Myocarditis - Dilated Cardiomyopathies: The Role of Endomyocardial Biopsy

Diagnostic, Prognostic and Therapeutic Implications

Stamatis Adamopoulos, MD, PhD

Onassis Cardiac Surgery Center, Athens, Greece
Evolution of Acute Viral Myocarditis

R Dennert et al, Eur Heart J 2008, July 9
Persistent or Increasing Cardiac Dysfunction

**Proposal of Diagnostic Approach for Patients with Suspected Myocarditis**

**Suspected myocarditis**

- Initial evaluation*
  - Detailed history
  - Electrocardiogram
  - Blood studies
    - Cardiac enzymes
    - Serum anti-heart auto-antibodies
  - Imaging
    - Echocardiogram
    - CMR

- Within 48 h
  - Progressive cardiac dysfunction
    - Coronary angiogram
    - Exclusion coronary artery disease
    - Diagnostic EMB

- After 48 h
  - Persistent cardiac dysfunction
  - Spontaneous Recovery
    - Follow-up for at least 3 years

*R Dennert et al, Eur Heart J 2008, July 9
The Role of Endomyocardial Biopsy in the Management of Cardiovascular Disease

AHA/ACC/ESC scientific statement, Eur Heart Journal 2007, October 24

Clinical scenario 1
EMB should be performed in the setting of unexplained new-onset HF of <2 weeks’ duration associated with normal-sized or dilated left ventricle in addition to hemodynamic compromise (dd: lymphocytic vs GCM vs necrotizing eosinophilic) (Class I, Evidence B)

Clinical scenario 2
EMB should be performed in the setting of unexplained new-onset HF of 2 weeks’ to 3 months’ duration associated with a dilated left ventricle and new ventricular arrhythmias, Mobitz type II 2nd- or 3rd-degree AV heart block, or failure to respond to usual care within 1 to 2 weeks (exclude GCM) (Class I, Evidence B)

Clinical scenario 4
EMB is reasonable in unexplained HF associated with a DCM of any duration with suspected allergic reaction in addition to eosinophilia (Class IIa, Evidence C)

Clinical scenario 9
EMB may be considered in the setting of unexplained, new-onset HF of 2 weeks’ to 3 months’ duration associated with a dilated LV, without new ventricular arrhythmias, Mobitz type II 2nd- or 3rd-degree AV heart block that responds to usual care within 1 to 2 weeks (Class IIb, Evidence B)
Complication Rate of RV Endomyocardial Biopsy via Femoral Approach

3048 Diagnostic Procedures over an 11-Year Period

Table 2. Major Complications of 2505 Retrospective and 543 Prospective EMB Procedures

<table>
<thead>
<tr>
<th>Major Complications of EMB Procedures</th>
<th>Retrospective, Absolute/%</th>
<th>Prospective, Absolute/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardial tamponade with pericardiocentesis</td>
<td>2/0.08</td>
<td>0/0</td>
</tr>
<tr>
<td>Permanent complete AV block with permanent pacemaker required</td>
<td>1/0.04</td>
<td>0/0</td>
</tr>
<tr>
<td>Urgent cardiac surgery</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Advanced cardiac life support</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Hemothorax or pneumothorax</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Death</td>
<td>0/0</td>
<td>0/0</td>
</tr>
</tbody>
</table>

M Holzmann et al, Circulation 2008, August 5
Myocarditis
Current Trends in Diagnosis and Treatment

JW Magnani and GW Dec
Circulation 2006, February 14
Probability for Myocarditis Patients of Remaining Free from Death or Transplantation According to Clinical and Histological Presentation

ALP Caforio et al, Eur Heart J 2007;28:1326-1333
Viral Persistence in the Myocardium is Associated with Progressive Cardiac Dysfunction

High Prevalence of Viral Genomes and Multiple Viral Infections in the Myocardium of Adults with “Idiopathic” Left Ventricular Dysfunction

