercise restriction**

**Commonly prescribed anti-inflammatory therapies for recurrent pericarditis**

Drug	Usual initial dose <sup>a</sup>	Tx duration <sup>b</sup>	Tapering <sup>a</sup>
Aspirin	500–1000 mg every 6–8 hours (range 1,5–4 g/day)	weeks-months	Decrease doses by 250–500 mg every 1–2 weeks <sup>b</sup>
Ibuprofen	600 mg every 8 hours (range 1200–2400 mg)	weeks-months	Decrease doses by 200–400 mg every 1–2 weeks <sup>b</sup>
Indomethacin	25–50 mg every 8 hours: start at lower end of dosing range and titrate upward to avoid headache and dizziness.	weeks-months	Decrease doses by 25 mg every 1–2 weeks <sup>b</sup>
Colchicine	0.5 mg twice or 0.5 mg daily for patients <70 kg or intolerant to higher doses.	At least 6 months	Not necessary, alternatively 0.5 mg every other day (<70 kg) or 0.5 mg once (≥70 kg) in the last weeks

Tx = treatment.

<sup>a</sup>Tapering should be considered for aspirin and NSAIDs.

<sup>b</sup>Longer tapering times for more difficult, resistant cases may be considered.

**Disease modifying**

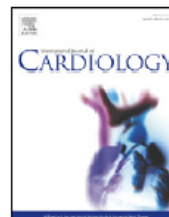
**Check CRP  
before  
tapering**



Contents lists available at [SciVerse ScienceDirect](http://SciVerse.ScienceDirect.com)

International Journal of Cardiology

journal homepage: [www.elsevier.com/locate/ijcard](http://www.elsevier.com/locate/ijcard)



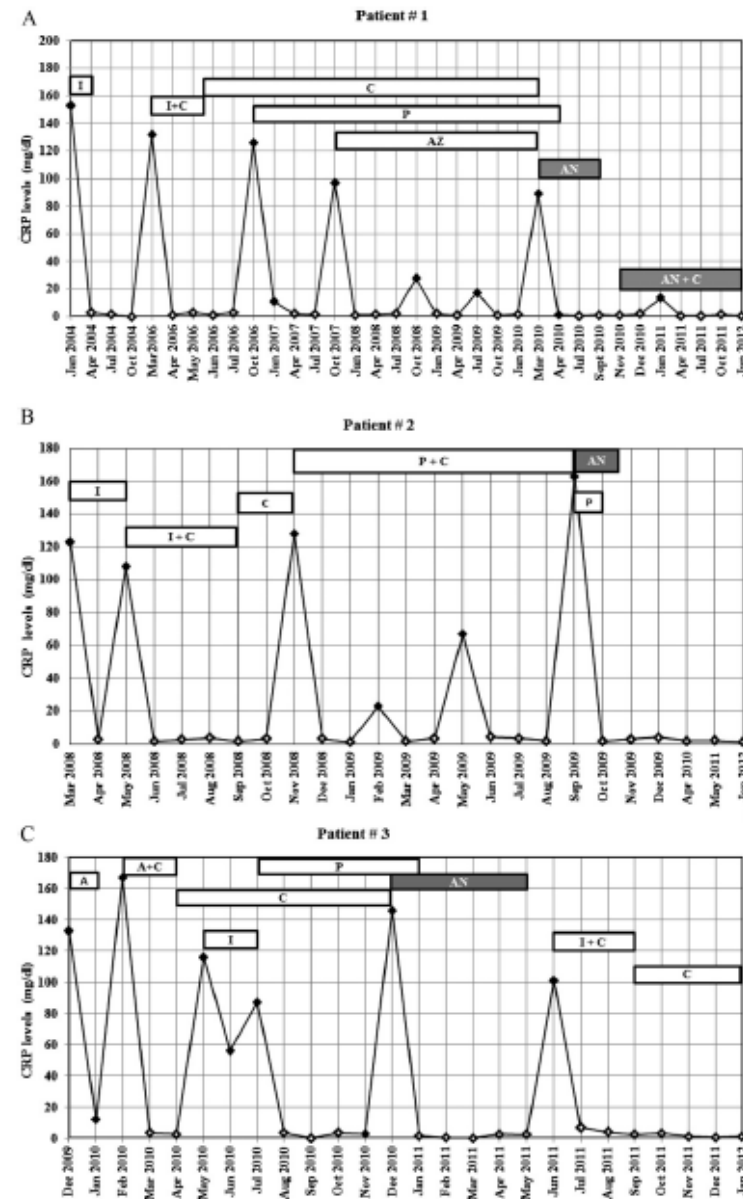
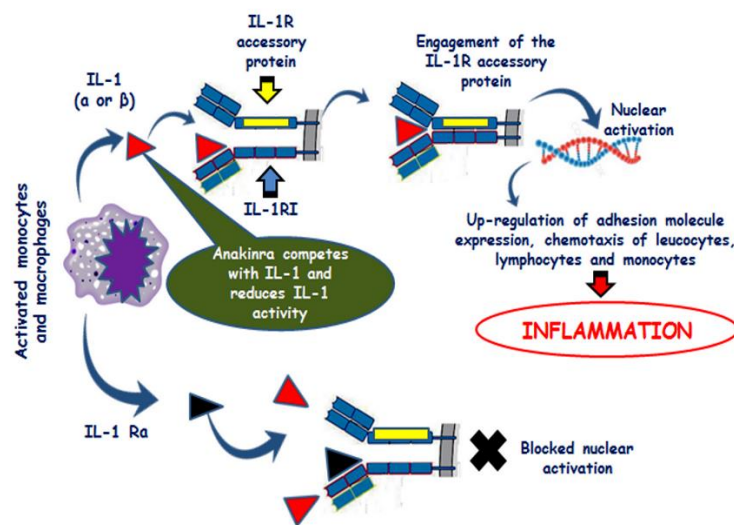
Letter to the Editor

