Guideline Title

Presentation, diagnosis, and medical management of heart failure in children: Canadian Cardiovascular Society guidelines.

Bibliographic Source(s)


Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The grading of evidence (High, Moderate, Low, Very Low) and strength of recommendations (Strong or Conditional) are defined at the end of the "Major Recommendations" field.

Presentation and Detection of Heart Failure (HF) in Children

Symptom Severity and Recognition

The New York Heart Association (NYHA)/Ross classification is a suitable basis for symptom stratification of patients with established chronic HF, but is not essential to establishing the diagnosis, or determining the prognosis of HF in children (Strong Recommendation, Moderate-Quality Evidence).

Values and preferences. This Recommendation places high value on the need for the development of reliable and valid prognostic indicators for pediatric HF.

Underlying cardiac disease should be considered and excluded in younger infants with feeding difficulties and growth failure when primary gastrointestinal and other common causes have been ruled out, and in infants, toddlers, and children with chronic calorie, protein, or trace element deficiency (Strong Recommendation, Moderate-Quality Evidence).
**Values and preferences.** This Recommendation places a high value on early diagnosis of underlying HF in situations of ambiguous clinical symptoms and signs, or when uncertainty is present. Early and repeated cardiovascular examination of infants is mandated as the most valuable screening tool available. Expert evaluation is considered preferable in situations of uncertainty, notwithstanding the potential for unnecessary referral: the trade-off of missed diagnosis at an earlier stage of disease being of such significant consequence to the patient and family.

**Presentation of Cardiomyopathies (CMs) in Children/Myocarditis in Children**

A high index of suspicion for CMs with acute decompensated HF is necessary in emergency and primary care settings, when evaluating infants with weakness, lethargy, abdominal pain, unexplained or disproportionate tachycardia, and tachypnea (Strong Recommendation, Low-Quality Evidence). In suspected muscular dystrophies, symptoms and signs of congestive HF might be concealed because of reduced physical activity. Careful evaluation of myocardial function (via serial echocardiography or magnetic resonance imaging [MRI]) beginning in mid-childhood is recommended (Strong Recommendation, Moderate-Quality Evidence). Myocarditis should always be considered in the differential diagnosis of children who present with a viral prodrome and nonspecific respiratory or abdominal symptoms associated with tachycardia, hypotension, or cardiac rhythm abnormalities, even in the absence of cardiomegaly on chest x-ray (CXR) (Strong Recommendation, Low-Quality Evidence).

**Values and preferences.** These Recommendations place a high value on a comprehensive approach to history-taking, examination, and differential diagnosis for children with suspected genetic or acquired CM and on a comprehensive approach to ongoing evaluation in suspected cases.

**Diagnosis of HF in Children**

**Chest Radiography**

Chest radiography is indicated as a first-line investigation in children with suspected HF (Strong Recommendation, Moderate-Quality Evidence).

**Biochemical and Routine Laboratory Testing**

Assessment of electrolytes (Na⁺, K⁺, Cl⁻, Ca²⁺), glucose, acid-base status, urea and creatinine, hepatic transaminases, thyroid hormone levels, and a complete blood count should be performed at initial presentation of HF and repeated as needed to assess ongoing clinical status (Strong Recommendation, Low-Quality Evidence).

**Electrocardiography**

All patients should have 12-lead electrocardiography (ECG) performed at the time of presentation with HF, to exclude features of congenital or ischemic heart disease, arrhythmia and pre-excitation (Strong Recommendation, Moderate-Quality Evidence). Holter/ambulatory ECG monitoring is not indicated as a primary diagnostic test in HF, unless hypertrophic CM (HCM), arrhythmogenic right ventricular (RV) CM, or tachycardia-induced CM is the suspected cause (Conditional Recommendation, Low-Quality Evidence). Holter/ambulatory ECG monitoring might be indicated during chronic follow-up, particularly in higher arrhythmia risk groups, including patients with primary restrictive CM or HCM, with tachycardia-induced CM, or those who are taking anti-arrhythmic therapy (Conditional Recommendation, Low-Quality Evidence).