U Kühl et al, Circulation 2005, February 22
Chlamydia Trachomatis 41%

Chlamydia Psittackie 4%

CMV 4%

Coxsackie B3k 9%

HSV6 4%

None 9%

CMV/myocardium/liver/Echoviruses 11 4%

PARVOB-19/HSV1/HSV2 5%

Chlamydia Trachomatis/HSV1/HSV2 5%

Coxsackie B3k/Echoviruses 11/HSV1/HSV2 5%

CMV/Coxsackie B3k/Echoviruses 11 5%

Chlamydia Trachomatis/HSV1/HSV2 5%

PARVOB-19/HSV1/HSV2 5%

HSV6/Chlamydia Trachomatis 5%

PARVOB-19 5%

HSV6 5%
Predictors of Outcome in Patients with Suspected Myocarditis

I. Kindermann et al, Circulation 2008, August 5

Graph showing survival rates based on NYHA class and IH status:
- NYHA I/II, IH negative, beta-blocker
- One or two unfavourable predictors
- NYHA III/IV, IH positive, no beta-blocker

Statistical comparisons:
- dotted line vs. dashed line, p = 0.020
- dotted line vs. solid line, p < 0.001
- solid line vs. --, p < 0.001

Months after biopsy:
- 0
- 40
- 80
- 120

Images A, B, C, D, E, F, G, H accompany the graph.
A Prospective Study of Biopsy-Proven Myocarditis

Prognostic Relevance of Clinical and Aetiopathogenic Features at Diagnosis

ALP Caforio et al, Eur Heart J 2007;28:1326-1333
Presentation, Patterns of Myocardial Damage and Clinical Course of Viral Myocarditis

H Mahrholdt et al, Circulation 2006;114:1581-1590

PVB 19

HHV 6

PVB + HHV

PVB19, Parvovirus B19; HHV6, Human Herpes Virus 6; EF, ejection fraction; EDV, end diastolic volume; FU, follow-up
Spatial Distribution of the Mean Values for Segmental Extent of LGE at Time of the Initial CMR Scan with Respect to the Viral Type

H Mahrholdt et al, Circulation 2006;114:1581-1590
### Summary of Recommended Components for the CMR Study Report

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LV volume and function</strong></td>
<td>LV end-diastolic volume and volume index &lt;br&gt;LV end-systolic volume and volume index &lt;br&gt;Ejection fraction &lt;br&gt;Cardiac index &lt;br&gt;LV mass and mass index</td>
</tr>
<tr>
<td><strong>Presence or absence of markers for inflammatory activity and injury</strong></td>
<td>T2 signal/edema (regional edema or global T2 ratio) &lt;br&gt;Calculated global myocardial early gadolinium enhancement ratio (hyperemia) &lt;br&gt;Myocardial late gadolinium enhancement with nonischemic regional distribution (necrosis)</td>
</tr>
<tr>
<td><strong>Conclusion</strong></td>
<td>On the basis of the presence or absence of 2 or more criteria, considering additional evidence by the presence of LV dysfunction and/or pericardial effusion</td>
</tr>
<tr>
<td><strong>Recommendation for follow-up</strong></td>
<td>Based on clinical setting &lt;br&gt;A follow-up 4 weeks after the onset of symptoms may have prognostic implications and thus is recommended.</td>
</tr>
</tbody>
</table>
Cardiovascular Magnetic Resonance in Myocarditis: A JACC White Paper

MG Friedrich et al,
J Am Coll Cardiol 2009, April 28
Diagnostic Synergy of Non-Invasive Cardiovascular Magnetic Resonance and Invasive Endomyocardial Biopsy in Troponin-Positive Patients without Coronary Artery Disease

<table>
<thead>
<tr>
<th>CMR diagnoses</th>
<th>EMR diagnoses</th>
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<tbody>
<tr>
<td></td>
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</tr>
<tr>
<td>Myocarditis</td>
<td>Myocarditis</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>Dilated cardiomyopathy</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>Amyloidosis</td>
</tr>
<tr>
<td>Non-conclusive</td>
<td>Non-conclusive</td>
</tr>
<tr>
<td>Tako-Tsubo-cardiomyopathy</td>
<td>Tako-Tsubo-cardiomyopathy</td>
</tr>
</tbody>
</table>

