ASE Clinical Recommendations for Multimodality CV Imaging of Patients with Pericardial Disease

A New Renaissance in Multimodality Imaging

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* No Conflicts to Declare
ASE Clinical Recommendations for Multimodality CV Imaging of Patients with Pericardial Disease

• Introduction
• Case presentations
• Clinical perspective
• Hemodynamics
• Multimodality Imaging
• Pitfalls
A New Renaissance in Pericardial Diseases
Edema/Inflammation

T2W STIR
LGE

“Rip-Roaring” Transient Constrictive Pericarditis
Transient Constrictive Pericarditis

Imaging Guided Therapy
Multimodality Pericardial Disease Guidelines

American Society of Echocardiography Clinical Recommendations for Multimodality Cardiovascular Imaging of Patients with Pericardial Disease

Endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography

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European Association of Cardiovascular Imaging (EACVI) position paper: multimodality imaging in pericardial disease

Bernard Cosyns1, Sven Plein1, Petros Nihoyannopoulos1, Otto Smiseth2, Stephan Achenbach3, Maria Joao Andrade4, Mauro Pepi5, Arsen Ristic6, Massimo Imazio7, Bernard Paelinck8, and Patrizio Lancellotti9 On behalf of the European Association of Cardiovascular Imaging (EACVI) and European Society of Cardiology Working Group (ESC WG) on Myocardial and Pericardial diseases

J Am Soc Echocardiogr 2013;26:965-1012

European Heart Journal CV imaging 2014
ESC Pericardial Guidelines

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-Escuvias (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)

‘Ten Commandments’ of 2015 ESC Guidelines for diagnosis and management of pericardial diseases

European Heart Journal 2015
Multimodality Imaging
Pericardial Disease Syndromes

- Pericarditis
  - Acute, incessant, recurrent, chronic
- Pericardial effusion/tamponade
- Constrictive pericarditis
- Effusive-constrictive
- Pericardial masses, diverticulum, cysts
- Congenital anomalies
Acute/Recurrent Pericarditis
Definitions and Diagnostic Criteria

- **Documented 1st episode**
- **Dx by same criteria as acute pericarditis**
- **CRP, (CT) and/or CMR may provide confirmatory findings**
- **Recurrence rate 15-30%**
  - Up to 50% in pts not treated with colchicine, especially if treated with steroids

**European Heart Journal 2015**

<table>
<thead>
<tr>
<th>Pericarditis</th>
<th>Definition and diagnostic criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute</strong></td>
<td>Inflammatory pericardial syndrome to be diagnosed with at least 2 of the 4 following criteria: (1) pericarditic chest pain (2) pericardial rubs (3) new widespread ST-elevation or PR depression on ECG (4) pericardial effusion (new or worsening) Additional supporting findings: - Elevation of markers of inflammation (i.e. C-reactive protein, erythrocyte sedimentation rate, and white blood cell count); - Evidence of pericardial inflammation by an imaging technique (CT, CMR).</td>
</tr>
<tr>
<td><strong>Incessant</strong></td>
<td>Pericarditis lasting for &gt;4–6 weeks but &lt;3 months without remission.</td>
</tr>
<tr>
<td><strong>Recurrent</strong></td>
<td>Recurrence of pericarditis after a documented first episode of acute pericarditis and a symptom-free interval of 4–6 weeks or longer.</td>
</tr>
<tr>
<td><strong>Chronic</strong></td>
<td>Pericarditis lasting for &gt;3 months.</td>
</tr>
</tbody>
</table>
Classification of Pericarditis by Time Scale

- Symptoms > 3 months: Chronic Pericarditis
- Symptoms > 4-6 weeks: Incessant pericarditis
- New-onset pericarditis: Acute pericarditis
  - Symptoms free interval 4-6 weeks
  - Symptoms recurrence: Recurrent Pericarditis