**Echocardiography**

All patients with symptoms consistent with HF should undergo transthoracic echocardiography in a pediatric cardiology facility at, or as soon as possible after, initial presentation. This initial echocardiographic study should include as a minimum (Strong Recommendation, High-Quality Evidence):
Ruling out congenital heart disease (with attention to coronary arteries)
Assessment of myocardial appearance for phenotypic patterns of CM
Assessment of the systolic function parameters of the left ventricle by determining the shortening fraction (SF) and/or ejection fraction (EF)
Measurement of the left ventricular (LV) end diastolic dimension Z-score
Determination of the presence of mitral regurgitation
Quantitative or qualitative assessment of RV function and RV pressure
Assessment of LV diastolic function
Exclusion of intracardiac thrombus

Populations at increased risk for ventricular dysfunction should undergo routine periodic screening echocardiography even in the absence of cardiac symptoms (Strong Recommendation, Moderate-Quality Evidence).
All patients with HF should undergo periodic follow-up echocardiography to reassess ventricular function with respect to response to medical therapy and to assess further progression of ventricular dysfunction. Follow-up echocardiography should also be repeated if there is a significant change in the clinical status of the patient, either in terms of improvement or deterioration (Strong Recommendation, Moderate-Quality Evidence).

Values and preferences. These Recommendations place a high value on the diagnostic accuracy of expert pediatric echocardiography done in a qualified facility, for primary evaluation and for follow-up assessment of at risk or affected patients. The trade-off of inconvenient access to such a facility is considered acceptable considering the benefits of early accurate diagnosis.

Biomarkers

Brain natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (NT-proBNP) levels are useful in distinguishing HF from respiratory or other non-cardiac disease and should be used as a confirmatory test in the acute evaluation of pediatric HF (Strong Recommendation, Moderate-Quality Evidence).

Metabolic and Genetic Testing

All pediatric patients presenting with HF require a thorough personal health history and a family history including a 3-generation pedigree (Strong Recommendation, High-Quality Evidence).
Metabolic laboratory testing in children with unexplained CM (of hypertrophic, dilated, or non-compaction phenotype) should be based on clinical presentation and assisted by specialist consultation: virtually all undiagnosed patients, whether there is a familial pattern or not, require primary screening tests, including serum amino acids, organic acids, total and free carnitine levels, lactate, and urine testing for ketones, mucopolysaccharides, and oligosaccharides (Strong Recommendation, High-Quality Evidence).
Specialty consultation with genetic and/or metabolic services is recommended to guide further testing such as muscle biopsy or specific gene screening, molecular, or cytogenetic testing.
Excluding familial CM is crucial, especially when the presentation is in the fetus or newborn (Strong Recommendation, High-Quality Evidence).
At-risk family members might require secondary diagnostic screening, including genetic testing, echocardiography, or other relevant modalities of screening, depending on the etiology identified (Conditional Recommendation, Low-Quality Evidence).

Endomyocardial Biopsy for Acute Myocarditis

A diagnosis of acute myocarditis should be considered in all children, regardless of age, who present with new onset HF without a history of decreased functional capacity, and specifically if echocardiographic ventricular dilation is less than expected for the degree of systolic dysfunction and clinical severity (Strong Recommendation, Moderate-Quality Evidence).
Endomyocardial biopsy (EMB) should only be performed if confirming the clinical diagnosis of myocarditis will have a clear effect on the patient treatment plan (for example, listing for transplantation). EMB is not recommended in infants weighing less than 10 kg, or in patients who
are hemodynamically unstable (Strong Recommendation, Moderate-Quality Evidence).

Values and Preferences. These Recommendations place a higher emphasis on clinical diagnosis supported by noninvasive imaging, and a lower emphasis on confirmation via biopsy, except in specific cases as outlined in this Recommendation. The trade-off is diagnostic confirmation for increased safety.

Cardiac MRI

Cardiac magnetic resonance imaging (CMRI) might assist in the clinical diagnosis of myocarditis, and might provide additional information in CMs by tissue and scar characterization. The prognostic value of CMRI findings is not yet known (Conditional Recommendation, Low-Quality Evidence).

Medical Treatment of the Child with Acute HF

Acute Therapy for HF

A loop diuretic, such as furosemide, is recommended for patients with HF and signs and symptoms of congestion. An initial starting dose of 0.5-1 mg/kg intravenously or orally every 6-12 hours is safe and effective (Strong Recommendation, Moderate-Quality Evidence).

Children presenting with HF because of reduced cardiac output with end-organ dysfunction are likely to benefit from inotropic therapy as a rescue strategy. In this setting, milrinone, dobutamine, and low dose epinephrine have all shown efficacy in children (Strong Recommendation, Low-Quality Evidence).

Inotropic therapy should be continued to patients with depressed systolic function and clinical evidence of low cardiac output syndrome who can be closely monitored for tachyarrhythmias and blood pressure lability (Strong Recommendation, Moderate-Quality Evidence).