## Successful treatment of adult patients with idiopathic recurrent pericarditis with an interleukin-1 receptor antagonist (anakinra)

Dimitrios Vassilopoulos<sup>a</sup>, George Lazaros<sup>b,\*</sup>, Costas Tsioufis<sup>b</sup>, Panagiotis Vasileiou<sup>b</sup>, Christodoulos Stefanadis<sup>b</sup>, Dimitrios Pectasides<sup>a</sup>

<sup>a</sup> 2nd Department of Medicine, Hippokraton General Hospital, Athens University School of Medicine, Athens, Greece

<sup>b</sup> 1st Department of Cardiology, University of Athens Medical School, Hippokraton Hospital, Athens, Greece



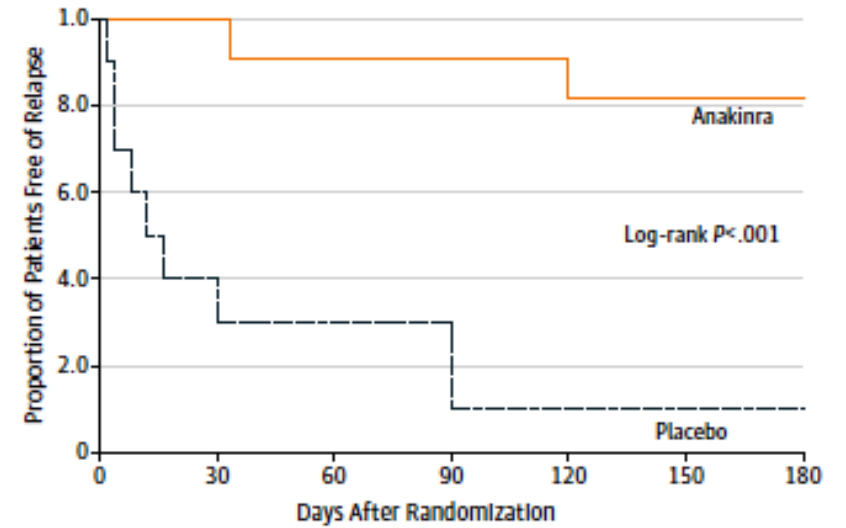


JAMA | Preliminary Communication

# Effect of Anakinra on Recurrent Pericarditis Among Patients With Colchicine Resistance and Corticosteroid Dependence The AIRTRIP Randomized Clinical Trial

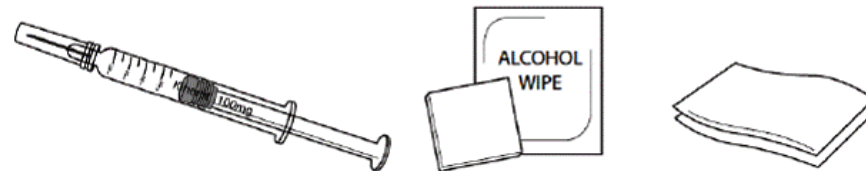
Antonio Brucato, MD; Massimo Imazio, MD, FESC; Marco Gattorno, MD; George Lazaros, MD; Silvia Maestroni, MD; Mara Carraro, RN; Martina Finetti, MD; Davide Cumetti, MD; Alessandra Carobbio, MSc; Nicolino Ruperto, MD, MPH; Renzo Marcolongo, MD; Monia Lorini, MD; Alessandro Rimini, MD; Anna Valenti, MD; Gian Luca Erre, MD; Maria Pia Sormani, PhD; Riccardo Belli, MD; Fiorenzo Gaita, MD; Alberto Martini, MD

