

Pericardial Disease: Key Concepts

Leonard S. Lilly, M.D.

Professor of Medicine

Harvard Medical School

Chief, Brigham/Faulkner Cardiology

Brigham and Women's Hospital



Mass General Brigham



HARVARD
MEDICAL SCHOOL

Leonard S. Lilly, M.D.



- Professor of Medicine
Harvard Medical School
- Chief, Brigham/Faulkner Cardiology Section
Brigham & Women's Hospital
- Clinician, Educator, Textbook Author
 - Clinical focus: General and preventive cardiology, noninvasive imaging, pericardial disease
 - Research interests: Novel approaches for pericardial disease, innovations in medical education

Disclosures

Member of Data Monitoring Committee for RHAPSODY trial
(Cleveland Clinic / Kiniksa Pharmaceuticals)

Objectives

Diagnosis and management of:

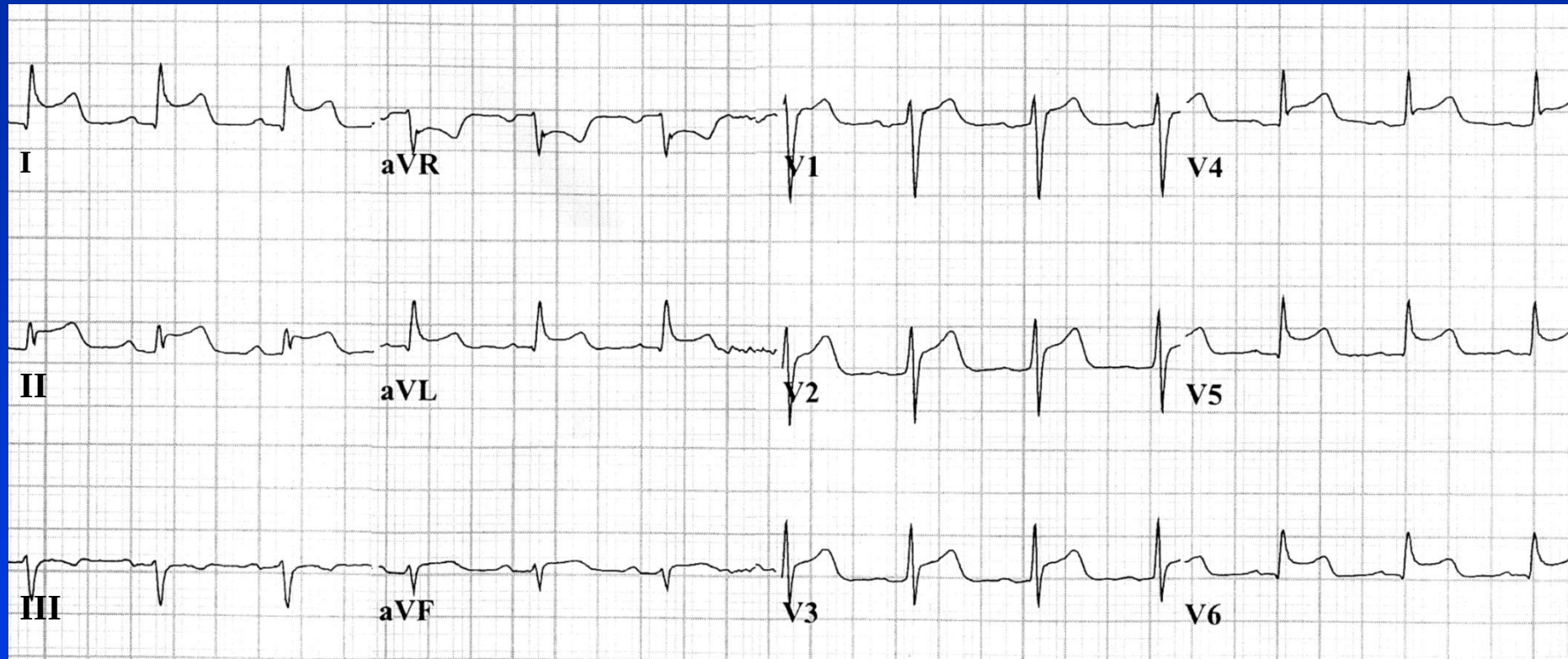
- Acute pericarditis
- Cardiac tamponade
- Constrictive pericarditis

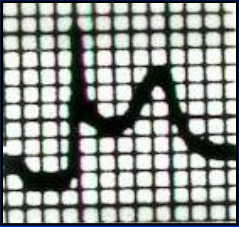
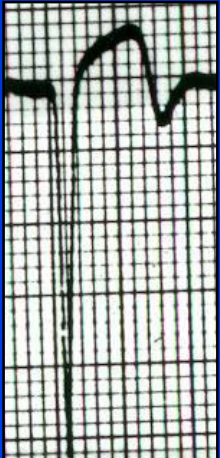
Case Presentation

42-year-old malpractice attorney presents to the emergency department with chest pain since awakening

- No history of angina
- Father had MI at age 55
- Had uncomplicated upper respiratory tract infection one month ago

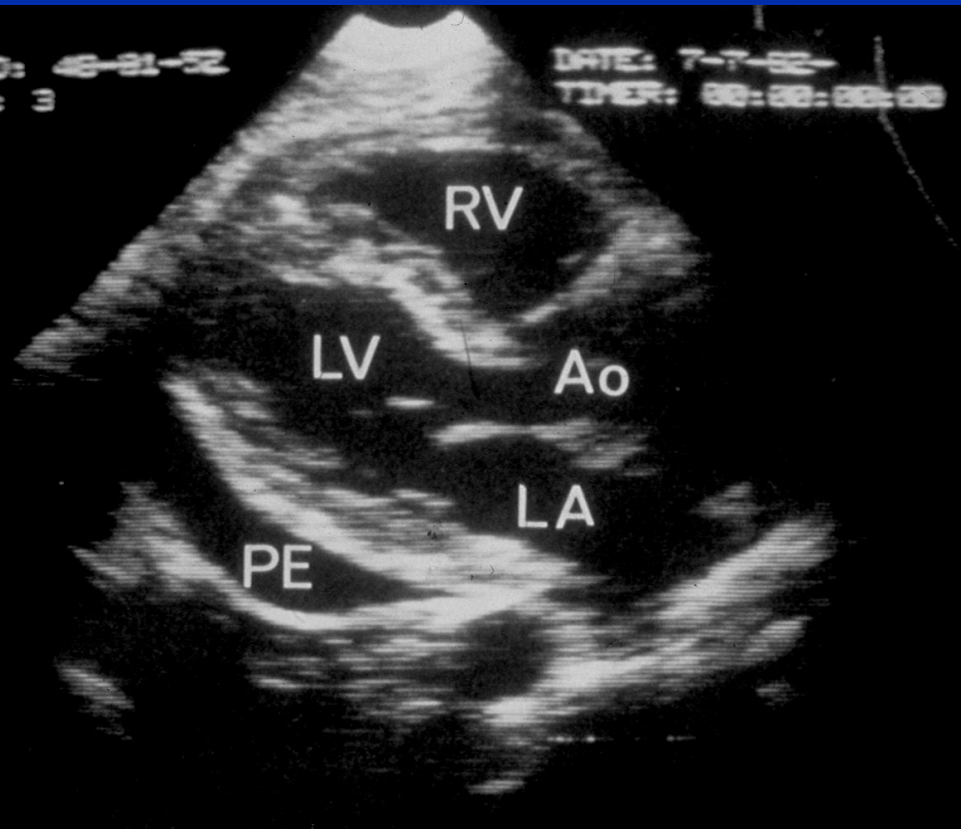
Electrocardiogram



	ST Coving	Which Leads?	ST-T Evolution	PR Segment
Pericarditis	 (STE < 5 mm)	Diffuse	Days- weeks	↓
Acute STEMI		Localized	Hours	Normal

PT ID: 48-91-52
CODE: 3

DATE: 7-7-92
TIME: 00:00:00:00



Acute Pericarditis

- >85% post-viral / idiopathic¹
- Usually self-limited: 1-3 weeks
- 15-30% recurrence rate²
- Several recent prospective trials offer evidence-based guidance

¹*Am J Cardiol* 1995;75:378.

²*Circulation* 2010;121:916.

Management of Acute Pericarditis

- Aspirin and other NSAIDs
- Colchicine
- Glucocorticoids

NSAIDs

- No prospective randomized trials

Aspirin ¹	650-975 mg TID-QID
Ibuprofen	400-800 mg TID
Indomethacin	50 mg TID
Ketorolac ²	IM or IV: 15-30 mg QID

- ~2 week course followed by taper

¹*J Am Coll Cardiol* 2004;43:1042.

²*Am Heart J* 1993;125:1455.