Fardman et al, Curr Cardiology Reports 2016
Normal Pericardium

Acute injury
Infectious
Autoimmune
Myocardial Infarction
Cardiac interventions
Trauma

Chronic injury
Radiation
Neoplasm
Drugs
Metabolic disorders
Chronic infections
Connective
Tissue/Systemic
Diseases

Pericarditis
Effusive
Dry
Fibrinous
Acute
Complete/Partial resolution
Recurrent
Effusive Constrictive

Effusive
Constrictive
Adhesive

Yingchoncharoen et al  Exp Cardiov Review 2013
Effect of Pericarditis on Pathology

Treatment of Pericarditis

- NSAIDs (ASA, Ibuprofen, Indomethacin)
- Colchicine
- Prednisone
- Triple therapy based on imaging
- DMARD’S (intractable cases)
- Biologicals (Anakinra)
- Surgery
Mechanism of Treatment for Recurrent Pericarditis

Anakinra competes with IL-1 and reduces IL-1 activity

Colchicine interferes with granulocyte function, blocking tubulin polymerization

Azathioprine blocks purine and DNA synthesis and inhibits lymphocyte proliferation

Intravenous immunoglobulins modulate the adaptive and innate immune systems, and increase the clearance of infectious agents

# Treatment (acute vs. recurrent)

## Acute

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual dosing(^a)</th>
<th>Tx duration(^b)</th>
<th>Tapering(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>750–1000 mg every 8h</td>
<td>1–2 weeks</td>
<td>Decrease doses by 250–500 mg every 1–2 weeks</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>600 mg every 8h</td>
<td>1–2 weeks</td>
<td>Decrease doses by 200–400 mg every 1–2 weeks</td>
</tr>
<tr>
<td>Colchicine</td>
<td>0.5 mg once (&lt;70 kg) or 0.5 mg b.i.d. (≥70 kg)</td>
<td>3 months</td>
<td>Not mandatory, alternatively 0.5 mg every other day (&lt;70 kg) or 0.5 mg once (≥70 kg) in the last weeks</td>
</tr>
</tbody>
</table>

## Recurrent

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual initial dose(^a)</th>
<th>Tx duration(^b)</th>
<th>Tapering(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>500–1000 mg every 6–8 hours (range 1.5–4 g/day)</td>
<td>weeks-months</td>
<td>Decrease doses by 250–500 mg every 1–2 weeks(^b)</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>600 mg every 8 hours (range 1200–2400 mg)</td>
<td>weeks-months</td>
<td>Decrease doses by 200–400 mg every 1–2 weeks(^b)</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>25–50 mg every 8 hours; start at lower end of dosing range and titrate upward to avoid headache and dizziness.</td>
<td>weeks-months</td>
<td>Decrease doses by 25 mg every 1–2 weeks(^b)</td>
</tr>
<tr>
<td>Colchicine</td>
<td>0.5 mg twice or 0.5 mg daily for patients &lt;70 kg or intolerant to higher doses.</td>
<td>At least 6 months</td>
<td>Not necessary, alternatively 0.5 mg every other day (&lt;70 kg) or 0.5 mg once (≥70 kg) in the last weeks</td>
</tr>
</tbody>
</table>
Interleukin-1 Receptor Antagonist

Long-Term Efficacy of Interleukin-1 Receptor Antagonist (Anakinra) in Corticosteroid-Dependent and Colchicine-Resistant Recurrent Pericarditis

Martina Finetti, MD\textsuperscript{1}, Antonella Insalaco, MD\textsuperscript{2}, Luca Cantarini, MD\textsuperscript{3}, Antonella Maini, MD\textsuperscript{4}, Luciana Breda, MD\textsuperscript{5}, Maria Alessio, MD\textsuperscript{6}, Matteo D’Alessandro, MD\textsuperscript{1}, Paolo Plocu, MD\textsuperscript{1}, Alberto Martini, MD\textsuperscript{1,7}, and Marco Gattorno, MD\textsuperscript{1}

Objective To evaluate the long-term response and safety of interleukin-1 receptor antagonist (anakinra) in recurrent pericarditis.