2016;316:1906-1912



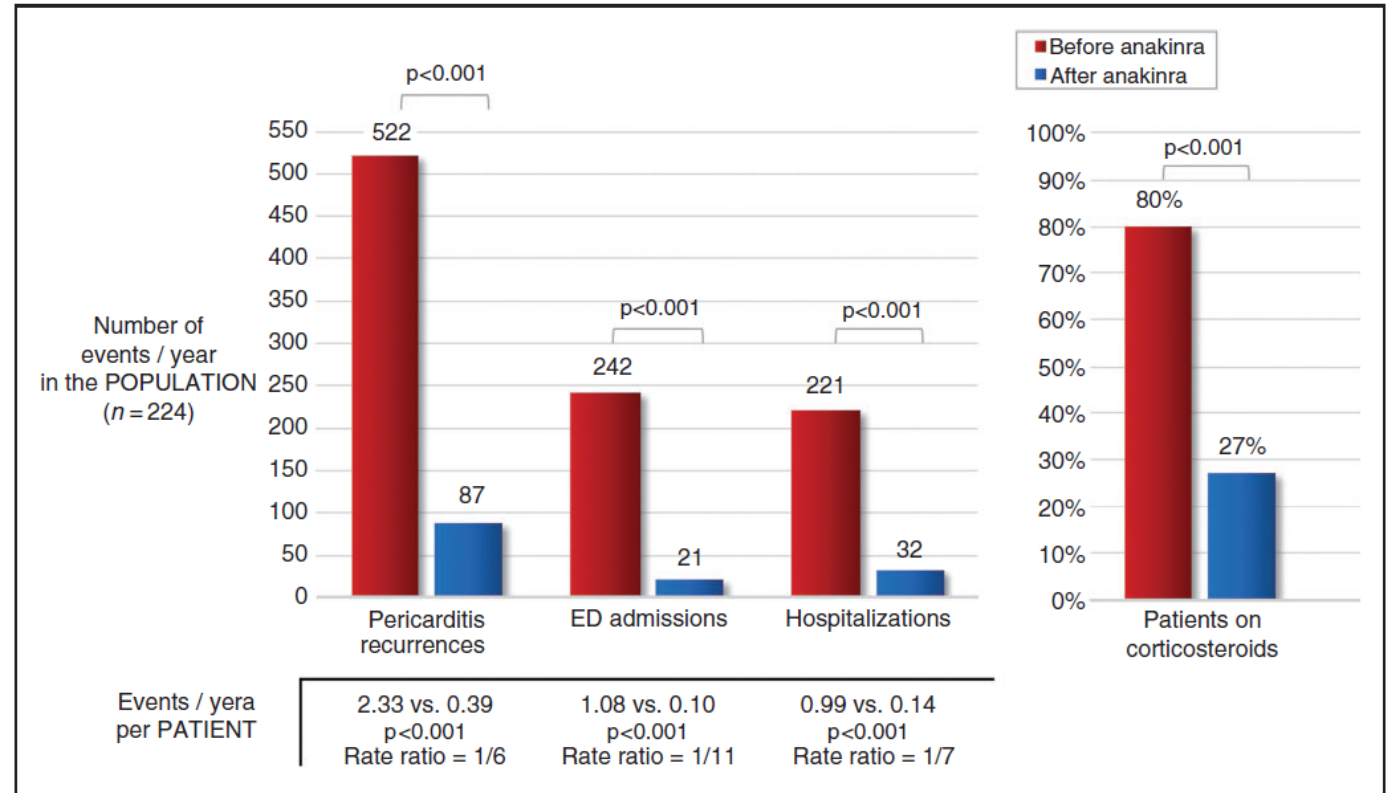
No. at risk		0	30	60	90	120	150	180
Placebo	10	4	3	3	1	1		
Anakinra	11	11	10	10	10	10	9	
No. of treatment failures								
Placebo		6	1	0	2	0		
Anakinra		0	1	0	0	1		

**Conclusion and relevance:** In this preliminary study of patients with recurrent pericarditis with colchicine resistance and corticosteroid dependence, the use of anakinra compared with placebo reduced the risk of recurrence over a median of 14 months. Larger studies are needed to replicate these findings as well as to assess safety and longer-term efficacy.