NSAIDs

- If symptoms or fever persist > 1 week, consider etiologies other than post-viral / idiopathic
- Imazio et al (*J Am Coll Cardiol* 2004;43:1042)
 - 254 pts with acute pericarditis treated as outpatients
 - 221 responded rapidly – presumably idiopathic
 - 33 (13%) had persistent symptoms
 - 14 Autoimmune disorder¹
 - 6 Tuberculosis

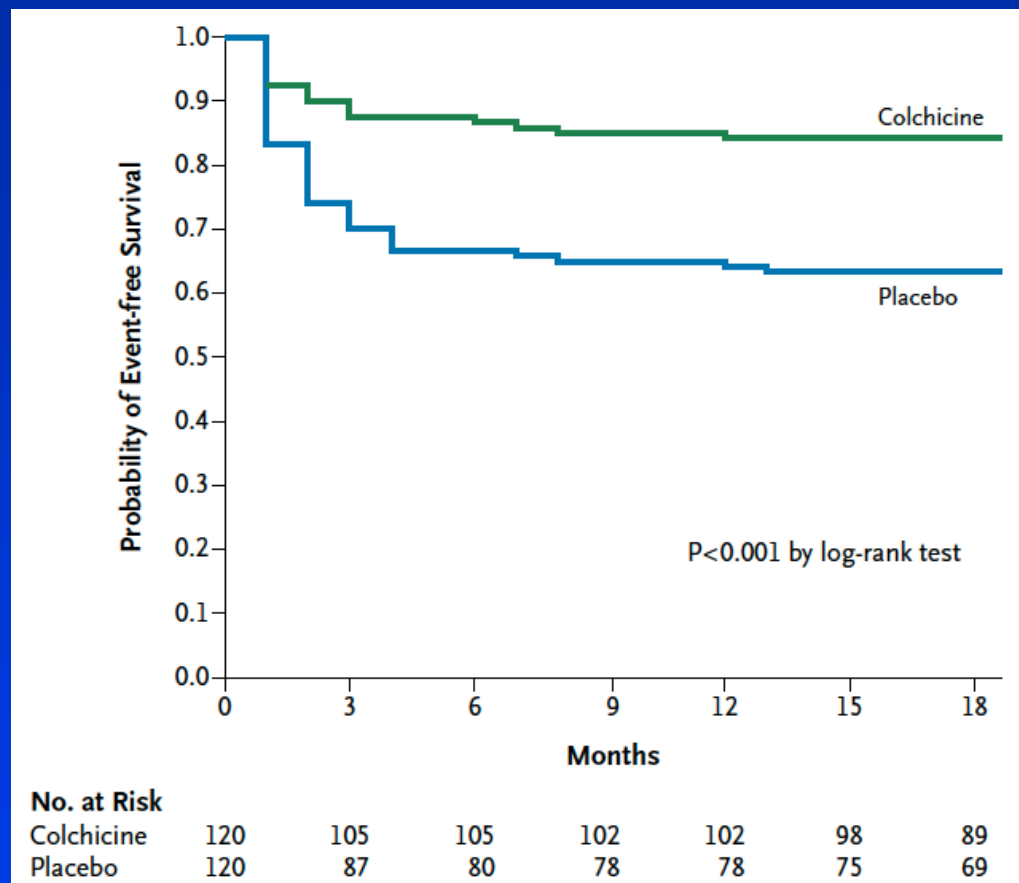
¹Connective tissue disease or post-pericardiotomy syndrome

ICAP: Double-blinded Trial of Colchicine in Initial Acute Pericarditis

(Imazio M et al. *N Eng J Med* 2013; 369:1522)

- Multicenter study of 240 men & women with 1st episode of pericarditis (idiopathic/ viral, CTD, or post-cardiac surgery)
- Randomized to colchicine (0.5-1.0 mg/d x 3 months) vs. placebo, in addition to ASA or ibuprofen
- Primary end point: Persistent or recurrent pericarditis

ICAP: Primary Outcome Results



Outcome	RRR	<i>P</i>
Persistent or recurrent pericarditis	0.56	<0.001
Symptoms at 72 hours	0.52	=0.001

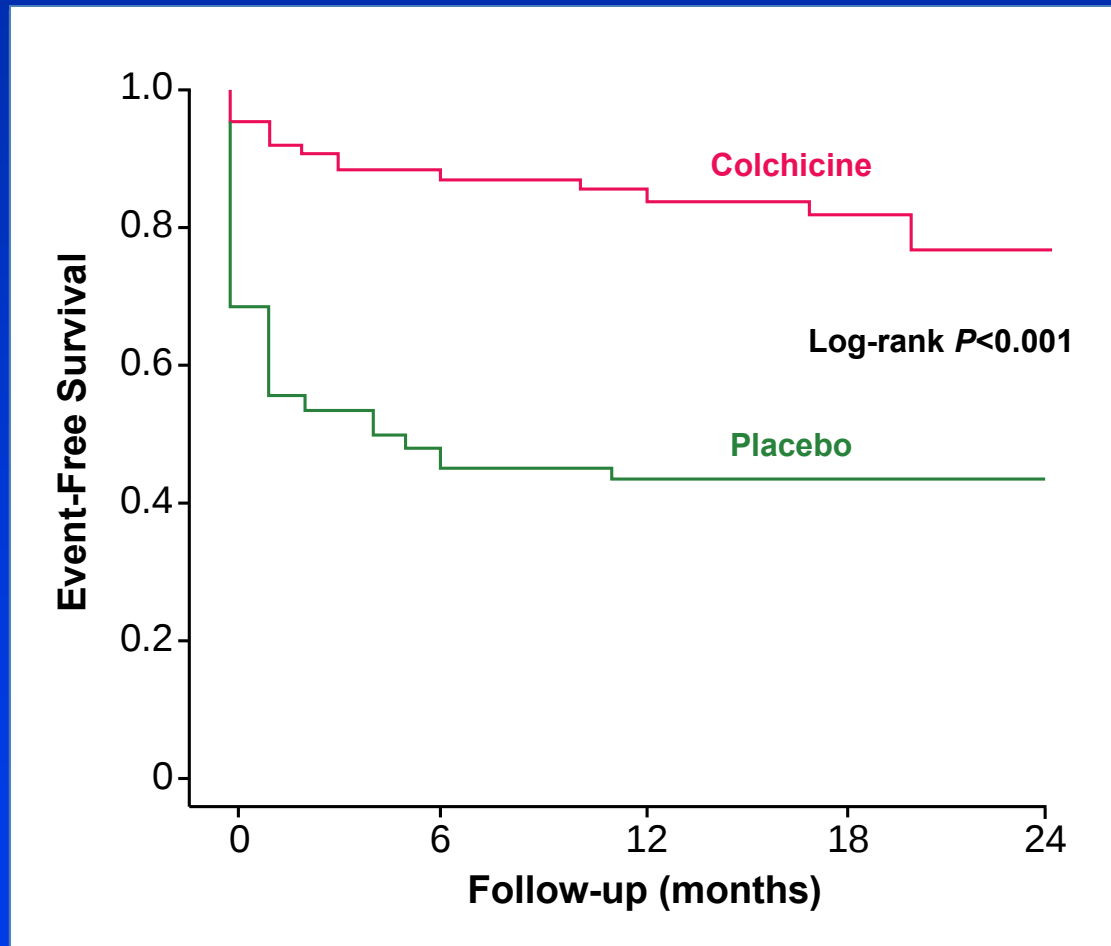
CORP: Double-blinded study of colchicine for secondary prevention

(Imazio M et al. *Ann Intern Med* 2011; 155:409)

- Prospective, placebo-controlled trial at four urban hospitals in Italy: 120 men & women with 1st recurrence of pericarditis
- Randomized to colchicine (1-2 mg x 1 day, then 0.5-1.0 mg/d x 6 months) vs. placebo, in addition to ASA or ibuprofen
- Primary end point: Recurrence of pericarditis at 18 months