Study design Fifteen patients (12 children, 3 adults) were enrolled in a multicenter retrospective study. All the patients were corticosteroid-dependent and 14 had received colchicine. Anakinra was given at 1-2 mg/kg/d. The primary outcome of the study was a reduction of at least 75% of disease flares after anakinra treatment compared with the pretreatment period. Secondary outcomes were: (1) number of complete or partial responders to anakinra and time for complete response; (2) number of patients who discontinued other ongoing treatments (non-steroidal anti-inflammatory drugs, corticosteroid, colchicine) and time needed for discontinuation; (3) number of relapses during continuous anakinra treatment; and (4) number of relapses during anakinra tapering or discontinuation.

Results All patients treated had a complete response within a few days and were able to rapidly withdraw concomitant treatments, including corticosteroids. During daily treatment, no patient had a relapse of the disease; 14 patients started tapering and 6 of them experienced a relapse, with a prompt response after anakinra reintroduction. Overall, after a median follow-up of 39 months (range 6-57), a 95% reduction of flares was observed compared with pretreatment period.

Conclusion The long-term use of anakinra in monotherapy is associated with persistent control of recurrent pericarditis. (J Pediatr 2014;164:1425-31)
Diagnosis of acute pericarditis
(2 of 4 clinical criteria: pericardial chest pain, pericardial rubs, ECG changes; pericardial effusion)

First line
Aspirin or NSAID + colchicine + exercise restriction

Second line
Low-dose corticosteroids
(in case of contraindications to aspirin/NSAID/colchicine and after exclusion of infectious cause)

Recurrent pericarditis
(after symptom-free interval 4-6 weeks)

First line
Aspirin or NSAID + colchicine + exercise restriction

Second line
Low-dose corticosteroids
(in case of contraindications to aspirin/NSAID/colchicine and after exclusion of infectious cause)

Third line
i.v. immunoglobulin or anakinra or azathioprine

Fourth line
Pericardiectomy

Low-dose corticosteroids are considered when there are contraindications to other drugs or when there is an incomplete response to aspirin/NSAIDs plus colchicine; in this case physicians should consider adding these drugs instead of replacing other anti-inflammatory therapies.

Azathioprine is steroid-sparing and has a slow onset of action compared with IVIG and anakinra. Cost considerations may apply considering the cheaper solution first (e.g., azathioprine) and resorting to more expensive options (e.g., IVIG and anakinra) for refractory cases.
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Constrictive Pericarditis

Definition

- Impaired diastolic filling due to pericardial disease
- Signs and symptoms of RHF with preserved RV and LV function
- Absence of previous or ongoing myocardial disease

Syed et al. Nat Rev Cardiol 2014;11: 530-544
Pathophysiology

Constrictive Pericarditis  
Restrictive Cardiomyopathy

Appleton CP et al. 1990
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Constrictive Pericarditis
Chest X-Ray
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Constrictive Pericarditis

Square Root Sign

LV pressure
LV/RV Interdependence

Discordance in Constriction

Concordance in Restriction

Talreja et al. JACC 2008
Survival Curves After Pericardiectomy by Etiology of Constriction

Figure 1

Survival Curves After Percardiection by Etiology of Constriction

- Idiopathic
- Misc
- Post SX
- Radiation

Survival

Years After Surgery

Bertog et al. J Am Coll Cardiol 2004;8:1445-52
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# Strengths and Limitations of Various Imaging Modalities in the Evaluation of Pericardial Disease