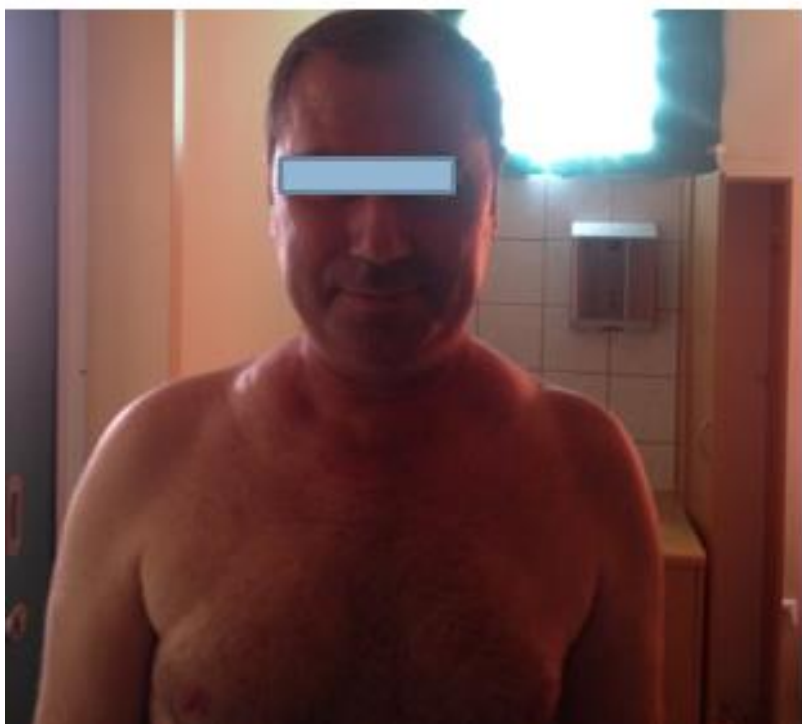
## Anakinra for corticosteroid-dependent and colchicine-resistant pericarditis: The IRAP (International Registry of Anakinra for Pericarditis) study

Massimo Imazio<sup>1</sup>, Alessandro Andreis<sup>1</sup>, Gaetano Maria De Ferrari<sup>1</sup>, Paul C Cremer<sup>2</sup>, Vartan Mardigyan<sup>3</sup>, Silvia Maestroni<sup>4</sup>, Sushil Allen Luis<sup>5</sup>, Giuseppe Lopalco<sup>6</sup>, Giacomo Emmi<sup>7</sup>, Dor Lotan<sup>8</sup>, Renzo Marcolongo<sup>9</sup>, George Lazaros<sup>10</sup>, Marzia De Biasio<sup>11</sup>, Luca Cantarini<sup>12</sup>, Lorenzo Dagna<sup>13</sup>, Andreja Cerne Cercek<sup>14</sup>, Emanuele Pivetta<sup>15</sup>, Beni Varma<sup>2</sup>, Laeora Berkson<sup>3</sup>, Enrico Tombetti<sup>16</sup>, Florenzo Iannone<sup>6</sup>, Domenico Prisco<sup>7</sup>, Alida Linda P Caforio<sup>9</sup>, Dimitrios Vassilopoulos<sup>10</sup>, Dimitrios Tousoulis<sup>10</sup>, Giacomo De Luca<sup>13</sup>, Carla Giustetto<sup>1</sup>, Mauro Rinaldi<sup>1</sup>, Jae K Oh<sup>5</sup>, Allan L Klein<sup>2</sup>, Antonio Brucato<sup>16</sup> and Yehuda Adler<sup>8</sup>



Recurrences, emergency department admissions, hospital admissions before and after anakinra (number of events/year per patient and in the population of the registry). Corticosteroid use before and after anakinra.

