Supplemental Material

Appendix

The Pediatric Cardiomyopathy Registry Study Group

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Table S1. Echocardiography criteria for study eligibility.

Measurements: (At least 2 must be present at the time of CM diagnosis for the patient to be eligible, unless otherwise noted)
1) Left ventricular fractional shortening or ejection fraction >2 s.d. below the normal mean for age. Fractional shortening is acceptable in patients with normal ventricular configuration and no regional wall motion abnormalities. Abnormal ejection fraction by echocardiography, radionuclide or contrast angiography, or MRI are acceptable alternatives, but age-appropriate norms for the individual laboratory must be employed.
2) Left ventricular posterior wall or septal thickness at end-diastole >3 s.d. above the normal mean for body-surface area. (This criterion applies to HCM only; Meeting this single criterion qualifies the patient as eligible)
3) Left ventricular end-diastolic posterior wall thickness-to- end-diastolic dimension ratio <0.12.
4) Left ventricular end-diastolic dimension or volume > 2 s.d. above the normal mean for body-surface area. Dimension data are acceptable under the conditions outlined in Measurement Criteria 1 for fractional shortening, and volume data may be derived from the imaging methods as in Measurement Criterion 1.
Patterns: (At least 1 must be met for the patient to be eligible if Measurement criteria are not met at the time of CM diagnosis)
1) Localized ventricular hypertrophy, such as septal thickness >1.5 x left ventricular posterior wall thickness with at least normal left ventricular posterior wall thickness, with or without dynamic outflow obstruction.
2) Restrictive cardiomyopathy: one or both atria enlarged relative to ventricles of normal or small size with evidence of impaired diastolic filling and in the absence of significant valvular heart disease.
3) Contracted form of endocardial fibroelastosis, similar to restrictive cardiomyopathy plus echo-dense endocardium.
4) Ventricular dysplasia/Uhl's anomaly: very thin right ventricle with dilated right atrium usually better assessed by MRI than echo.
5) Left ventricular myocardial noncompaction: very trabeculated spongiform left ventricular myocardium with multiple interstices.

Table S2. Inclusion and exclusion criteria.

Inclusion criteria:
1) Patient is alive A. Patients who are status-post heart transplant are eligible if pre-transplant longitudinal data is available.
2) Under age 18 years of age at the time of the diagnosis.
3) Either primary or idiopathic Dilated Cardiomyopathy, Hypertrophic Cardiomyopathy, Restrictive Cardiomyopathy, or Left Ventricular Noncompaction.
4) A diagnosis of cardiomyopathy which, at the time of diagnosis, was confirmed by: ● Echocardiographic criteria, OR ● Cardiac MRI

Exclusion criteria:
Arrhythmogenic right ventricular dysplasia
Neuromuscular disease (defined by the specific conditions listed in Appendix A)
Endocrine disease known to cause heart muscle disease (including infants of diabetic mothers)
History of rheumatic fever

Toxic exposures known to cause heart muscle disease (anthracyclines, mediastinal radiation, iron overload, or heavy metal exposure)
HIV infection or born to an HIV positive mother
Kawasaki disease
Immunologic disease
Invasive cardiothoracic procedures or major surgery during the preceding month, except those specifically related to cardiomyopathy including LVAD, ECMO, and AICD placement
Uremia, active or chronic
Abnormal ventricular size or function that can be attributed to intense physical training or chronic anemia
Chronic arrhythmia, unless there are studies documenting inclusion criteria prior to the onset of an arrhythmia (except a patient with a chronic arrhythmia, subsequently ablated, whose cardiomyopathy persists after two months is not to be excluded)
Malignancy
Systemic hypertension

Pulmonary parenchymal or vascular disease (e.g., cycstic fibrosis, cor pulmonale, or pulmonary hypertension)
Ischemic coronary vascular disease
Association with drugs known to hypertrophy (e.g., growth hormone, corticosteroids, cocaine)
Genetic syndrome or chromosomal abnormality known to be associated with cardiomyopathy

Table S3. Exome sequencing metrics. See Excel file.

Table S4. Variants identified in 37 clinically relevant genes. See Excel file.

Figure S1. Variation across the sites.