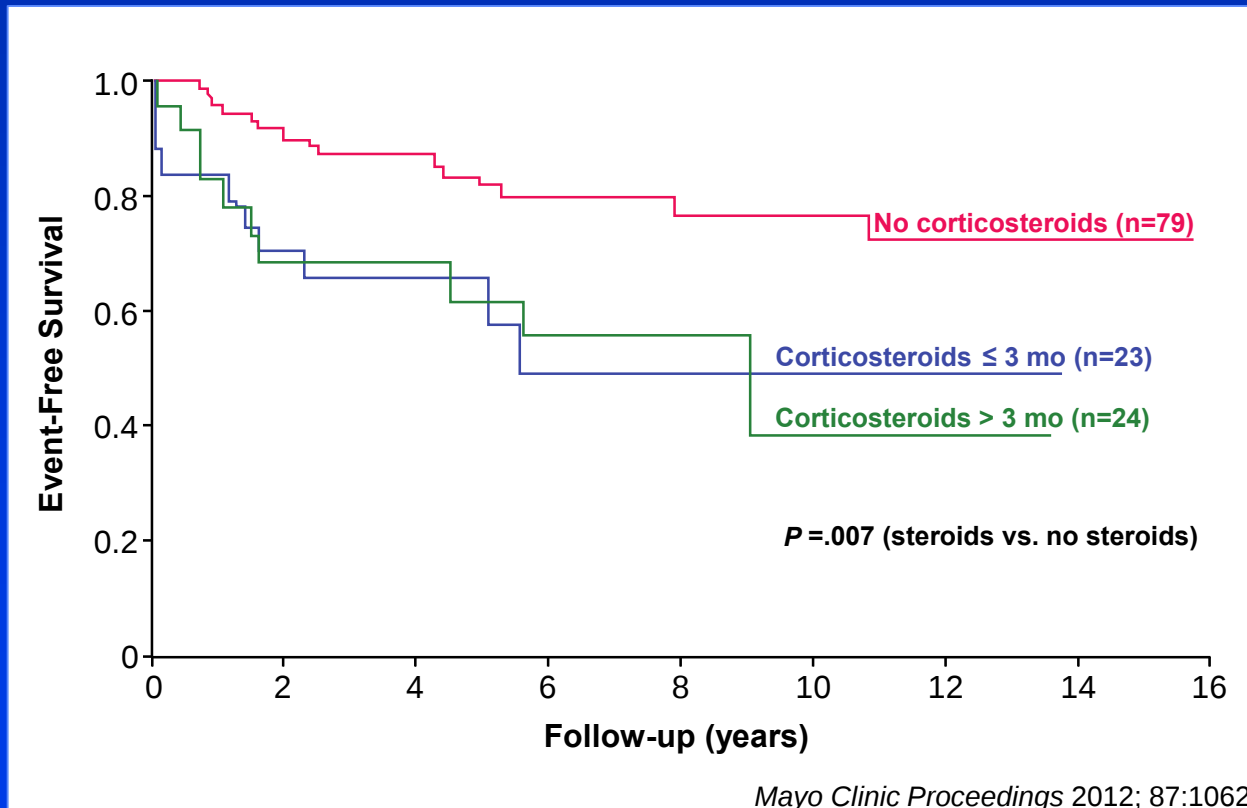
CORP: Double-blinded study of colchicine for secondary prevention

(Imazio M et al. *Ann Intern Med* 2011; 155:409)



Glucocorticoid Therapy in Pericarditis

- Rapidly improves symptoms, but should **not** be used as primary therapy for pericarditis: Increases risk of recurrences¹



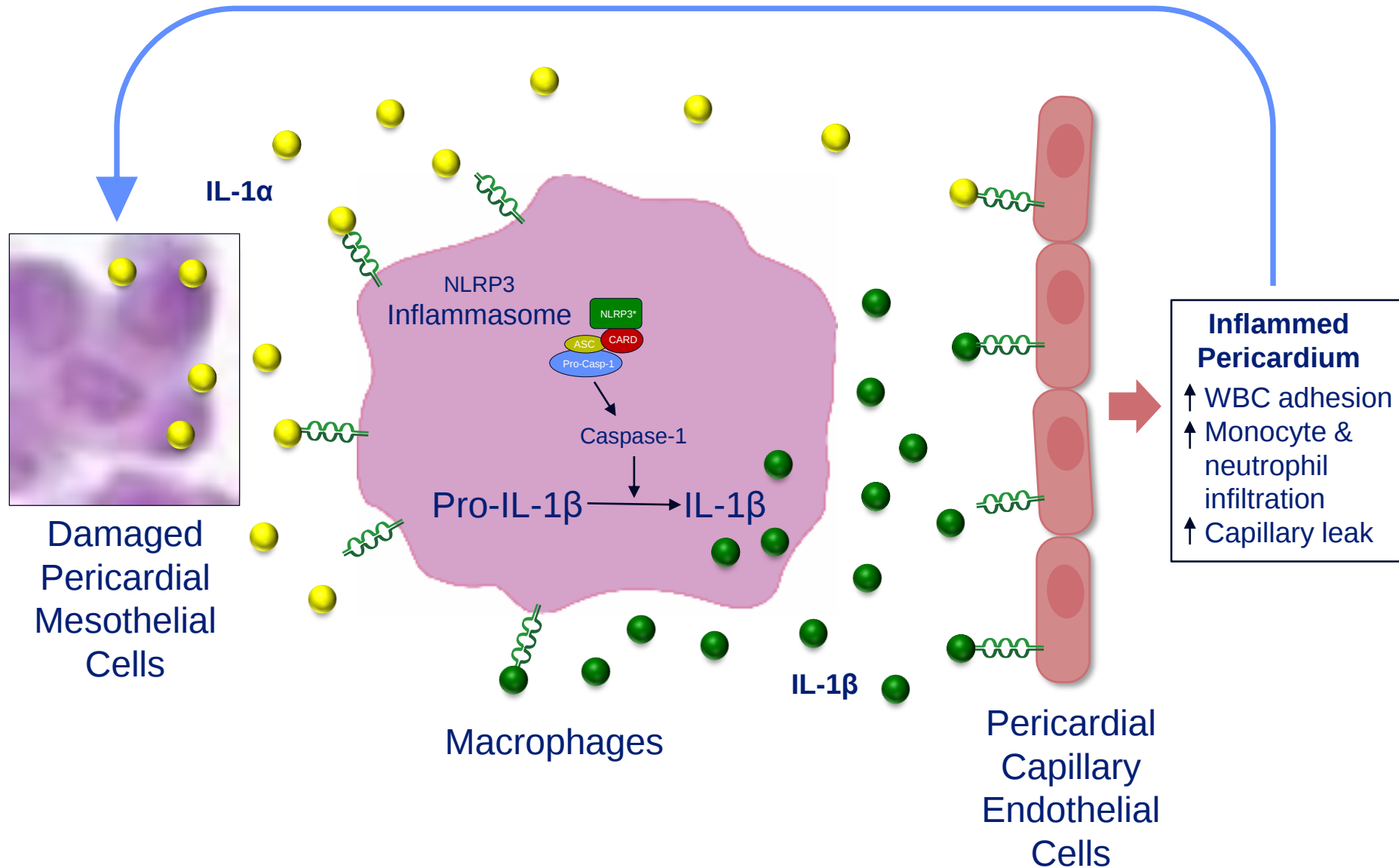
Glucocorticoid Therapy in Pericarditis

Restrict use to patients truly
refractory to, or intolerant of,
NSAID + colchicine
(and taper slowly)

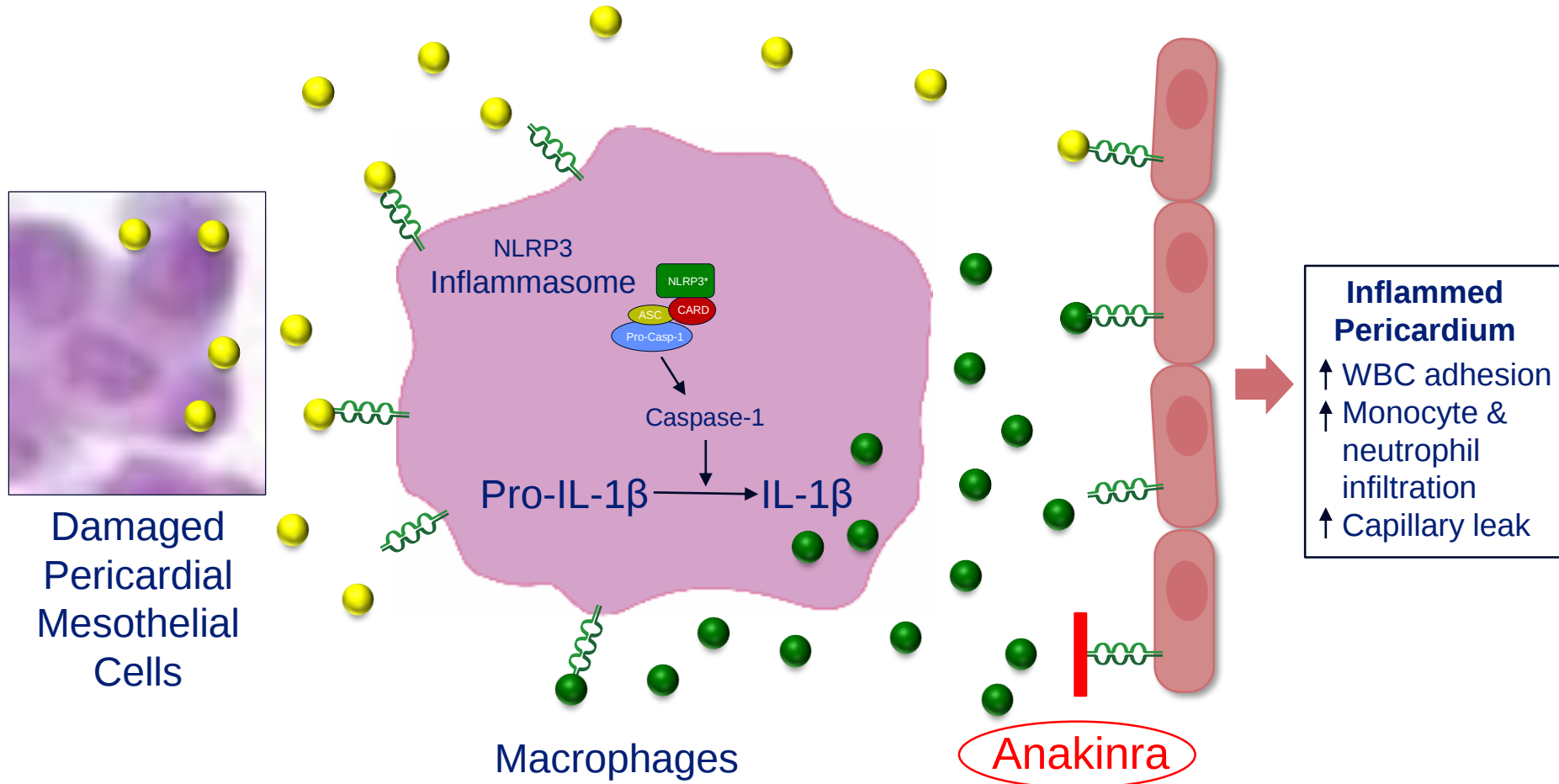
Approach to Colchicine-Refractory or Steroid-Dependent Patients