Values and preferences. These Recommendations place a high priority on improving cardiac output in an emergency setting, and acknowledge the deleterious effect of sustained inotropic stimulation on myocardial survival.

Chronic Therapy for HF: Angiotensin-Converting Enzyme Inhibitor and Angiotensin II Receptor Blocker Therapy

The use of angiotensin-converting-enzyme inhibitor (ACEi) therapy is indicated in children with HF because of primary heart muscle disease of the systemic left ventricle (Strong Recommendation, Moderate-Quality Evidence).

Values and preferences. The Recommendation favors commitment to a course of medical therapy, which, although of uncertain duration, is associated with symptom improvement, and possibly with survival benefit in certain patient groups.

β-Adrenergic Antagonists

Treatment with a β-adrenergic antagonist such as carvedilol, metoprolol, or bisoprolol might be initiated in the treatment of moderate to severe systolic dysfunction of a systemic left ventricle (Conditional Recommendation, Moderate-Quality Evidence).

Values and preferences. This Recommendation is based on the premise that patients are willing to accept a relatively low rate of side effects for potential clinical benefits in the absence of conclusive evidence for benefit.

Aldosterone Antagonist Therapy

Aldosterone antagonist therapy is reasonable in children with chronic systolic HF, provided renal function is normal or only mildly impaired. Close monitoring of renal function and serum potassium is required when co-administering aldosterone antagonist therapy with ACEi therapy (Conditional Recommendation, Low-Quality Evidence).

Medical Management of Myocarditis
A standard approach to HF management should be applied in patients with myocarditis including inotropic support and diuretic therapy (Strong Recommendation, Moderate-Quality Evidence). For fulminant myocarditis, mechanical circulatory support should be considered. Invasive therapies are considered acceptable considering the prospect of spontaneous recovery (Strong Recommendation, Moderate-Quality Evidence).

Corticosteroids are not recommended as a routine treatment for myocarditis, particularly in the absence of robust randomized controlled trial evidence. Continued speculative use of immunosuppressive therapy in the absence of a prospective clinical trial will not contribute to the evidence base of management for this disorder (Conditional Recommendation, Low-Quality Evidence).

Intravenous immunoglobulin G (IVIG) is not recommended as a routine treatment for myocarditis (Conditional Recommendation, Low-Quality Evidence).

Values and preferences. These Recommendations place a high priority on conservative management in an observed and monitored hospital setting when this disease is in evolution.

Definitions:

Quality of Evidence*
High: Further research is very unlikely to change confidence in the estimate of effect.
Moderate: Further research is likely to have an important influence on confidence in the estimate of effect and might change the estimate.
Low: Further research is very likely to have an important influence on confidence in the estimate of effect and is likely to change the estimate.
Very low: Any estimate of effect is very uncertain.

Strength of Recommendations*
Strong: The desirable effects clearly outweigh the undesirable effects, or clearly do not.
Conditional: The trade-offs are less certain, either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced.

*The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used for grading quality of evidence and strength of recommendations.

Clinical Algorithm(s)
An algorithm titled "Simplified Algorithm for Heart Failure Management" is provided in the original guideline document.

Scope

Disease/Condition(s)
Pediatric heart failure (HF) including HF caused by cardiomyopathies, congenital heart defects, or myocarditis

Guideline Category
Diagnosis
Guideline Objective(s)

- To present guidelines for the recognition, diagnosis, and early medical management of heart failure (HF) in infancy, childhood, and adolescence
- To assist practitioners in office-based or emergency room practice, who encounter children with undiagnosed heart disease and symptoms of possible HF, rather than those who have already received surgical palliation

Target Population

Children (aged 0-18 years) with undiagnosed heart disease and symptoms of possible heart failure (HF) and children with confirmed HF

Interventions and Practices Considered

Diagnosis/Evaluation/Screening

Evaluation of symptom severity and symptom stratification
Early diagnosis of underlying cardiac disease in younger infants
Evaluation for cardiomyopathies
Evaluation of myocardial function (via serial echocardiography or magnetic resonance imaging [MRI])
Consideration of myocarditis in the differential diagnosis of children who present with a viral prodrome
Chest radiography
Biochemical and routine laboratory testing
12-lead electrocardiography (ECG)
Holter/ambulatory ECG monitoring
Transthoracic echocardiography
Assessment of brain natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (NT-proBNP) levels
Family history, 3-generation pedigree mapping, and genetic testing
Metabolic laboratory testing in children with unexplained cardiomyopathy
Screening of at-risk family members
Endomyocardial biopsy for acute myocarditis
Cardiac MRI