- CMR diagnoses: 58% Myocarditis, 15% Hypertrophic cardiomyopathy, 15% Dilated cardiomyopathy, 1% Amyloidosis, 5% Non-conclusive, 20% Tako-Tsubo-cardiomyopathy
- EMR diagnoses: 81% Myocarditis, 12% Hypertrophic cardiomyopathy, 1% Dilated cardiomyopathy, 1% Amyloidosis, 4% Non-conclusive, 1% Tako-Tsubo-cardiomyopathy

*H Baccouche et al, Eur Heart J 2009, August 20*
The degree of sampling error depends on

(a) the number of biopsies taken per patient and
(b) the methods applied for ex vivo analysis
...in the patient with borderline myocarditis cardiovascular magnetic resonance was not able to diagnose myocarditis due to low extent of inflammation...

Limitations and Failure of CMR
Pathogenesis of Myocarditis

The Progression from Acute Injury to Chronic Dilated Cardiomyopathy May Be Simplified into a Three-Stage Process
A Clinical Trial of Immunosuppressive Therapy for Myocarditis

Interferon-β Treatment Eliminates Cardiotropic Viruses and Improves LV Function in Patients with Myocardial Persistence of Viral Genomes and LV Dysfunction

U Kühl et al, Circulation 2003, June 10
Randomized, Placebo-Controlled Study for Immunosuppressive Treatment of Inflammatory Dilated Cardiomyopathy

Two-Year Follow-up Results

R Wojnicz et al, Circulation 2001, July 3
Immunosuppressive Therapy for Active Lymphocytic Myocarditis

Virological and Immunologic Profile of Responders vs Nonresponders

A Frustaci et al, Circulation 2003, February 18
Proposal of Treatment Algorithm Based on Endomyocardial Biopsy Results

R Dennert et al, Eur Heart J 2008, July 9
Randomized Study on the Efficacy of Immunosuppressive Therapy in Patients with Virus-Negative Inflammatory Cardiomyopathy: the TIMIC Study

Frustaci A et al, Eur Heart J 2009, August
Prevention of Cardiac Dysfunction in Acute Coxsackievirus B3 Cardiomyopathy by Inducible Expression of a Soluble Coxsackievirus-Adenovirus Receptor

S Pinkert et al, Circulation 2009, December 8
Myocarditis and Heart Failure

Need for Better Diagnostic, Predictive and Therapeutic Tools

“...A combined effort of clinicians, pathologists and immunologists must contribute to the development of new criteria of myocarditis, which should include clinical presentation, auto-antibodies, imaging and cardiac biopsies for detailed study of inflammation, auto-immunity and virus presence. These new criteria to be developed will help to better classify, treat and predict the prognosis of a given patient with myocarditis...”

S Heymans, Eur Heart Journal 2007, June - Editorial

The heat is off: immunosuppression for myocarditis revisited

“...If the results of Frustaci and colleagues are replicated in a larger, multicentre designed trial with clinical endpoints such as death and heart transplantation, the class I indications for heart biopsy will expand to a much larger population...”

Leslie T. Cooper, Eur Heart J 2009, August - Editorial
Propranolol Ameliorates and Epinephrine Exacerbates Progression of Acute and Chronic Viral Myocarditis

**Indications for Cardiovascular Magnetic Resonance in Patients With Suspected Myocarditis**

<table>
<thead>
<tr>
<th>New Onset or Persisting Symptoms Suggestive of Myocarditis</th>
<th>Plus</th>
<th>Evidence for Recent/Ongoing Myocardial Injury</th>
<th>Plus</th>
<th>Suspected Viral Etiology</th>
</tr>
</thead>
</table>
| Dyspnea  
or  orthopnoea  
or  palpitations  
or  effort intolerance/malaise  
or  chest pain | | Ventricular dysfunction  
or  new or persisting ECG abnormalities  
or  elevated troponin | | History of recent systemic viral disease or previous myocarditis  
or  absence of risk factors for CAD  
or  age < 35 years  
or  symptoms not explained by coronary stenosis on coronary angiogram  
or  recent negative ischemic stress test |