1. Confirm pericarditis is actual cause of symptoms
2. Very slow prednisone taper
3. Immunosuppressive therapy
(case reports and nonrandomized data:
methotrexate, azathioprine, mycophenolate, IV
immunoglobulin)
4. IL-1 antagonist therapies
5. Pericardiectomy

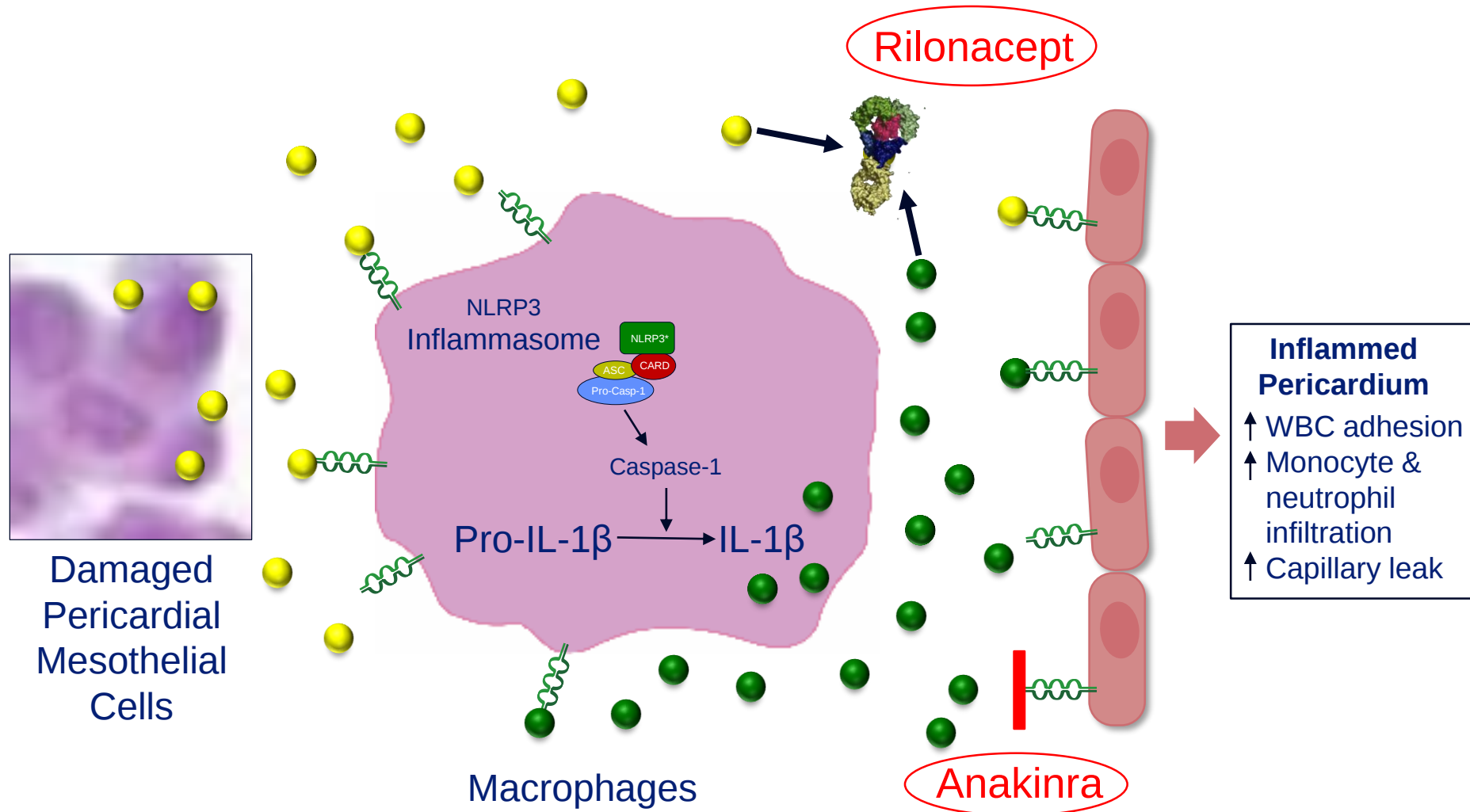
Role of IL-1 in Pericarditis



Role of IL-1 in Pericarditis



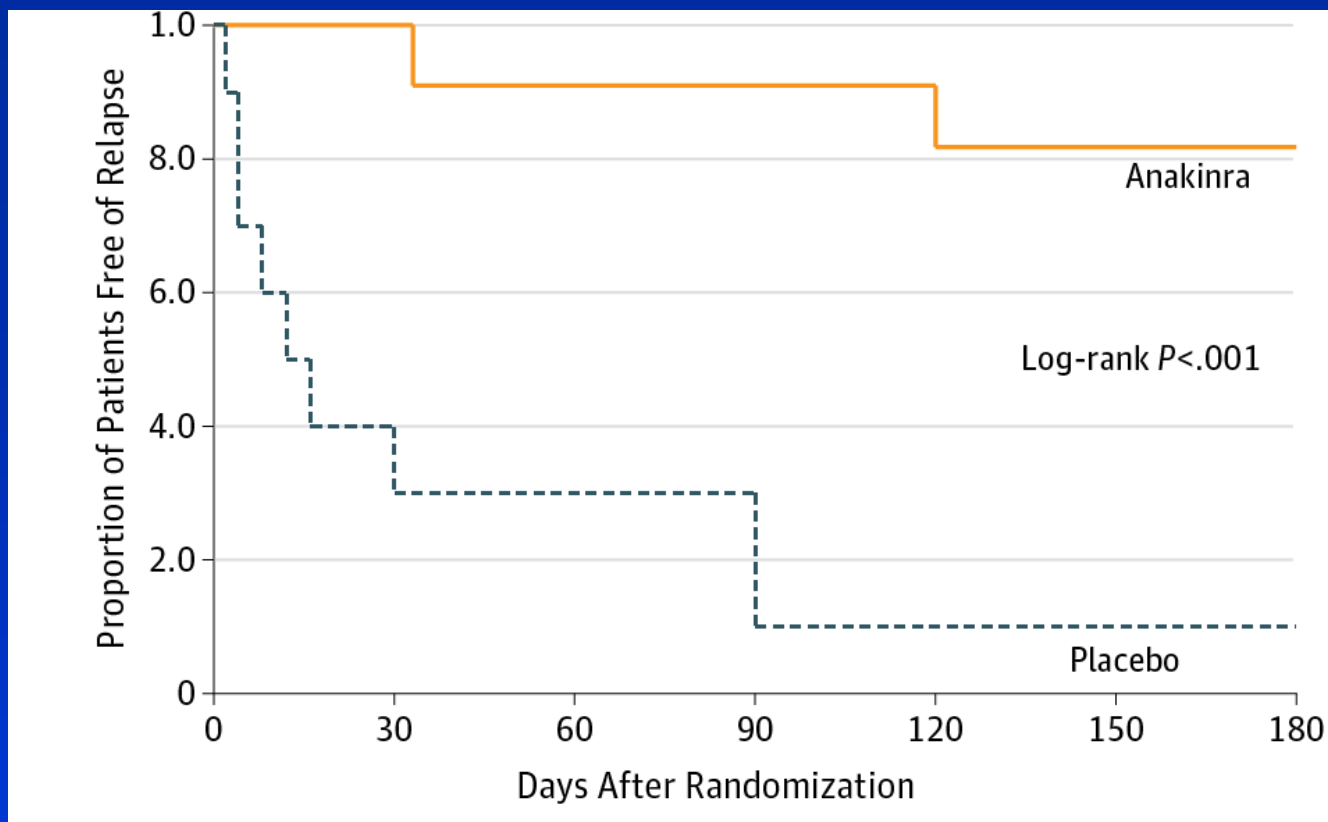
Role of IL-1 in Pericarditis



Anakinra in Recurrent Pericarditis

(AIRTRIP Trial *JAMA* 2016; 316:1906)

