Guideline
pediatric congenital heart disease

DEUTSCHE GESELLSCHAFT
FÜR PÄDIATRISCHE KARDIOLOGIE

Leitlinien Pädiatrische Kardiologie

Vorwort

In den letzten beiden Jahren arbeitete und vom Vorstand beschlossene neue Leitlinien:

- Periphere Pulmonalarterienstenosen
- Valvuläre Pulmonalstenose
- Pulmonalinsuffizienz
- Subvalvuläre Aortenstenose
- Aortenklappenstenose
- Aortenklappeninsuffizienz
- Supravalvuläre Aortenstenose
- Aortenisthmusstenose
- Vorhofseptumdefekt (ASD)
- Ventrikelseptumdefekt
- Persistierender Ductus arteriosus
- Bradykardie Herzrhythmusstörungen
- Tachykardie Herzrhythmusstörungen
- Tachykardie Herzrhythmusstörungen: Indikationen zur ICD-Therapie
- Familienorientierte Rehabilitation (FOR) bei Herz- und Kreislauferkrankungen im Kindes- und Jugendalter und spezielle Rehabilitations im Jugend- und jungen Erwachsenenalter (JHWA-Patienten)
- Abklingen eines Herzgeräusches
- Abklingen einer Cyanose
- Univentrikuläres Herz
- Pulmonalarterielle Hypertonie (PAH) im Kindes- und Jugendalter
- Myokarditis
- Rheumatisches Fieber – Poststreptokokkenarthritis
- Primäre Kardiomyopathien

LL 28 Leitlinie Pädiatrische Kardiologie: Primäre Kardiomyopathien
Autoren: S. Dittrich (Erlangen), S. Klaassen (Berlin), R. Kandolf (Tübingen), T. Doenst (Jena), L. Sieverding (Tübingen)

Beschlossen vom Vorstand der Deutschen Gesellschaft für Pädiatrische Kardiologie am 13.06.2012

www.kinderkardiologie.org/dgpkLeitlinien.shtm
Guideline
primary cardiomyopathies

Content

- Definition of primary cardiomyopathies
- Dilated cardiomyopathy
- Hypertrophic cardiomyopathy
- Genetic testing and prevention
Definition of cardiomyopathies

- Cardiomyopathies are defined as diseases of the myocardium associated with cardiac dysfunction

- (WHO 1995): They are classified as
  - dilated cardiomyopathy
  - hypertrophic cardiomyopathy
  - restrictive cardiomyopathy
  - arrhythmogenic right ventricular cardiomyopathy

Classification of primary cardiomyopathies
AHA statement 2006

PRIMARY CARDIOMYOPATHIES
(predominantly involving the heart)

Genetic
- HCM
- ARVC/D
- LVNC
- PRKAG2
- Danon
- Glycogen storage
- Conduction Defects
- Mitochondrial myopathies

Mixed*
- DCM
  - Restrictive (non-hypertrophied and non-dilated)

Acquired
- Inflammatory (myocarditis)
- Stress-provoked ("tako-tsubo")
- Peripartum
- Tachycardia-induced
- Infants of insulin-dependent diabetic mothers

Ion Channel Disorders
- LQTS
- Brugada
- SQTS
- CVPT
- Asian SUNDS

Secondary cardiomyopathies

Secondary Cardiomyopathies

- Infiltrative*: Amyloidosis (primary, familial autosomal dominant†, senile, secondary forms), Gaucher disease†, Hunter's disease†, Hurler's disease†, Storage†: Hemochromatosis, Fabry's disease†, Glycogen storage disease† (type II, Pompe), Niemann-Pick disease†, Toxicity: Drugs, heavy metals, chemical agents, Endomyocardial: Endomyocardial fibrosis, Hypereosinophilic syndrome (Löeffler's endocarditis), Inflammatory (granulomatous): Sarcoidosis, Endocrine: Diabetes mellitus†, Hyperthyroidism, Hypothyroidism, Hyperparathyroidism, Pheochromocytoma, Acromegaly, Cardiofacial: Noonan syndrome†

- Lenticulost†, Neuromuscular/neurological: Friedreich's ataxia†, Duchenne-Becker muscular dystrophy†, Emery-Dreifuss muscular dystrophy†, Myotonic dystrophy†, Neurofibromatosis†, Tuberous sclerosis†, Nutritional deficiencies: Beriberi (thiamine), pellagra, scurvy, selenium, carotene, kwashiorkor, Autoimmune/collagen: Systemic lupus erythematosus, Dermatomyositis, Rheumatoid arthritis, Scleroderma, Polyarteritis nodosa, Electrolyte imbalance

*Accumulation of abnormal substances between myocytes (i.e., extracellular). †Genetic (familial) origin. ‡Accumulation of abnormal substances within myocytes (i.e., intracellular).