Management/Treatment

Loop diuretic, such as furosemide
Inotropic therapy (milrinone, dobutamine, and low-dose epinephrine)
Angiotensin-converting enzyme inhibitors (ACEis)
Angiotensin II receptor blockers
β-adrenergic antagonists (carvedilol, metoprolol, or bisoprolol)
Aldosterone antagonists
Medical management of myocarditis (inotropic support and diuretic therapy, mechanical circulatory)
(corticosteroids and intravenous immunoglobulin were considered but not recommended as a routine treatment for myocarditis)

Major Outcomes Considered

- Clinical symptoms and signs of heart failure in children
- Diagnostic accuracy and yield of biochemical, laboratory, imaging, metabolic, and genetic tests
- Mortality
- Effectiveness of medications in relieving symptoms, increasing exercise capacity, reducing episodes of worsening heart failure
- Survival
- Need for heart transplantation or insertion of a left ventricular assist device
- Adverse effects and intolerance associated with medications

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Methodology

Searches in Ovid MEDLINE and Ovid EMBASE were performed using database subject headings and, when appropriate text words, to create a base set of references on the topic of heart failure in the context of
congenital heart disease or cardiomyopathy, excluding heart assist devices, heart transplants, case reports or reviews, and limited to English, ages 18 and under, and the publication years 1982 to April 2012. The base set was combined with concepts for symptoms, diagnosis, treatments and quality of life. Four additional searches were conducted for heart failure and symptoms, heart failure and beta blockers, myocarditis and (gamma globulin or corticosteroids or interferon or immunosuppression or steroids), and cardiomyopathies and (supplements or co-factors).

The literature searches resulted in 2716 unique citations, acquired in three separate searches. These were clustered into 3 datasets, and each abstract was reviewed separately by the three primary authors of this manuscript. Of these 615 were deemed appropriate for complete review based on relevance, and specific criteria established prospectively.

The 615 manuscripts were distributed to three working groups, dealing with the three topic areas. Each working group comprised 6 primary and a variable number of secondary panelists. Of the 615 identified by abstract review, only 260 were deemed of sufficient quality or relevance to merit formal review using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method.

Additional information on the development process, including evidence inclusion criteria, search methods, consensus-building procedure, and evidence appraisal is available in Supplemental Appendix S1 (see the "Availability of Companion Documents" field).

Number of Source Documents

A total of 260 manuscripts were deemed of sufficient quality or relevance to merit formal review.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence*

High: Further research is very unlikely to change confidence in the estimate of effect.

Moderate: Further research is likely to have an important influence on confidence in the estimate of effect and might change the estimate.

Low: Further research is very likely to have an important influence on confidence in the estimate of effect and is likely to change the estimate.

Very low: Any estimate of effect is very uncertain.

*The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used for grading quality of evidence and strength of recommendations.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

These guidelines were developed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system of evidence evaluation, in order to make practice recommendations to clinicians that accounted for the variable strength of evidence, and the co-existing need to highlight the
values and preferences implicit in these recommendations.

Of the 615 manuscripts identified by abstract review, only 260 were deemed of sufficient quality or relevance to merit formal review using the GRADE method. Each working group reviewed these manuscripts in parallel, and constructed a formal structured assessment of the strength of the evidence, and quality of the data using a customized appraisal tool developed to apply GRADE (see Supplemental Appendix I [see the "Availability of Companion Documents" field]). These reviews were then abstracted into a database.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The evidence was discussed at a series of teleconferences, with recommendations drafted, and the level of evidence, and strength of recommendation assigned by consensus.

Although the evidentiary base determined the strength of the recommendations, the guideline panel recognizes that the treatment-related values and preferences of patients and families also play a role in clinical decision-making. The panel has therefore made the values and preferences of the team explicit, as they pertain to each group of recommendations.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations*

Strong: The desirable effects clearly outweigh the undesirable effects, or clearly do not.

Conditional: The trade-offs are less certain, either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced.

*The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used for grading quality of evidence and strength of recommendations.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Internal peer review of the recommendations and evidentiary support was reviewed at working group, steering committee and internal and external reviewer level.