<table>
<thead>
<tr>
<th>Echocardiography</th>
<th>Cardiac CT</th>
<th>CMR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main indications/advantages</strong></td>
<td><strong>Need for better anatomic description</strong></td>
<td><strong>Need for better anatomic description</strong></td>
</tr>
<tr>
<td>• First-line diagnostic imaging test in the evaluation and follow-up of pericardial disease</td>
<td>• Evaluation of associated/extracardiac disease</td>
<td>• Superior tissue characterization</td>
</tr>
<tr>
<td>• Widely available</td>
<td>• Preoperative planning</td>
<td></td>
</tr>
<tr>
<td>• Low cost</td>
<td>• Detection of pericardial calcification</td>
<td></td>
</tr>
<tr>
<td>• Safe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Can be performed bedside or in hemodynamically unstable patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Main limitations/disadvantages</strong></td>
<td><strong>Use of ionizing radiation</strong></td>
<td><strong>Time consuming, high cost</strong></td>
</tr>
<tr>
<td>• Limited windows, narrow field of view</td>
<td>• Use of iodinated contrast (unless visualization of related anatomy is not needed)</td>
<td>• Preferably stable heart rhythms</td>
</tr>
<tr>
<td>• Technical difficulties in case of obesity, obstructive lung disease or immediately post-cardiothoracic surgery</td>
<td>• Functional evaluation only possible with retrospectively gated studies (higher radiation dose, suboptimal temporal resolution)</td>
<td>• Contraindicated in case of pacemaker or defibrillators</td>
</tr>
<tr>
<td>• Operator dependent</td>
<td>• Difficulties in case of tachycardia or unstable heart rhythm (particularly for prospectively gated studies)</td>
<td>• Lung tissue less well visualized</td>
</tr>
<tr>
<td>• Low signal-to-noise ratio of the pericardium</td>
<td>• Need for breath-hold</td>
<td>• Calcifications less well visualized</td>
</tr>
<tr>
<td>• Limited tissue characterization</td>
<td>• Hemodynamically stable patients only</td>
<td>• Use of Gadolinium contrast contra-indicated in case of advanced renal dysfunction (glomerular filtration rate &lt;30 mL/min)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Use of some breath-hold sequences</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hemodynamically stable patients only</td>
</tr>
</tbody>
</table>

Mitral Inflow

E insp

E exp

Tricuspid Inflow

E insp

E exp

TDI septal

s'

e'

a'
HV Flow

[Image of an echocardiogram showing flow dynamics with annotations for Insp, Exp, S, D, AR, and a graph with flow velocity across the heart cycle.]
Diagnosis of Constriction Algorithm

Nagueh et al  JASE 2016
CONCLUSIONS: Regional longitudinal systolic strain ratios are robust novel diagnostic tools for CP. Regional myocardial mechanics inversely correlates with adjacent pericardial segment thickness detected by CMR and pericardiectomy leads to systolic strain improvement, which is more pronounced in RV and LV free walls. (Circ Cardiovasc Imaging 2013;6:2399-406)
2-D Strain

Pre Pericardiectomy

Post Pericardiectomy

| GLPS_LAX   | -6.8 % | AVC_MEAS   | 234 msec |
| GLPS_A4C  | -10.7 % | HR_ApLAX   | 90.0 bpm |
| GLPS_A2C  | -10.1 % |            |          |
| GLPS_Avg  | -9.2 %  |            |          |

| GLPS_LAX   | -11.6 % | AVC_MEAS   | 374 msec |
| GLPS_A4C  | -14.3 % | HR_ApLAX   | 67.4 bpm |
| GLPS_A2C  | -14.0 % |            |          |
| GLPS_Avg  | -13.3 % |            |          |
Constriction

CT

CMR
Interventricular Dependence CMR

Free breathing sequence

Normal

Constrictive Pericarditis
Histology of Pericardial Inflammation

Normal Organizing Pericarditis with Fibroplasia

Organizing Pericarditis

Organized Fibrous Pericarditis

Movat stain

Immunostain with Cd-34
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Mixed Constriction/Restriction
“Mixed Bag”

Constrictive Pericarditis

Mixed

Restrictive Cardiomyopathy

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Exciting Times