Incidence of cardiomyopathies in patients <19 yrs.: 1.13 on 100,000 children (8.34 on 100,000 in infants)

dilative cardiomyopathy
definition and clinical symptoms

- Dilation of left and later right ventricle
- severe systolic dysfunction

- Congestive heart failure
- Cold sweating
- Dyspnoea
- Lung odema
- Peripheral cyanosis
- Hepatomegaly
- Failure to thrive

Clinical differential diagnosis:
- Pneumonia
- Sepsis
**dilative cardiomyopathy**

**primary diagnostics**

<table>
<thead>
<tr>
<th><strong>Echocardiography</strong></th>
<th><strong>Cardiac catheterization</strong> (necessary after primary stabilization)</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Left ventricular diameter/function</td>
<td></td>
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<tr>
<td>▪ Mitral regurgitation</td>
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<tr>
<td>▪ Coronary morphology</td>
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<tr>
<td>▪ Pulmonary artery pressure (tricuspid/pulmonary regurgitation)</td>
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</tbody>
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<thead>
<tr>
<th><strong>ECG</strong> (not specific)</th>
<th><strong>Myocardial biopsy</strong></th>
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<tbody>
<tr>
<td>▪ left heart strain</td>
<td></td>
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<tr>
<td>▪ Arrhythmias</td>
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<thead>
<tr>
<th><strong>Thoracic X-ray</strong> (not specific)</th>
<th><strong>Cardiac MRI</strong></th>
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<tbody>
<tr>
<td>▪ Cardiomegaly</td>
<td></td>
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<tr>
<td>▪ Pulmonary congestion</td>
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<tr>
<td>▪ DD: myocarditis (late enhancement)</td>
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<thead>
<tr>
<th><strong>Biomarkers</strong></th>
<th><strong>Genetic testing</strong></th>
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<tbody>
<tr>
<td>▪ NT-pro/BNP</td>
<td></td>
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<tr>
<td>▪ Not recommended in isolated CMP</td>
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<tr>
<td>▪ Meaningful in patients with combination of AV-block or myopathy</td>
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dilative cardiomyopathy
- possible causes

- Hereditary/geneically caused disease
- Post-myocarditis
- Metabolic disease
- Other secondary cardiomyopathy
- Coronary artery disease (ALCAPA)
- Tachycardia induced cardiomyopathy