*MG Friedrich et al, J Am Coll Cardiol 2009, April 28*
Cardiac Magnetic Resonance Monitors
Reversible and Irreversible Myocardial Injury in Myocarditis

A Zagrosek et al, JACC Cardiovascular Imaging 2009, February
Concordant Normalization of LV Global Function and Tissue Parameters of Acute Myocardial Injury in Myocarditis

A Zagrosek et al, JACC Cardiovascular Imaging 2009, February
Diagnostic Synergy of Non-Invasive Cardiovascular Magnetic Resonance and Invasive Endomyocardial Biopsy in Troponin-Positive Patients without Coronary Artery Disease

H Baccouche et al, Eur Heart J 2009, August 20
Conclusions

Diagnostic synergy of non-invasive cardiovascular magnetic resonance and invasive endomyocardial biopsy

i) EMB is superior to LGE-CMR in diagnosing myocarditis because of its ability to capture minor forms of myocarditis

ii) The value of LGE in the CMR-based diagnosis of myocarditis is related to the histological degree and extent of inflammation as detected on EMB

iii) The degree of *sampling error* depends on (a) the number of biopsies taken per patient and (b) the methods applied for *ex vivo* analysis

iv) The combined approach seems superior to each single technique and can overcome some of the well-known limitations of CMR and EMB as individually applied techniques

v) The use of CMR only to establish the diagnosis of myocarditis will result in less detailed information about the degree of inflammation, the presence of special forms of myocarditis (such as *giant cell* or *eosinophilic myocarditis*), or the presence and type of *virus*
Cardiovascular MRI Assessment of Human Myocarditis
A Comparison to Histology and Molecular Pathology

Viral Persistence in the Myocardium is Associated with Progressive Cardiac Dysfunction


![Graph showing EF change (%) with virus clearance and persistence](image-url)
Myocarditis in Hypertrophic Cardiomyopathy Patients Presenting Acute Clinical Deterioration

Recognition can potentially affect disease prognosis and treatment

A Frustaci et al, Eur Heart J 2007;28:733-740
η Εμφάνιση Νόσου

- 27 ετών Ιταλός
  Αμυγδαλίτιδα σε αποδρομή (αντιβίωση)
- Νοσοκομείο Κερκύρας
  προκάρδιο άλγος, ↑ST-T V₂-V₆
  θετική ενζυμική κίνηση, περικαρδιακή συλλογή και LVEF:25%
- Διακομιδή Νοσοκομείο Ιωαννίνων
  Αιμοδυναμικά ασταθής, χορήγηση ινοτρόπων (Dopamine –Dobutamine )
  → διακομιδή ΩΚΚ
- Εργαστηριακός Έλεγχος
  WBC: 27.400, CRP: 559, CPK:1083, CPK-MB:69, RCTNI :11
  Υποπληθυσμοί Λεμφοκυττάρων
  CD₃: 796 (960-2570) - CD₄: 541 (544-1660) - CD₈: 260 (350-900)
  CD₄/CD₈: 2,1 (0.93-3,50) - CD₁₉: 147 (122-350)
  NK: 49 (250-650)
- CxR: εικόνα πνευμονικού οιδήματος (συμφόρηση)
Πορεία Νόσου

✓ Αιμοδυναμικός έλεγχος
CAA, Δεξιός καθετηριασμός + βιοψία
PA: 46/29/38, PCWP: 38/37/35
LVEF: 25%, MR: 2+/4+

✓ PCR σε μυοκαρδιακό ιστό και αίμα
CMV (+)
CMV Copies: 4809/ml αίματος ή 601 copies/10^6 WBC

✓ Θεραπεία
Valgancyclovir 900 mg
↑LVEF: 45%
Αφαίρεση IABP, ↓CMV copies (327 copies/ml αίματος ή 45 copies/10^6 WBC)

✓ Νοσηλεία 15 ημερών
✓ LVEF (εξόδου): 60%
Clinical Scenario 12

AHA/ACC/ESC scientific statement, Eur Heart Journal 2007, October 24

✓ EMB may be considered in the setting of suspected ARVD/C

*Class of Recommendation IIb, Level of Evidence C*
Clinical Scenario 6

AHA/ACC/ESC scientific statement, Eur Heart Journal 2007, October 24

✓ EMB is reasonable in the setting of heart failure associated with unexplained restrictive cardiomyopathy