- Double-blind, placebo-controlled, randomized withdrawal trial (n=21, mean age 45.4 y)
- Patients with ≥ 3 recurrences (colchicine resistant, glucocorticoid dependent, elevated CRP)
- Initial open label treatment with daily subcutaneous anakinra: All patients able to stop steroids, CRP normalized
- At 60 days: randomized to continued anakinra vs. placebo x 6 months
- Primary end point: Recurrent pericarditis



18% recurrence

90% recurrence

Anakinra side effects:

- Local skin reaction common (resolved with topical Rx)
- 3 pts: transaminitis (<2xULN), reversed with ↓dose

Conclusion:

- Anakinra allows rapid withdrawal from steroids
- Prolonged therapy is necessary

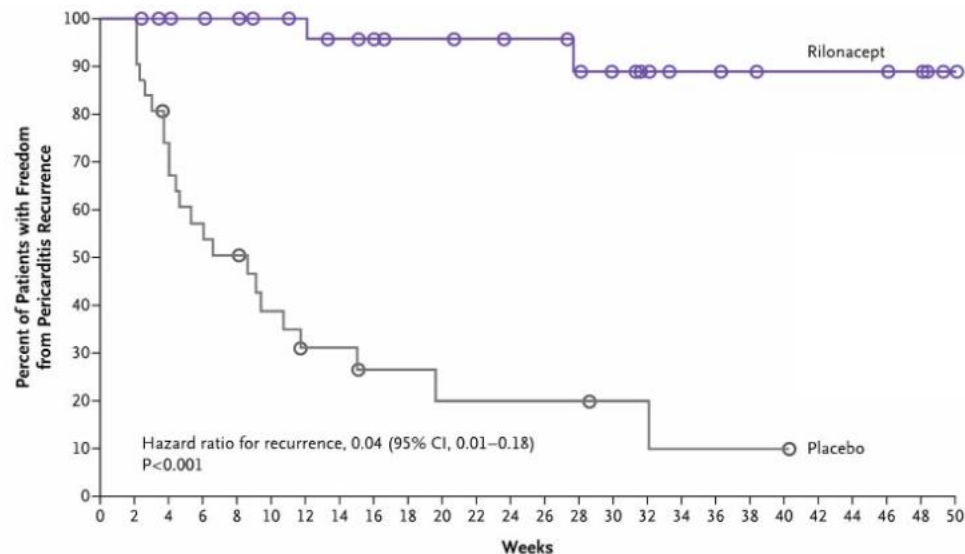
Rilonacept in Recurrent Pericarditis

(RHAPSODY Trial *N Engl J Med* 2021; 384:31)

- Double-blind, placebo-controlled, randomized withdrawal trial (n=61, mean age 44.7 y)
- Patients with ≥ 2 recurrences and elevated CRP (~47% on glucocorticoid therapy)
- Initial open label treatment with weekly subcutaneous rilonacept: All patients able to wean off steroids, colchicine
- At 12 weeks: randomized to continued rilonacept vs. placebo
- Primary end point: Recurrent pericarditis

RHAPSODY: Time to the First Adjudicated Pericarditis Recurrence

Primary Efficacy Endpoint (Randomized Withdrawal Period; n = 61)



No. at Risk

Rilonacept	30	30	28	27	26	24	23	21	20	17	17	16	15	15	13	11	9	7	7	6	5	5	5	5	4	1
Placebo	31	31	22	17	15	10	7	7	4	4	3	3	3	3	3	2	2	1	1	1	1					

2

23

RHAPSODY AEs:

Event	Run-In Period	Randomized Withdrawal Period				Total (N = 86)
	Rilonacept (N = 86)	Rilonacept, Including Bailout (N = 30)	Placebo, Including Bailout (N = 31)	Rilonacept, Before Bailout (N = 30)	Placebo, Before Bailout (N = 31)	
Any AE	69 (80)	24 (80)	22 (71)	24 (80)	13 (42)	74 (86)
Serious AE	1 (1)	1 (3)	3 (10)	1 (3)	1 (3)	5 (6)
Cancer	0	1 (3)	0	1 (3)	0	1 (1)
Injection-site reaction	28 (33)	6 (20)	2 (6)	5 (17)	0	29 (34)
Infection or infestation	14 (16)	12 (40)	7 (23)	12 (40)	3 (10)	29 (34)
URTI	12 (14)	7 (23)	2 (6)	7 (23)	0	19 (22)