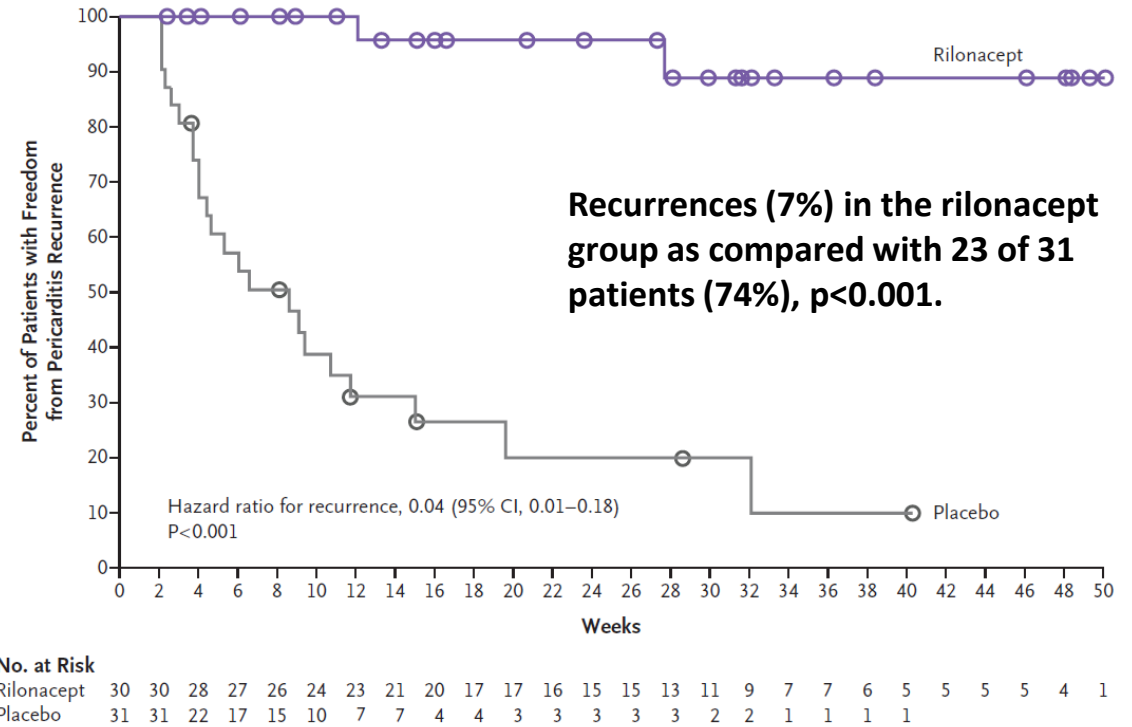
- 224 patients (46 ± 14 years old, 63% women, 75% idiopathic).
- Follow-up of 3889 patient-months.



ORIGINAL ARTICLE

# Phase 3 Trial of Interleukin-1 Trap Rilonacept in Recurrent Pericarditis

Allan L. Klein, M.D., Massimo Imazio, M.D., Paul Cremer, M.D., Antonio Brucato, M.D., Antonio Abbate, M.D., Ph.D., Fang Fang, Ph.D., Antonella Insalaco, M.D., Martin LeWinter, M.D., Basil S. Lewis, M.D., David Lin, M.D., Sushil A. Luis, M.B., B.S., Stephen J. Nicholls, M.B., B.S., Ph.D., Arian Pano, M.D., Alistair Wheeler, M.D., and John F. Paolini, M.D., Ph.D., for the RHAPSODY Investigators\*



- 61 patients underwent randomization.
- The median duration of exposure to rilonacept was 9 months.

**Conclusions:** Among patients with recurrent pericarditis, rilonacept led to rapid resolution of recurrent pericarditis episodes and to a significantly lower risk of pericarditis recurrence than placebo.

# Concerns related to anakinra (IL-1 inhibitors) administration

- Daily injections
- In ~10% discontinuation due to side effects
- With abrupt discontinuation after the full dose regimen for 6-12 months 70% of patients relapse
- With slow tapering ~45% of patients relapse. Those who relapse they do so when they switch from 3 injection/week to 2 injections /week
- Thus with 10-12 injections daily in most cases we are able to achieve stable disease remission



Please review the Supplemental Files folder to review documents not compiled in the PDF.