*Class of Recommendation IIa, Level of Evidence C*
Quantitative Assessment of Endomyocardial biopsy in Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia: an in Vitro Validation of Diagnostic Criteria

C Basso et al, Eur Heart J 2008, September 26
Quantitative Assessment of EMB in ARVC/D: an *in Vitro* Validation of Diagnostic Criteria
Immunohistological Diagnosis of Myocarditis

Potential Role of Sarcolemmal Induction of the MCH and ICAM-1 in the Detection of Autoimmune Mediated Myocyte Injury

R Wojnicz et al, Eur Heart Journal 1998;19:1564-1572
Cardiac Troponin I but not Cardiac Troponin T Induces Severe Autoimmune Inflammation in the Myocardium

S Göser et al, Circulation 2006;114:1693-1702
Myocarditis
Current Trends in Diagnosis and Treatment

Cardiology - Suspected NEW Heart Failure

Patient Presentation
- New onset breathlessness
- Ankle oedema
- Dyspnoea on exertion/rest
- Orthopnoea
- Fatigue/tiredness

GP
- History including previous cardiac history and examination to exclude red flag signs and symptoms.
- Tests required: 12 Lead ECG, full blood count, U&E, TFTs, LFTs, glucose, chest x-ray, urinalysis
- if ECG is not available
- Normal ECG but still suspect heart failure
- Abnormal ECG

RED FLAG SYMPTOMS:
- Previous cardiac history
- Paroxysmal nocturnal dyspnoea
- Tachycardia/new onset AF
- Increased jugular venous pressure
- Gallop rhythm
- New heart murmur with symptoms
- Lung crepitations
- Sleep snore

Secondary Care
- Consider hospital admission dependent on severity of symptoms

Useful information for patients with confirmed LVSD
- Record daily weight
- Change to low sodium diet
- Early symptom recognition and reporting
- Importance of medication compliance
- Flu & Pneumococcal immunisations

GP
- Consider starting appropriate therapies: ACEI, diuretic therapy (if not already initiated).
- Once stable introduce beta-blocker.
- Assess future cardiovascular risk: cholesterol, smoking, diabetes, hypertension and diet.

Perform BNP (B-Type Natriuretic Peptide) test
- Abnormal BNP
- Normal BNP

Cardiology Consultant
- Refer for Specialist opinion

Obtain echocardiogram (and ECG if not already done) and refer
- Confirmed left ventricular systolic dysfunction (LVSD)
- No LVSD

Heart Failure Service
- Refer for further specialist assessment and consideration for long term follow-up by Nurse Specialist (see “useful information for patients with confirmed LVSD”)
# Criteria for Diagnosis of Heart Failure

## HISTORY

<table>
<thead>
<tr>
<th>Points</th>
<th>Points</th>
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<tbody>
<tr>
<td>rest dyspnea</td>
<td>4</td>
</tr>
<tr>
<td>orthopnea</td>
<td>4</td>
</tr>
<tr>
<td>PND</td>
<td>3</td>
</tr>
<tr>
<td>dyspnea walking on level</td>
<td>2</td>
</tr>
<tr>
<td>dyspnea on climbing</td>
<td>1</td>
</tr>
</tbody>
</table>

## CHEST X-Ray

<table>
<thead>
<tr>
<th>Points</th>
<th>Points</th>
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</thead>
<tbody>
<tr>
<td>alveolar pulmonary edema</td>
<td>4</td>
</tr>
<tr>
<td>interstitial pulmonary edema</td>
<td>3</td>
</tr>
<tr>
<td>bilateral pleural effusion</td>
<td>3</td>
</tr>
<tr>
<td>CT ratio &gt; 0.50</td>
<td>3</td>
</tr>
<tr>
<td>flow redistribution</td>
<td>2</td>
</tr>
</tbody>
</table>