Complications of Acute Pericarditis

Cardiac tamponade

*(Pericardial fluid
under pressure)*

Constrictive pericarditis

*(Scarred, rigid
Pericardium)*

```
graph TD; A[Cardiac tamponade  
(Pericardial fluid under pressure)] --> C[Impaired diastolic ventricular filling]; B[Constrictive pericarditis  
(Scarred, rigid Pericardium)] --> C; C --> D[Elevated venous pressures]; C --> E[Reduced stroke volume]; D --> F[Jugular venous distension & Pulmonary congestion]; E --> G[Decreased Cardiac output];
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Impaired diastolic
ventricular filling

Elevated venous
pressures



Jugular venous distension
&
Pulmonary congestion

Reduced stroke
volume

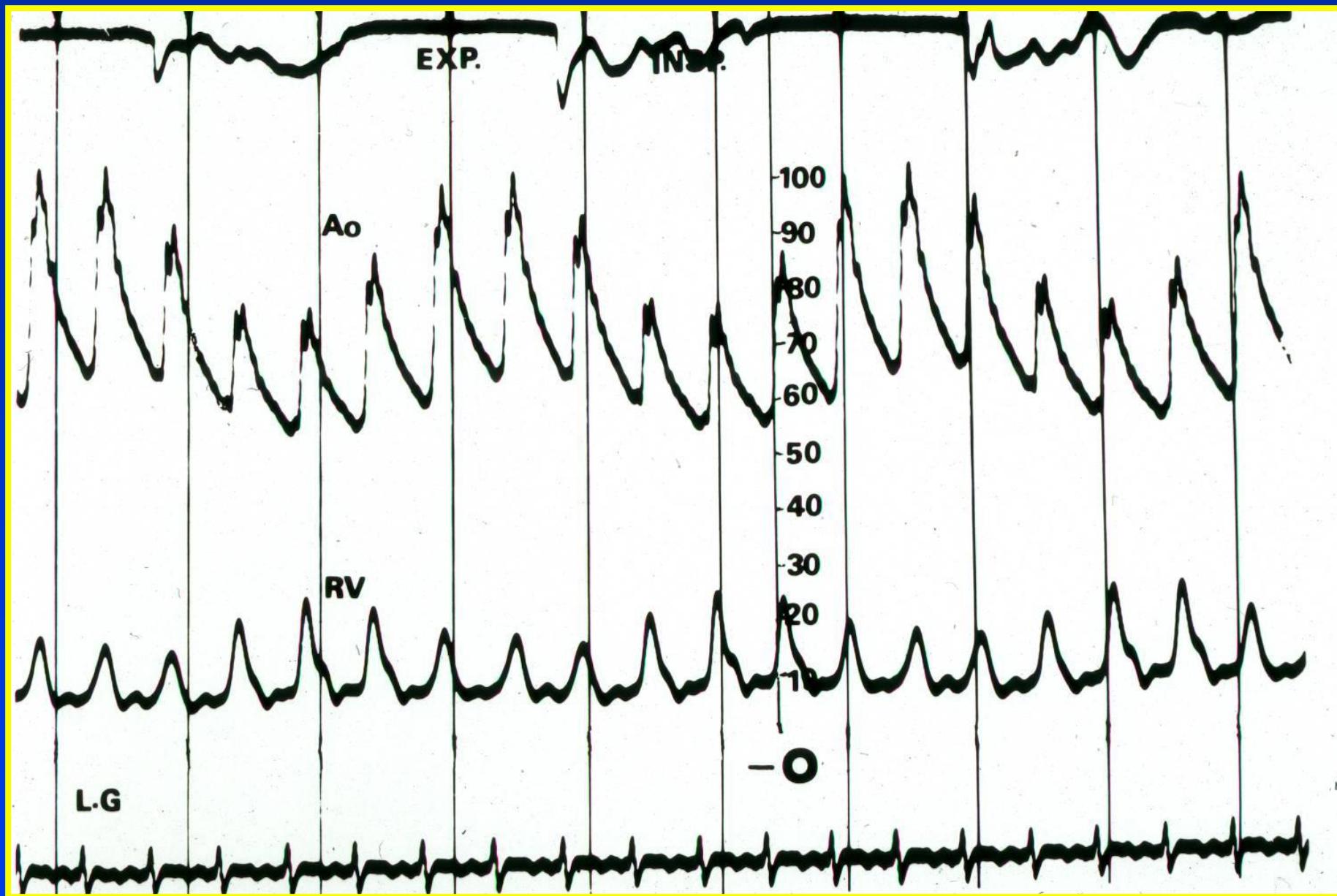


Decreased
Cardiac
output

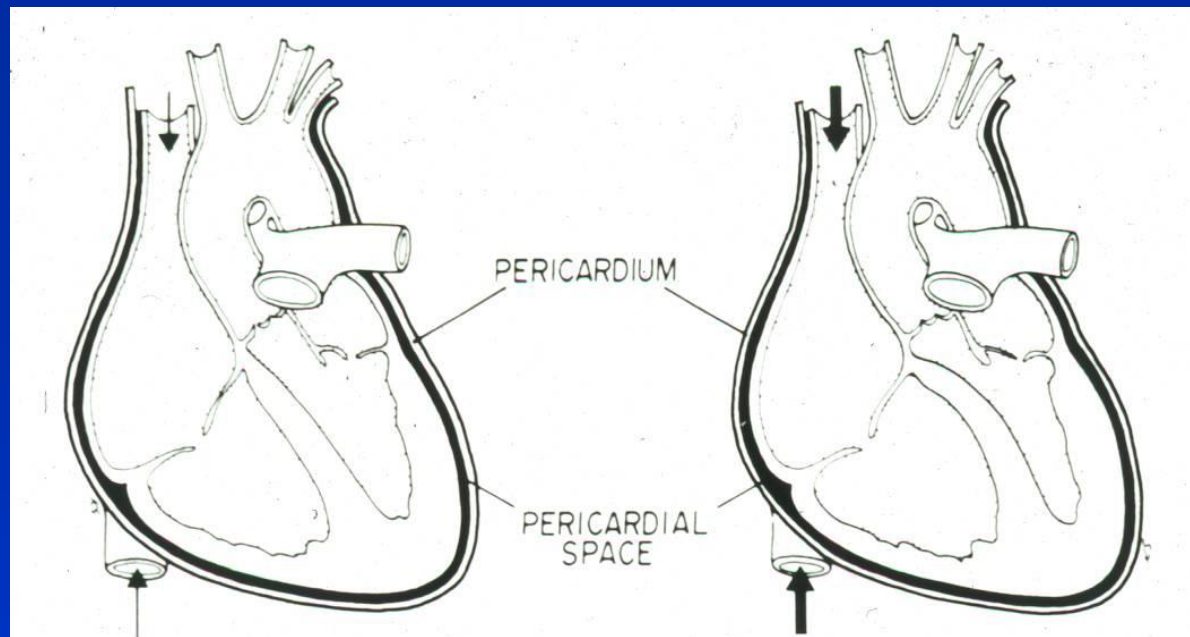
Cardiac Tamponade

(Beck, 1935)

- Jugular venous distention
- “Small, quiet heart”
- Hypotension



Normal

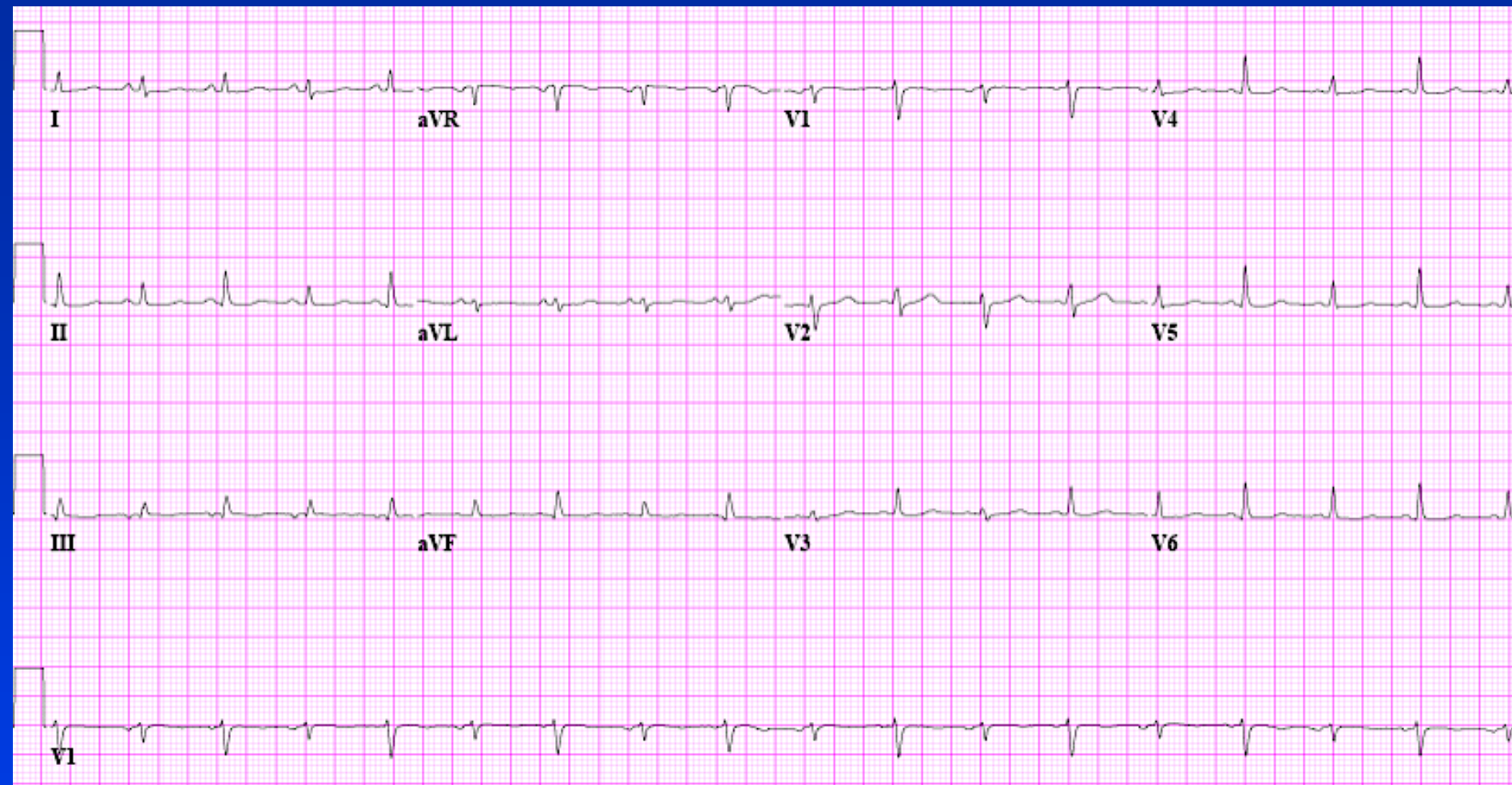


Expiration

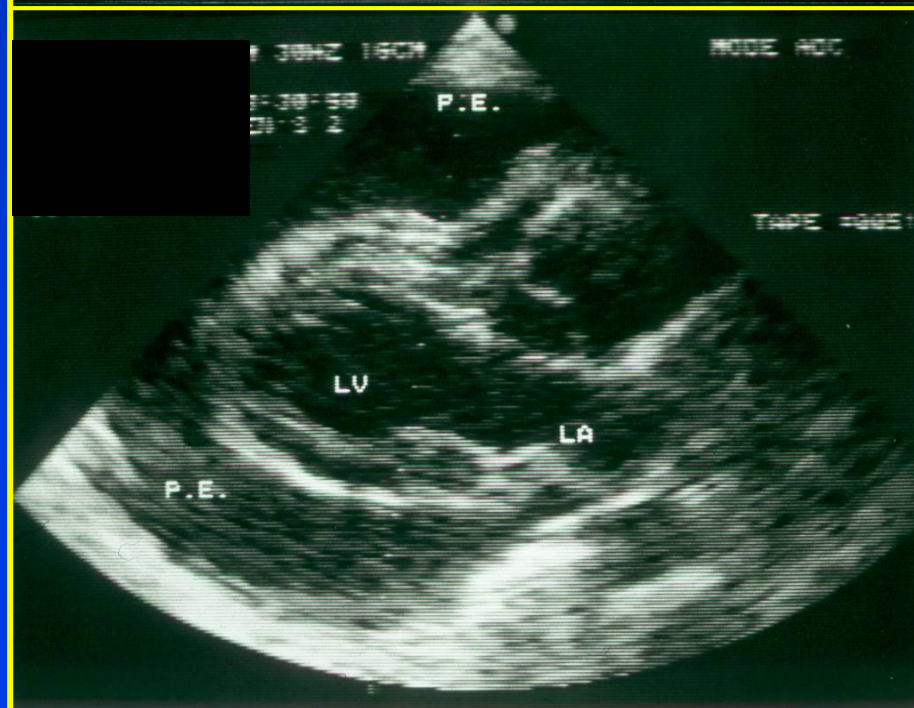
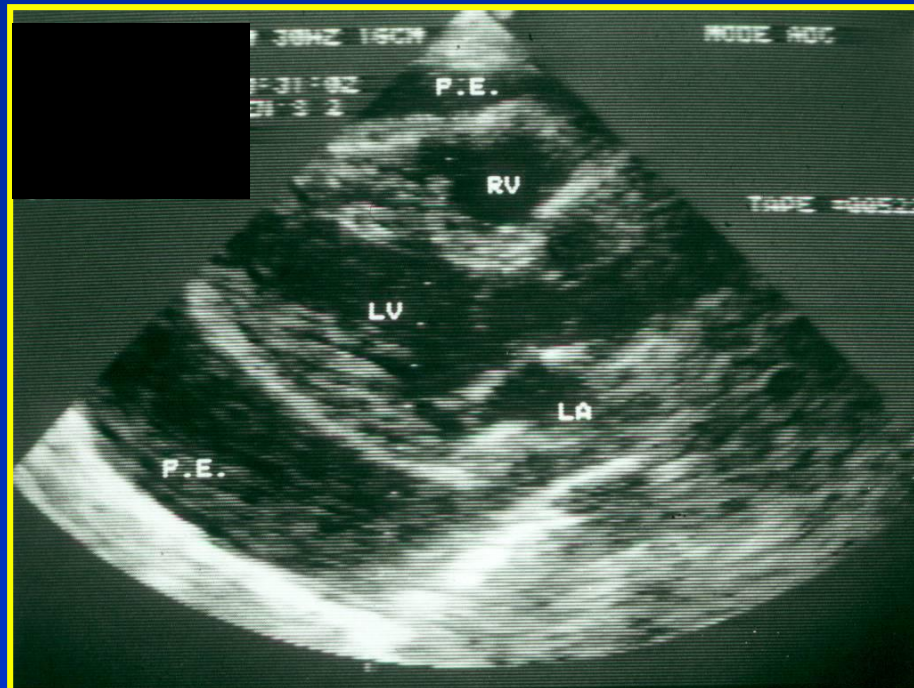
Inspiration

Cardiac
Tamponade

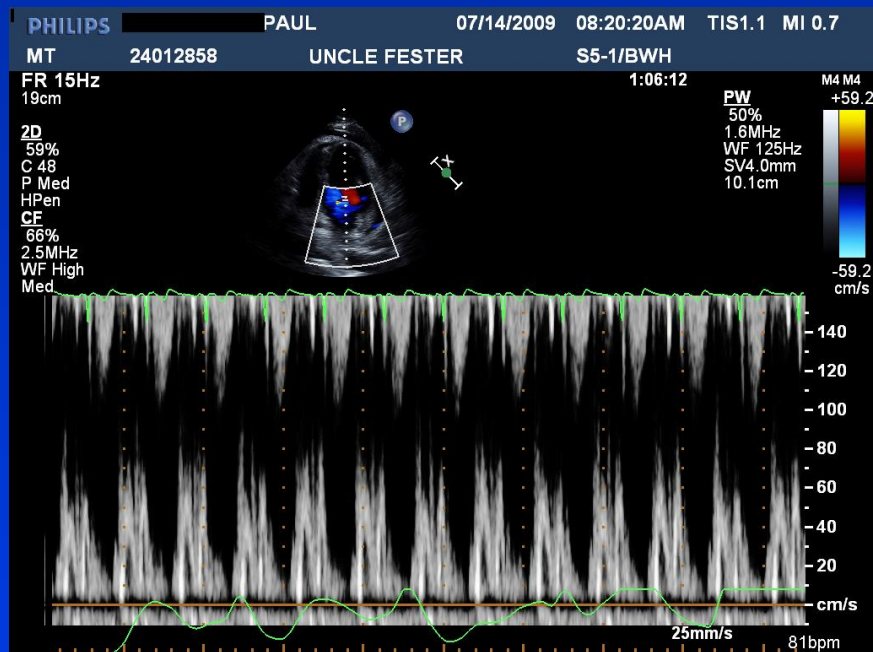




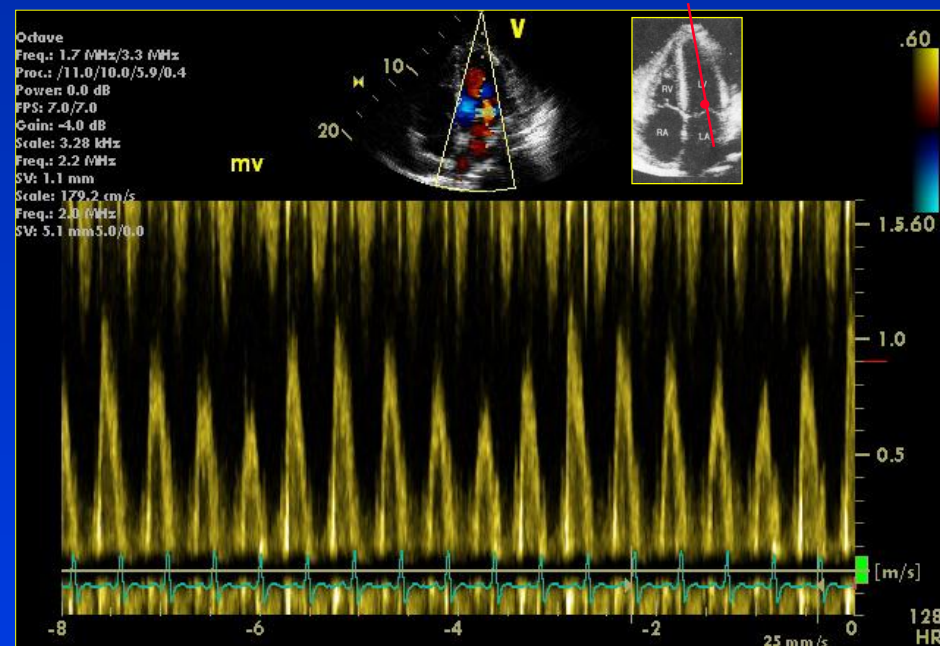
- Low limb lead voltage
- Electrical alternans



Excessive Respiratory Variation (Flow velocity paradox)



No Tamponade



Tamponade

Cardiac Tamponade

1. Pericardial pressure elevated
2. Equalization of diastolic pressures:

Pericardial pressure = RA
= RV
= PCW
= LV

Age: 066Y
Sex: M

Study Date: 14-Dec-2020
IM Time: 10:08:47
Zoom Factor: 0.42



1/1
IM #: 1
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WL : W:44992 L:20448

Inst: BWH

Constrictive Pericarditis Etiologies

(Cleveland Clinic Series; n=163)

Postviral / idiopathic	46%
Post–cardiac surgical	37%
Mediastinal irradiation	9%
Miscellaneous (e.g., collagen vascular disease)	8%