## Interleukin-1 Inhibition in Recurrent Pericarditis

Journal:	<i>New England Journal of Medicine</i>
Manuscript ID	Draft
Article Type:	Letter about NEJM Article
Date Submitted by the Author:	n/a
Complete List of Authors:	Lazaros, George; University of Athens Medical School, Hippokraton General Hospital, Cardiology Tsioufis, Costas; First Cardiology Clinic, University of Athens, Hippokraton Hospital, ; Vassilopoulos, Dimitrios; Hippokraton Hospital, 2nd Academic Department of Medicine
Abstract:	

**J Cardiovasc Med (Hagerstown). 2016;17:256-262.**

**Front Med 12 June 2017doi.org/103389.fmed.2017.00078.**

**EULAR CONGRESS 2016 (ABSTRACT)**

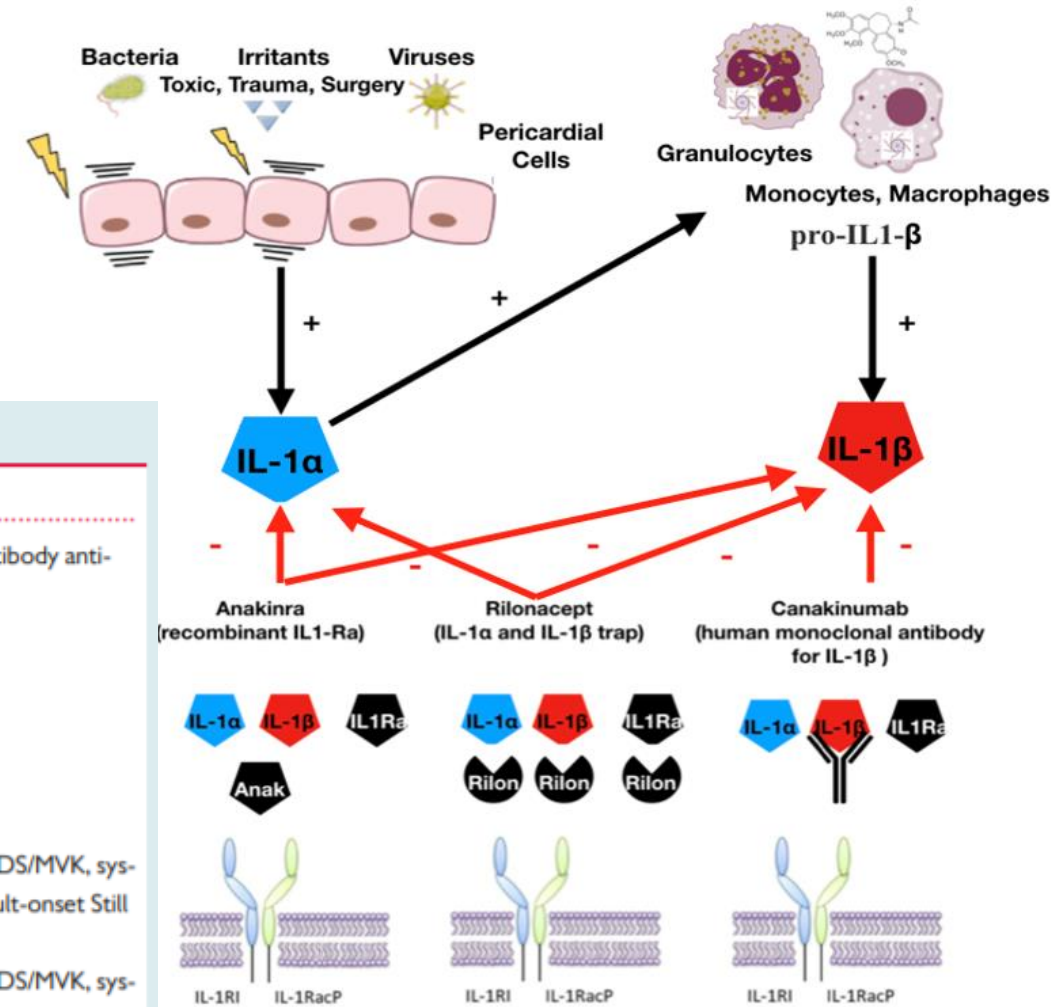
**N Engl J Med. 2021;384:1474-1475.**

# Anti-interleukin-1 agents for pericarditis: a primer for cardiologists

Massimo Imazio <sup>1\*</sup>, George Lazaros <sup>2</sup>, Marco Gattorno <sup>3</sup>, Martin LeWinter <sup>4</sup>, Antonio Abbate <sup>5</sup>, Antonio Brucato <sup>6†</sup>, and Allan Klein <sup>7†</sup>