Goodwin, Muntoni, Muscle Nerve 2005;32:577-88
<table>
<thead>
<tr>
<th>Virusinfektionen (Myokarditis)</th>
<th>Coxsackie B, Adenovirus, Echo-Virus, EBV, CMV, HIV Röteln, Masern, Mumps Varizellen Influenza, Parovirus B19, Hepatitis-C-Virus, Polio, Tollwut</th>
</tr>
</thead>
<tbody>
<tr>
<td>bakterielle Infektionen</td>
<td>Diphtherie, Mykoplasmen, Tbc, Borrelien, Sepsis</td>
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<tr>
<td>Parasiten</td>
<td>Toxoplasmen, Ascariden</td>
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<tr>
<td>Pilzinfektionen</td>
<td>Histoplasmen, Aspergillen, Candida, Cryptcoccus</td>
</tr>
<tr>
<td>neuromuskuläre Erkrankungen</td>
<td>Muskeldystrophie Becker, Duchenne, Emery-Dreifuss, Glieder-Gürtel-Typ; Myotonoe Dystrophie, Friedreich-Ataxie, Kearns-Sayre-Syndrom, kongenitale Myopathie, Barth-Syndrom</td>
</tr>
<tr>
<td>Erkrankungsgruppe</td>
<td>Differentialdiagnosen</td>
</tr>
<tr>
<td>-----------------------------------</td>
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<tr>
<td>Mangelzustände</td>
<td>Anorexia nervosa, Mangel an Kupfer, Eisen, Selen, Thiamin</td>
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<tr>
<td>immunologische Erkrankungen</td>
<td>rheumatisches Fieber, rheumatoide Arthritis, systemischer Lupus erythematodes, Dermatomyositis, Kawasaki-Syndrom</td>
</tr>
<tr>
<td>Hämatologische Erkrankungen</td>
<td>Thalassämie, Sichelzell-Erkrankung</td>
</tr>
<tr>
<td>Medikamente oder Toxine</td>
<td>Anthrazykline, Cyclophosphamid, Choroquin, Kokain, trizyklische Antidepressiva, Interferon, Alkohol, Anabolika</td>
</tr>
<tr>
<td>endokrinologische Erkrankungen</td>
<td>Hypo-/Hyperthyreose, Hypoparathyreoidismus, Phäochromozytom, Hypoglykämie</td>
</tr>
<tr>
<td>metabolische Erkrankungen</td>
<td>Glykogenspeicherkrankheiten, Carnitin-Mangel, Störungen der Beta-Oxidation oder des Fettsäuretransports, Refsum-Krankheit, Mukopolysaccharidosen, Oligosaccharidosen, Mitochondriopathien, Defekte im Glukose-/Pyruvat-Stoffwechsel und Zitratzyklus, Hämoglobinopathien</td>
</tr>
<tr>
<td>Myokardischämie</td>
<td>Bland-White-Garland-Syndrom (ALCAPA), Myokardinfarkt</td>
</tr>
<tr>
<td>Arrhythmien</td>
<td>supraventrikuläre/ventrikuläre Tachykardien</td>
</tr>
<tr>
<td>Fehlbildungssyndrome</td>
<td>Katzenschrei-Syndrom</td>
</tr>
<tr>
<td>familiäre DCM</td>
<td>unterschiedliche Erbgänge, am häufigsten autosomal dominant: betroffen sind v.a. Gene, die myokardiale Proteine codieren (Actin, Desmin, Dystrophin)</td>
</tr>
</tbody>
</table>

Nikolaus A. Haas; Ulrich Kleideiter - Kinderkardiologie: Klinik und Praxis der Herzerkrankungen bei Kindern, Jugendlichen und jungen Erwachsenen, Thieme 2011
Drug therapy for congestive heart failure (look at guideline)
  - ACE-inhibitor
  - β-blocker
  - Aldosteron-antagonists
  - Diuretics

- Anti-coagulants
- Anti-arrhythmics (guideline)
- ICD-implantation (guideline)
- Cardiac resynchronisation therapy
- Cardiac-assist-system
- Heart transplantation (HTX)
dilative cardiomyopathy follow-up examinations

- Echocardiography
  - Left ventricle
  - Mitral valve
  - Pulmonary artery hypertension (PAH)
- Biomarkers (1x/y)
- Holter-ECG (every 2 yrs.)
- Repeated catheterizations if signs of PAH are existent
- Spiroergometry (every 3 yrs.)
- Involvement of HTX-center
hypertrophic cardiomyopathy
definition and clinical symptoms

- Asymmetric hypertrophy of the left ventricle
- +/- obstruction of left ventricular outflow tract
- Disease of the sacomer
- 90% hereditary disease (autosomal dominant)

- Systolic heart murmur
- palpitations
- Fatigue
- Dyspnoea (on exertion)
- Syncope (on exertion)
hypertrophic cardiomyopathy
primary diagnostics

- **Echocardiography**
  - Left ventricular measurements
  - Thickness of the septum and different wall segments
  - Distribution of hypertrophy (asymmetric/concentric)
  - Assessment of left ventricular apex
  - Systolic anterior movement of mitral valve (SAM phenomenon)
  - Thickness of right ventricular wall
  - PW-/CW-Doppler: left ventricular obstruction (subaortal, mid-ventricular, apical)

- **Stress echocardiography**
  - Recommended in symptomatic patients with LVOTO-rest-gradient < 30 mmHg