Constrictive
pericarditis

Cardiac
tamponade

Pulsus
paradoxus

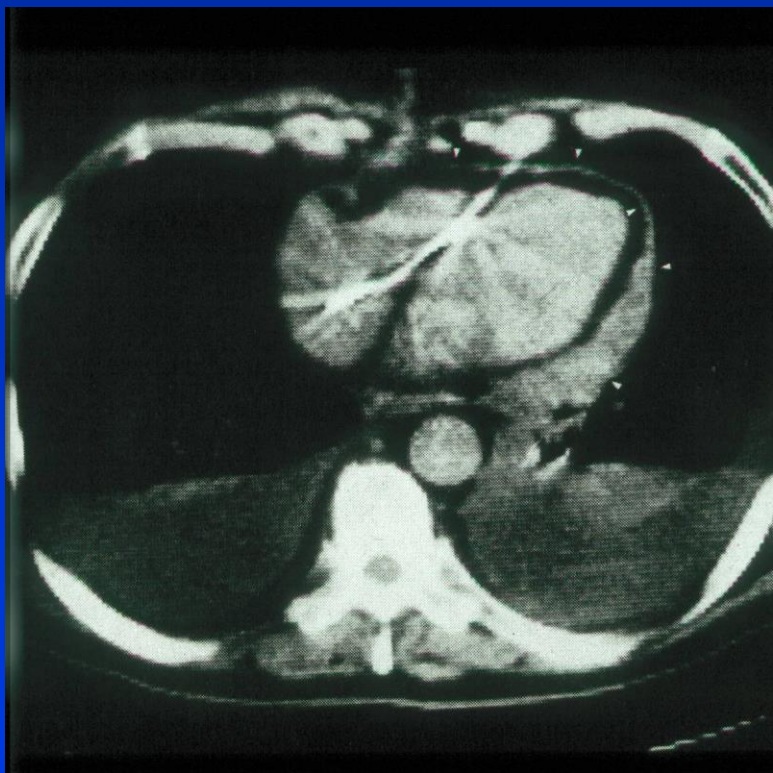
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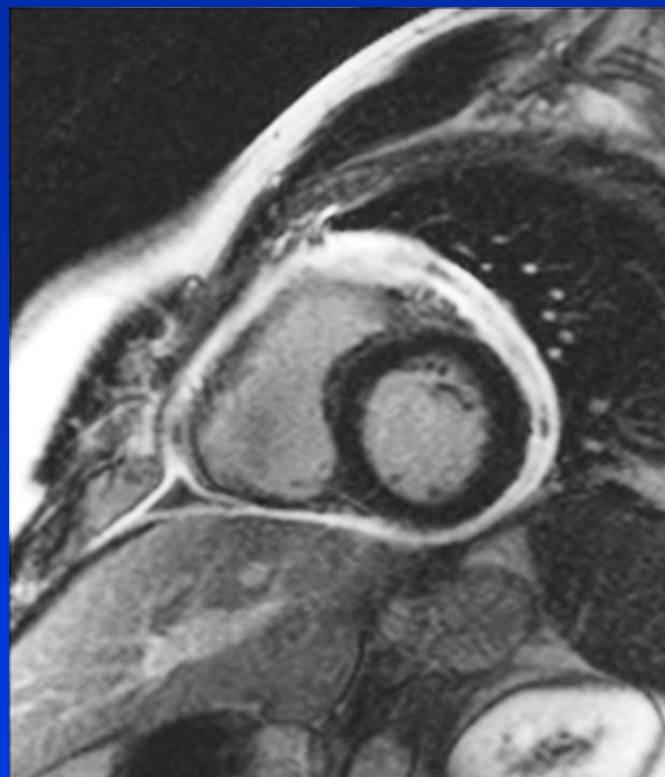
Kussmaul
Sign

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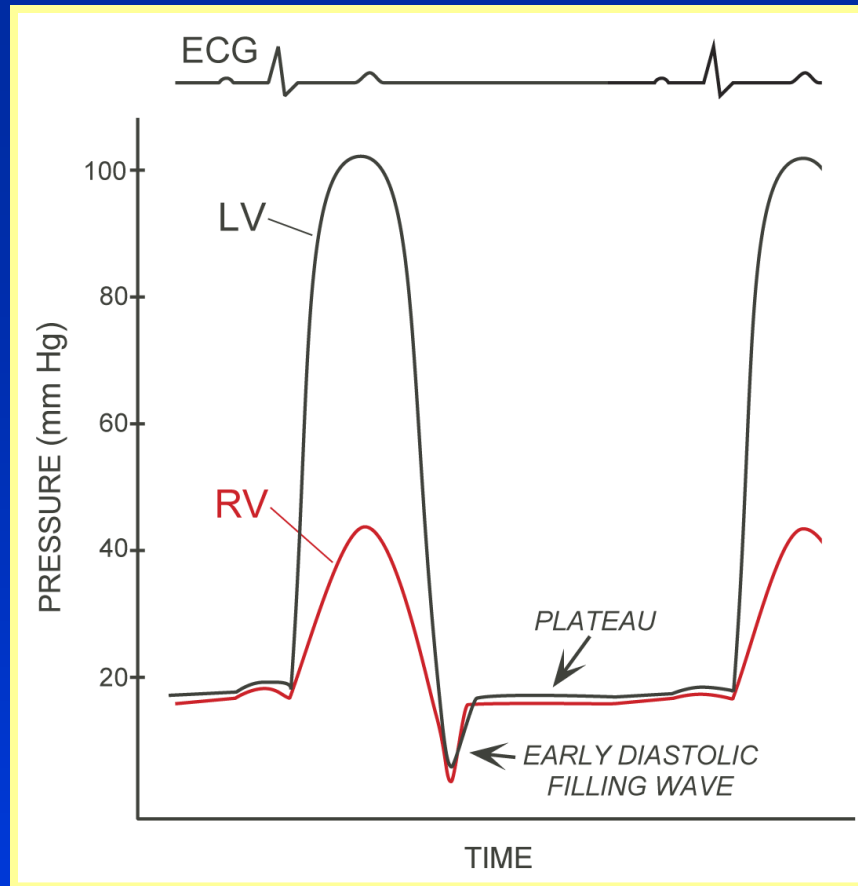
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CT



CMR



1. Elevation of diastolic pressure in ventricles
2. Equalization of diastolic pressure in ventricles
3. “Dip and plateau” pressure pattern



Question #1

38 year old woman, previously healthy, presents with fever, pleuritic anterior chest pain and a pericardial friction rub.

ECG shows diffuse ST elevation and PR segment depression.

Echocardiography demonstrates a small posterior pericardial effusion, without cardiac chamber compression.

Which of the following is correct?

- A. Glucocorticoid therapy is indicated to prevent progression of the effusion
- B. A bacterial etiology is most likely responsible
- C. The relapse rate is $> 15\%$
- D. Kussmaul sign is an expected physical finding

Which of the following is correct?

- A. Glucocorticoid therapy is indicated to prevent progression of the effusion
- B. A bacterial etiology is most likely responsible
- C. The relapse rate is $> 15\%$
- D. Kussmaul sign is an expected physical finding

Question #2

56 year old man presents with exertional dyspnea, marked jugular venous distention and peripheral edema; no pulsus paradoxus.

History of Hodgkin Disease 18 years earlier, treated with chemotherapy and thoracic radiation therapy.

As part of evaluation, right-sided heart catheterization was performed:

<i>Chamber</i>	<i>Pressure (mm Hg)</i>	<i>Normal (mm Hg)</i>
Right atrium (mean)	16	≤ 8
Right ventricle	30/17	$\leq 30/8$