## Anti-IL-1 agents in clinical use

	Anakinra	Riloncept	Canakinumab
Form	Recombinant human IL-1Ra	IL-1 $\alpha$ and IL-1 $\beta$ trap	Human monoclonal antibody anti-IL-1 $\beta$
IL-1 target	IL-1 $\alpha$ and IL-1 $\beta$	IL-1 $\alpha$ and IL-1 $\beta$	IL-1 $\beta$
Half-life	4–6 h	7 days	26 days
Administration	SC or IV	SC	SC
Dosing	Every day	Weekly	Every 1–2 months
Dose adjustment for renal failure	Yes	No	No
Anti-inflammatory potency	+++	++	+++
FDA-approved indications	CAPS, RA	CAPS	CAPS, TRAPS, FMF, HIDS/MVK, systemic juvenile IA, adult-onset Still disease
EMA-approved indications	CAPS, systemic juvenile IA, adult-onset Still disease, RA	None	CAPS, TRAPS, FMF, HIDS/MVK, systemic juvenile IA, adult-onset Still disease, gout flare
Adverse Events	Injection site reactions, hepatitis, infections	Injection site reactions, infections, neutropenia, hyperlipidemia	Injection site reactions, infections, neutropenia



# Are there alternative solutions in refractory cases?



## Hydroxychloroquine for colchicine-resistant glucocorticoid-dependent idiopathic recurrent pericarditis: A pilot observational prospective study

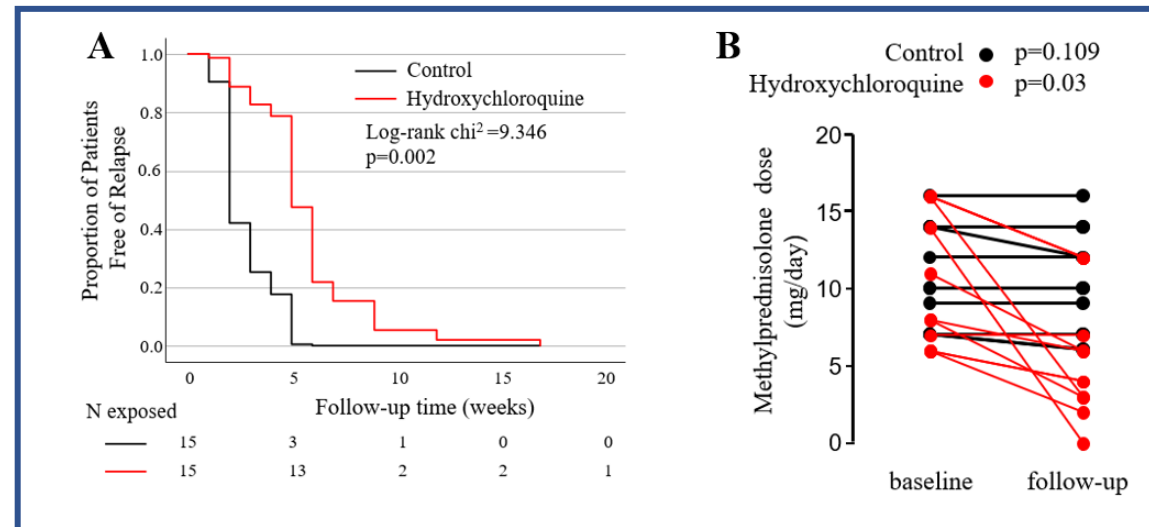
George Lazaros<sup>a,\*</sup>, Alexios S. Antonopoulos<sup>a,1</sup>, Katerina Antonatou<sup>b</sup>, Panagiotis Skendros<sup>c</sup>, Konstantinos Ritis<sup>c</sup>, Emilia Hadziyannis<sup>b</sup>, Emilia Lazarou<sup>a</sup>, Ioannis Leontsinis<sup>a</sup>, Spiros Simantiris<sup>a</sup>, Charalambos Vlachopoulos<sup>a</sup>, Dimitris Tousoulis<sup>a</sup>, Dimitrios Vassilopoulos<sup>b</sup>

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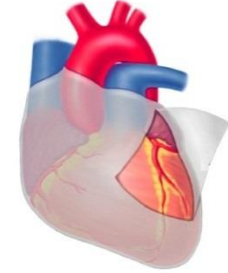
<sup>c</sup> First Department of Internal Medicine, Democritus University of Thrace, University Hospital of Alexandroupolis, Alexandroupolis, Greece

- HCQ acts through inhibition of autophagy, a key regulatory mechanism in innate immunity and autoinflammation leading to a reduced expression of IL-1 $\beta$ .
- HCQ was also associated with a higher proportion of patients obtaining a  $\geq 50\%$  dose reduction of GCs (33.3% vs. 0% in the control group,  $p=0.037$ ) and reduced GC dose (HCQ: -43.5% vs. control: -4.5%,  $p<0.001$ ).