- **Valsalva´s manoeuvre**
Cardiac MRI
- Recommended in patients with insufficient echo-window
- Verification of fibrosis (late gadolinium enhancement)

ECG (left ventricular hypertrophy, repolarisation patterns)

Holter-ECG, Ergometry (arrhythmias)

Thoracic X-ray (not necessary for primary diagnostics)

Cardiac catheterization
- LV-Angiography/coronary imaging recommended before surgery in patients with LVOTO

Endomyocardial biopsy
- uncertain phenotype/etiology
- Elimination of secondary hypertrophy in cases of uncertain concentric myocardial hypertrophy

Genetic testing
- Limited indication in patients <18 yrs. of age
- Only for clarification of differential diagnoses in uncertain phenotypes
Differential diagnoses

- Storage diseases (e.g. Pompe disease)
- Genetic disorders (e.g. Noonan diseases)
- Neuromuscular diseases
- PRKAG2-syndrom (cardiac glycogenosis associated with Wolff-Parkinson-White Syndrom)
- Danon disease (X-chromosomal inherited lysosomal storage disease)
Hypertrophic cardiomyopathy (HCM) - risk factors

- Main risk factors for sudden cardiac death (according to adult patients)
  - Resuitation for cardiac arrest or non-sustained ventricular tachycardia
  - Sudden cardiac death in family history
  - History of non-sustained ventricular tachycardia (>3 Schläge < 30 sec, HF >120/min.)
  - Profound thickness of the septum >30 mm (controversially discussed)
  - Insufficient rise of systolic blood pressure under exertion (syst. ≤ 20 mmHg)
  - Rapid progression of the disease

Follow-up-visits
- At least annually (ECG, echocardiography)

High risk patients
- LVOT-peak echo-gradient >30 mmHg
- moderate or profound LV-wall hypertrophy
- rapid progress of the disease
- unfavorable patient or family history
- Holter-ECG and ergometry annually

Hypertrophic cardiomyopathy (HCM) – sports and primary prevention

- No competitive sport \(^*1\)
- No isometric muscular exertion \(^*1\)
- For detailed recommendations look at the current guideline of the European Society of Cardiology \(^*2\)

- Early detection and medical screening before athletic activities
  - HCM, ARVC and ion-channel disorders are mean reasons for sudden cardiac death in athletes <35 yrs. of age
  - Preliminary medical examination before athletic sports should include patients medical and family history, physical examination, ECG
  - Guideline committee recommends a medical screening examination (including ECG) for all adolescents at the age of 12-14 yrs. and in the „Jugendarbeitsschutzuntersuchung“ (strong agreement of the committee)

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Hypertrophic cardiomyopathy (HCM) – therapeutic options

- Lipophilic β-blockers (e.g. Propranolol, Metoprolol or Bisoprolol): recommended in symptomatic patients
- CA-antagonists (e.g. Verapamil): increased risk for deterioration of congestive heart failure/death in patients with severe hypertrophy; contraindication for use in infants
- Amiodarone: protection against sudden cardiac death not shown; side effects of permanent application are more serious in children/adolescents
- ICD-Implantation: only reliable primary and secondary prevention for sudden cardiac death (look at guideline)
- Septal myectomy to treat LVOTO
- Transcatheter intervention in individual cases/controversially discussed
- Rarely heart transplantation

**Primary cardiomyopathies – family members and prevention**

- Family history (3 generations)
- Medical examination of first-degree relatives (incl. children)
- Conspicuous medical finding/carrier of mutation: annually controls
- Time interval for controls in inconspicuous siblings during childhood:
  - Every 3 yrs.
  - in hypertrophic cardiomyopathy annually from the age of 12. yrs.

Primary cardiomyopathies – family members and prevention

- Genetic testing
  - Counseling (institut for human genetics) recommended for patients and families
  - Children and adolescents show larger number of
    - Inherited/gentically caused cardiomyopathies
    - Mitochondrial or metabolically caused cardiomyopathies
    - Chromosomal defects, dysmorphic syndroms
- Family-screening and -management (adjustment of risk in asymptomatic carriers of mutation)
  - Predictive genetic testing in children/adolescents is rated very controversially
  - Predictive genetic testing is legal exclusively after qualified genetic counseling