## PHYSICAL

<table>
<thead>
<tr>
<th>Points</th>
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</thead>
<tbody>
<tr>
<td>HR 91-110</td>
<td>1</td>
</tr>
<tr>
<td>HR &gt; 110</td>
<td>2</td>
</tr>
<tr>
<td>JVP &gt; 6 cm</td>
<td>2</td>
</tr>
<tr>
<td>JVP &gt; 6 cm &amp; hepatomeg</td>
<td>3</td>
</tr>
<tr>
<td>lung crackles in base</td>
<td>1</td>
</tr>
<tr>
<td>lung crackles above base</td>
<td>2</td>
</tr>
<tr>
<td>wheezing</td>
<td>3</td>
</tr>
<tr>
<td>S3</td>
<td>3</td>
</tr>
</tbody>
</table>

8-12 points - definite CHF
5-7 points - possible CHF
<5 points - unlikely CHF
B-Type Natriuretic Peptide and Clinical Judgement in Emergency Diagnosis of Heart Failure

Analysis from BNP Multinational Study

PA McCullough et al, Circulation 2002;106:416
Indications for Coronary Angiography in New Onset Cardiomyopathy

✓ Patients with Known Coronary Artery Disease/Angina Pectoris
  – Revascularization recommended in vast majority of such individuals with multivessel disease; little role for non-invasive testing
  – Coronary angiography considered (Class I, Evidence: B)

✓ Patients with Known Coronary Artery Disease Who Lack Angina
  – No controlled trials have examined whether coronary revascularization can improve outcomes in this population
  – Many centers first evaluate patient for myocardial hibernation
  – Coronary angiography considered (Class IIa, Evidence: C)

✓ Patients with or without Chest Pain in Whom Coronary Artery Disease has not Been Evaluated
  – Approximately 35% of patients with IDCM will report angina-like pain
  – Coronary angiography should be considered (Class IIa, Evidence: C)
Left Ventricular Non-Compaction

Insights from Cardiovascular MRI

SE Petersen et al,
J Am Coll Cardiol 2005;46:101-105
ACE Inhibitors Asymptomatic LV Dysfunction

SOLVD (prevention) 12-year survival and life expectancy

Lancet 2003;361:1843-48
Metoprolol Reverses Left Ventricular Remodeling in Patients with Asymptomatic Systolic Dysfunction

REVERT Trial

**WS Colucci et al, Circulation 2007, June 18**
Primary Endpoint: LVESVI
Comparison Between Treatments (CARMEN Study)

- Carvedilol
- Enalapril

P values for $\Delta$ BL to M6, M12, M18:
- $P < 0.05$
- $P < 0.002$
- NS
Eplerenone, a Selective Aldosterone Blocker, after Myocardial Infarction (EPHESUS TRIAL)

Symptomatic Heart Failure + Reduced Ejection Fraction

Diuretic + ACEI (or ARB)
Titrate to clinical stability

β-Blocker

Persisting signs and symptoms?

Yes

ADD aldosterone antagonist OR ARB

Persisting symptoms?

Yes

QRS >120 ms?

Yes

Consider: CRT-P or CRT-D

No

Consider: digoxin, hydralazine/nitrate, LVAD, transplantation

No

LVEF <35%?

Yes

Consider ICD

No

No further treatment indicated
Oxygen/NIV
Loop diuretic ± vasodilator
Clinical evaluation

- SBP >100 mmHg: vasodilator (NTG, nitroprusside, nesiritide, levasimendan)
- SBP 90-100 mmHg: vasodilator and/or inotrope (dobutamine, PDEI, levasimendan)
- SBP <90 mmHg: consider preload correction with fluids, inotrope (dopamine)