Fourth line

## Pericardiectomy



- Pericardiectomy should be reserved only for frequent, strongly symptomatic recurrences (especially recurrent tamponade) resistant to medication.
- Referral of these patients to centers with specific expertise in this surgery is recommended.
- During surgery every effort should be made to remove the complete pericardium..
- In a retrospective study in 184 pts (1994-2005) pericardiectomy was very effective in reducing the rate of recurrences with a perioperative mortality of 0% and rate of major complications 3%.



# Prognosis in recurrent pericarditis

- Despite detrimental effects on the patients' quality of life, the long-term prognosis is good.
- In specific forms, prognosis depends on the underlying condition. Overall in-hospital mortality rate for acute pericarditis was 1.1% in a recent Finnish national registry.
- In a metanalysis of 230 patients with idiopathic recurrent pericarditis, during a mean follow-up period of 61 months, cardiac tamponade was recorded in 3.5% of cases, while there were no cases of constrictive pericarditis or left ventricular dysfunction.

## 3.3.2 Prognosis

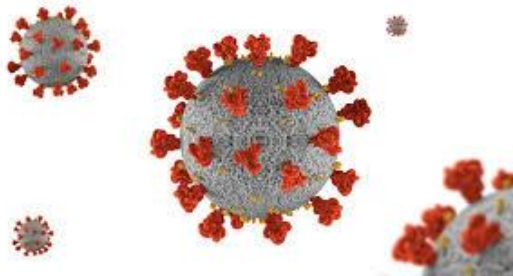
Severe complications are uncommon in idiopathic recurrent pericarditis.<sup>37,60,61</sup> Cardiac tamponade is rare and generally occurs at the beginning of the disease. Constrictive pericarditis has never been reported in these patients, despite numerous recurrences, and the overall risk is lower than that recorded after a first episode of acute pericarditis (<1%).<sup>36,37,61</sup> Thus it is important to reassure patients about their prognosis, explaining the nature of the disease and its likely course. The complication rates are related to the aetiology and not to the number of recurrences. Drug treatment should take into account this favourable outcome to avoid more toxic agents. However, quality of life can be severely affected in patients with repeated recurrences, subacute or incessant pericarditis and glucocorticoid dependence.

**2015 ESC Guidelines for the diagnosis and management of pericardial diseases** 

Imazio M, et al. *Circulation* 2007;115:2739-2744.  
Imazio M, et al. *Am J Cardiol* 2007;100:1026-1028.  
Kytö et al. *Circulation* 2014;130:1601-1606.

## Anti-inflammatory therapies for pericardial diseases in the COVID-19 pandemic: safety and potentiality

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### Current treatments for pericarditis and Coronavirus disease 2019 infection

Drug	Attack dose	Duration	LOE	Effect on COVID-19 <sup>a</sup>
NSAIDs <sup>2</sup>	Aspirin 750–1000 mg × 3/day Ibuprofen 600–800 mg × 3/day Indomethacin 25–50 mg × 3/day	1–2 weeks but till symptoms resolution and CRP normalization	A	Harmful (?) <sup>10,11</sup>
Colchicine <sup>2,5,6</sup>	0.5 mg × 2/day (0.5 mg /day if <70 kg)	3 months (acute) 6 months (recurrent)	A	Potential therapy
Corticosteroid <sup>2</sup>	0.2–0.5 mg/kg/day of prednisone	Up to 1 month	B	Therapy for advanced cases <sup>12</sup>
Azathioprine <sup>2,9</sup>	Up to 2 mg/kg	>6 months	B	Unknown
NHIG <sup>2,8</sup>	400–500 mg/kg/day	5 days (can be repeated after 1 month)	B	Potential therapy
Anakinra <sup>2–4</sup>	2 mg/kg/day up to 100 mg/day	3–6 months then tapered	B	Potential therapy <sup>12</sup>

## Periodical reevaluation is important in patients with idiopathic recurrent pericarditis!

- 61 patients who were referred to a tertiary hospital for resistant idiopathic recurrent pericarditis were followed for an average of 8.3 years:



- During follow-up in ~90% of cases pericarditis remained idiopathic, whereas a new secondary diagnosis [namely Sjogren's syndrome – 8.3% and rheumatoid arthritis 2.1%), emerged in the rest.



### ***Key message***

Idiopathic recurrent pericarditis is not a life-long diagnosis in all cases



**Thank you for your attention**