Pulmonary wedge (mean)	16	≤ 10

Which of the following is true?

- A. Pericardiocentesis should be performed urgently
- B. Therapy should include diuretic, ACE inhibitor and beta-blocker
- C. CT scan would be more helpful than echocardiography in confirming diagnosis
- D. Sinus bradycardia is likely present

Which of the following is true?

- A. Pericardiocentesis should be performed urgently
- B. Therapy should include diuretic, ACE inhibitor and beta-blocker
- C. CT scan would be more helpful than echocardiography in confirming diagnosis
- D. Sinus bradycardia is likely present

Additional Reading

1. Adler Y, Charron P, Imazio M, et al. 2015 ESC guidelines for the diagnosis and management of pericardial diseases. *Eur Heart J* 2015;36:2921-64.
2. Brucato A, Imazio M, Gattorno M, et al. Effect of anakinra on recurrent pericarditis among patients with colchicine resistance and corticosteroid dependence: the AIRTRIP randomized clinical trial. *JAMA* 2016;316:1906-12.
3. Chiabrando JG, Bonaventura A, Vecchié A, et al. Management of acute and recurrent pericarditis: JACC state-of-the-art review. *J Am Coll Cardiol* 2020;75:76-92.
4. Cremer PC, Kumar A, Kontzias A, et al. Complicated Pericarditis: Understanding Risk Factors and Pathophysiology to Inform Imaging and Treatment. *J Am Coll Cardiol* 2016 (68):2311–28
5. Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. *N Engl J Med* 2021;384:31.
6. Lilly LS. Treatment of acute and recurrent idiopathic pericarditis. *Circulation* 2013;127:1723.
7. Leung, YY, Yao Hui LL, Kraus VB. Colchicine--Update on mechanisms of action and therapeutic uses. *Semin Arthritis Rheum* 2015 Dec;45(3):341-50.
8. LeWinter M, Kontzias A, Lin D et al. Burden of Recurrent Pericarditis on Health-Related Quality of Life. *Am J Cardiol* 2021 (141): 113-119.