Evidence Supporting the Recommendations
Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

These guidelines included systematic (Cochrane) reviews, single randomized controlled trials (RCTs), and quasi-experimental and pre-post intervention studies. The guideline development group also included observational/descriptive and retrospective, studies where the study was conducted with appropriate scientific rigor to allow generalization of the findings to the pediatric heart failure population.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and medical management of heart failure (HF) in children

Potential Harms

- Hyperkalemia might result in patients who receive spironolactone and an angiotensin-converting enzyme inhibitor, especially if renal function is already compromised. Therefore, potassium levels and renal function indices should be checked before starting spironolactone, within 7-14 days after introduction, and periodically thereafter. Any potassium supplementation should be carefully re-evaluated. Male gynaecomastia is a nonreversible complication of spironolactone, and must be closely monitored.
- Caution is advised when angiotensin-converting enzyme inhibitors (ACEis) are used in the first 4 months of life, because renal dysfunction is more common, and therefore uptitration must be carefully monitored. A small drop in systolic blood pressure is typically noted in patients who take an ACEi. This might occasionally exceed the expected 5%-10% drop in baseline values, necessitating observation for up to 2 hours after the first dose.
- There is a low rate of side effects with β-adrenergic antagonist therapy.
- The diagnostic accuracy of right ventricular endomyocardial biopsy for suspected myocarditis tends to be low, and is affected by the length of time from presentation of symptoms to time of biopsy, variation in pathological interpretation, and sampling errors. The addition of left ventricular biopsy or magnetic resonance imaging-guided biopsy might increase yield, but also the hazards of the procedure. Endomyocardial biopsy is associated with an increased risk of adverse events in children with suspected myocarditis who are using inotropic support.
- The goal of inotropic agent therapy needs to be carefully considered: although there is good empirical evidence that inotropes can bridge patients to mechanical circulatory support or cardiac transplantation, their toxicities prohibit routine use and limit their utility to only the sickest patients, who genuinely require rescue from low cardiac output with organ dysfunction with metabolic acidosis. The requirement for inotropic support for more than 48 hours requires a plan for weaning of support, transition to a more viable means of circulatory support, and consideration of the need for cardiac transplantation.
- Milrinone might cause peripheral dilation and should be used with caution in hypotensive patients.
- Prolonged administration (>72 hours) of nitroprusside sodium, especially when associated with renal failure, can result in thiocyanate toxicity.

Contraindications
Contraindications

It is important to note that indiscriminate administration of intravenous resuscitation is contraindicated in many, if not most, patients with heart failure (HF) syndrome, and will frequently worsen the condition of children with acute HF.

Qualifying Statements

This statement was developed following a thorough consideration of medical literature and the best available evidence and clinical experience. It represents the consensus of a Canadian panel comprised of multidisciplinary experts on this topic with a mandate to formulate disease-specific recommendations. These Recommendations are aimed to provide a reasonable and practical approach to care for specialists and allied health professionals obliged with the duty of bestowing optimal care to patients and families, and can be subject to change as scientific knowledge and technology advance and as practice patterns evolve. The statement is not intended to be a substitute for physicians using their individual judgment in managing clinical care in consultation with the patient, with appropriate regard to all the individual circumstances of the patient, diagnostic and treatment options available and available resources. Adherence to these Recommendations will not necessarily produce successful outcomes in every case.

These guidelines do not deal with advanced interventions or device therapies for heart failure in children, nor do they offer recommendations for treatment of all underlying disease etiologies. Background information is provided for context, but is not intended to be exhaustive. Important practice points and figures which will be of assistance are provided for illustration.

This document is intended to enhance, but not replace, expert physician judgment in individual scenarios. Finally, the authors acknowledge that the content of these guidelines reflects a literature and clinical experience that borrows much from that of adult medicine. It is hoped that further research in pediatric heart failure, particularly in the area of congenital heart diseases, will result in refinement of these guidelines.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

For information about availability, see the Availability of Companion Documents and Patient Resources fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need
Identifying Information and Availability

Bibliographic Source(s)


Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Dec

Guideline Developer(s)

Canadian Cardiovascular Society - Medical Specialty Society

Source(s) of Funding

Canadian Cardiovascular Society

Guideline Committee

The Children’s Heart Failure Study Group

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Financial Disclosures/Conflicts of Interest

The disclosure information of the authors and reviewers is available from the Canadian Cardiovascular Society on the following websites: [www.ccs.ca](http://www.ccs.ca) and/or [www.ccsguidelineprograms.ca](http://www.ccsguidelineprograms.ca).

Guideline Status

This is the current release of the guideline.

Guideline Availability

Available from the [Canadian Journal of Cardiology Web site](http://www.ccs.ca).

Availability of Companion Documents

Supplemental material, including tables and the literature search strategy, is available from the [Canadian Journal of Cardiology Web site](http://www.ccs.ca).

Patient Resources

None available

NGC Status

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