Good response
stabilize and initiate diuretic, ACEI/ARB, β-blocker

Poor response
inotrope, vasopressor
mechanical support
consider PAC
Patients at risk:
- Withdrawn: 79, 77, 73, 68, 66, 26, 10
- Not Treated: 303, 275, 269, 262, 242, 114, 51
- Continued: 1350, 1303, 1268, 1236, 1123, 596, 224
- NewlyStarted: 632, 600, 591, 575, 531, 274, 110
<table>
<thead>
<tr>
<th>Educational topics</th>
<th>Skills and self-care behaviours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition and etiology of heart failure</td>
<td>Understand the cause of heart failure and why symptoms occur</td>
</tr>
<tr>
<td>Symptoms and signs of heart failure</td>
<td>Monitor and recognize signs and symptoms</td>
</tr>
<tr>
<td></td>
<td>Record daily weight and recognize rapid weight gain</td>
</tr>
<tr>
<td></td>
<td>Know how and when to notify healthcare provider</td>
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<tr>
<td></td>
<td>Use flexible diuretic therapy if appropriate and recommended</td>
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<tr>
<td>Pharmacological treatment</td>
<td>Understand indications, dosing, and effects of drugs</td>
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<td>Recognize the common side-effects of each drug prescribed</td>
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<tr>
<td>Risk factor modification</td>
<td>Understand the importance of smoking cessation</td>
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<tr>
<td></td>
<td>Monitor blood pressure if hypertensive</td>
</tr>
<tr>
<td></td>
<td>Maintain good glucose control if diabetic</td>
</tr>
<tr>
<td></td>
<td>Avoid obesity</td>
</tr>
<tr>
<td>Diet recommendations</td>
<td>Sodium restriction if prescribed</td>
</tr>
<tr>
<td></td>
<td>Avoid excessive fluid intake</td>
</tr>
<tr>
<td></td>
<td>Modest intake of alcohol</td>
</tr>
<tr>
<td></td>
<td>Monitor and prevent malnutrition</td>
</tr>
<tr>
<td>Exercise recommendations</td>
<td>Be reassured and comfortable about physical activity</td>
</tr>
<tr>
<td></td>
<td>Understand the benefits of exercise</td>
</tr>
<tr>
<td></td>
<td>Perform exercise training regularly</td>
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<tr>
<td>Sexual activity</td>
<td>Be reassured about engaging in sex and discuss problems with healthcare professionals</td>
</tr>
<tr>
<td></td>
<td>Understand specific sexual problems and various coping strategies</td>
</tr>
<tr>
<td>Immunization</td>
<td>Receive immunization against infections such as influenza and pneumococcal disease</td>
</tr>
<tr>
<td>Sleep and breathing disorders</td>
<td>Recognize preventive behaviour such as reducing weight, obese, smoking cessation, and abstinence</td>
</tr>
<tr>
<td></td>
<td>from alcohol</td>
</tr>
<tr>
<td></td>
<td>Learn about treatment options if appropriate</td>
</tr>
<tr>
<td>Adherence</td>
<td>Understand the importance of following treatment recommendations and maintaining motivation to</td>
</tr>
<tr>
<td></td>
<td>follow treatment plan</td>
</tr>
<tr>
<td>Psychosocial aspects</td>
<td>Understand that depressive symptoms and cognitive dysfunction are common in patients with heart</td>
</tr>
<tr>
<td></td>
<td>failure and the importance of social support</td>
</tr>
<tr>
<td></td>
<td>Learn about treatment options if appropriate</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Understand important prognostic factors and make realistic decisions</td>
</tr>
<tr>
<td></td>
<td>Seek psychosocial support if appropriate</td>
</tr>
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</table>
Classification of the Cardiomyopathies: a Position Statement from the ESC Working Group on Myocardial and Pericardial Diseases

Cardiomyopathies

- HCM
- DCM
- ARVC
- RCM
- Unclassified

Familial/Genetic

- Unidentified gene defect
- Disease sub-type*

Non-familial/Non-genetic

- Idiopathic
- Disease sub-type*
(A) Chest pain

I
II
III
avr
avl
avf

I
II
III
avr
avl
avf

400 ms

(B) After 1 day

V1
V2
V3
V4
V5
V6

V1
V2
V3
V4
V5
V6
Human Phospholamban Mutation and Dilated Cardiomyopathy

Leu^{39} \rightarrow \text{Stop Codon:TTA}^{39} \rightarrow \text{TGA}

Haghighi et al, J Clin Invest March 2003
Prospective Familial Assessment in DCM
Cardiac Autoantibodies Predict Disease Development in Asymptomatic Relatives

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Presentation, Patterns of Myocardial Damage and Clinical Course of Viral Myocarditis

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