The impact of malnutrition on idiopathic dilated cardiomyopathy in children

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Abstract

Objective: To analyze the prognostic value of malnutrition in children with idiopathic dilated cardiomyopathy.

Methods: This is a retrospective study of 165 patients with idiopathic dilated cardiomyopathy, diagnosed from September 1979 to March 2003. It analyzed the following variables: gender, age, previous viral illness in the preceding 3 months, functional class according to the New York Heart Association (NYHA), evaluation of nutritional status (normal vs malnutrition), percentile and standard deviation (z index) of weight. Weight was measured 744 times during the first 72 months, 93 during the first month. Statistical analysis was performed by chi-squared, Student t test and analysis of variance for repeated measures (ANOVA). Ninety-five percent confidence intervals (CI95) and odds ratios (OR) were calculated. An alpha value of 0.05 and beta of 0.80 were used.

Results: Mean age at presentation was 2.2±3.2 years with higher incidence in those younger than 2 years (75.8%-CI95 = 68.5% to 82.1%) (p < 0.0001). NYHA classes III and IV were observed in 81.2% (CI95 = 74.4% to 86.9%) (p < 0.0001) and all 40 deaths were this group (p = 0.0008). At presentation, myocarditis occurred in 39.4% (CI95 = 31.9% to 47.3%) (p = 0.0001) and a high level of association between myocarditis and previous viral illness was observed (p = 0.0005) (OR = 3.15-CI95 = 1.55 to 6.44). Malnutrition at presentation did not influence death (p = 0.10), however progressive malnutrition was a marker for death (p = 0.02) (OR = 3.21-CI95 = 1.04 to 9.95). No significant differences weight percentiles (p = 0.15) or in z scores (p = 0.14) were observed. Observed mean weight percentiles (34.9±32.6 vs 8.6±16.0) (p < 0.0001) and z scores (-0.62±1.43 vs -2.02±1.12) (p < 0.0001) during the study period were greater among survivors. ANOVA demonstrated significant differences in weight percentile progression (p = 0.0417) and z scores (p = 0.0005) from the first month onwards.

Conclusion: The evaluation of nutritional status is easy to perform, it does not imply additional costs and should become routine for children with chronic heart failure.


Introduction

Heart failure (HF) can be defined as a clinical syndrome in which the heart is unable to adequately fulfill its pumping function and cannot supply enough oxygenated blood to meet demand necessary for normal tissue metabolism, including that necessary for growth and development.¹

Ventricular dysfunction may be caused by increased preload (severe stenosis of the aorta, coarctation of the aorta or chronic systemic arterial hypertension), by increased afterload (mitral insufficiency or left-right shunt as in intraventricular communication) or because of an intrinsic cardiac muscle injury (myocarditis or idiopathic dilated cardiomyopathy).² If we list the primary etiologies of childhood HF, congenital heart disease, rheumatic disease, arrhythmia, myocarditis and idiopathic dilated cardiomyopathy (IDCM) stand out.³

According to the World Health Organization, dilated cardiomyopathy is characterized by inadequate dilation and contraction of the left ventricle or of both ventricles,⁴

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and can be defined as idiopathic, familial or genetic, associated or not with an innate metabolic defect, viral and/or immunological, alcohol/toxin induced or associated with known cardiovascular diseases in which the degree of myocardial dysfunction cannot be explained by abnormal load conditions or by the extent of ischemic injury. Histology is non-specific. Presentation is normally by congestive heart failure, generally progressive. Arrhythmia, thromboembolism and sudden death are common and may occur at any stage of the disease.5-7

Within the pediatric group, IDCM is responsible for a large number of consultations and hospitalizations for HF not associated with congenital heart disease and, among under two-year-olds it is responsible for up to 29% of consultations.8 It results in a high mortality rate, with figures in published literature varying from 16%9 at 10 years to rates as high as 49%10 66%11 and even 80%12 at 5 years. For patients who progress badly with clinical treatment heart transplantation is the treatment of choice; global experience is currently exhibiting a survival curve of 75 to 80% at one year and 60 to 75 % at 5.13-15

Malnutrition is a serious complication of chronic diseases including cancer, the acquired immunodeficiency syndrome and chronic heart failure. Since as long ago as the era of Hippocrates (460-370 BC),16 it has been known that weight loss, weakness and little resistance to physical exercise, accompanied by muscular atrophy, is part of the presentation of HF. Doubt persists in relation to the significance of malnutrition as a marker and predictor of death from IDCM in childhood.

With the intention of defining the significance of malnutrition as a marker and predictor for death in IDCM, the sample was analyzed in terms of epidemiological characteristics, weight percentile and standard deviation for weight (z score) as predictors of progress..

**Patients and methods**

A retrospective study based on the Instituto Nacional de Cardiologia database, from which the medical records of 165 patients were extracted consecutively for posterior analysis. The patients had been diagnosed with IDCM between September 1979 and March 2003, aged from day to 15.4 years. Inclusion criteria were the presence of HF associated with cardiomegaly in chest teleradiography and/or left ventricle (LV) dilation with reduced contractility observed by echocardiogram. Patients with a clinical diagnosis of myocarditis were not excluded from the study. Clinical criteria used to indicate myocarditis were: fever, chest pains, electrocardiogram (ECG) showing low QRS complex voltage or conductive or rhythmic anomalies or abnormal findings from laboratory tests for creatine phosphokinase (CK) and its myocardial fraction (CKmb).8 Patients were excluded if they had congenital heart disease, anomalous origin of the coronary arteries, Kawasaki disease, arrhythmogenic right ventricular cardiomyopathy, ischemic injury from neonatal asphyxia or after cardiorespiratory resuscitation, primary arrhythmias, congenital valve defects or defects caused by rheumatic disease, neuromuscular diseases, arterial hypertension, septicemia, HIV infection, Chagas’ disease or diphtheria or if antineoplastic drugs had been used.

The variables analyzed were: sex, age and age group at onset (before 2 years vs. 2 years or older), previous history of viral illness during the 3 months preceding diagnosis and clinical myocarditis diagnosis. Patients were classified by functional class (FC) at onset according to the New York Heart Association (NYHA) criteria. These are: FC I – with no limitations to appropriate activity for age; FC II – comfortable at rest, but physical activity that is normal for age result in HF symptoms; FC III – comfortable at rest, but physical activity results in symptoms of HF and FC IV – HF symptoms, even at rest, any physical activity increases discomfort.17

Weight and nutritional status assessment. Weight was measured 817 times during the follow-up period (x = 4.95/patient); 744 weight measurements were taken during the first 72 months (x = 4.51/patient). Initial weight was defined as that obtained before the end of the first month of progress, during which period 73 children were weighed 93 times (x = 1.27/patient). The relationship between number of weight measurements per patient and the duration of follow-up was: 3 months = 1.27; 6 months = 1.61; 12 months = 1.48; 18 months = 1.56; 24 months = 1.85; 36 months = 1.52; 48 months = 1.44; 60 months = 1.33 and 72 months = 1.57. Weight percentiles and standard deviations for patient age and sex (z scores) were calculated using the EPINUT 2.0 anthropometry module of Epi-Info 6.04c by the CDC (Centers for Disease Control & Prevention). The diagnostic criteria for malnutrition were either weight below the 2nd standard deviation (SD or z < -2) or the fifth percentile. Weight percentiles and z scores were grouped at start (month zero) and at the 3rd, 6th, 12th, 18th, 24th, 36th 48th and 72nd months.

Classic pharmaceutical heart failure treatment was employed; consisting of oral digoxin, furosemide, spironolactone, captopril and acetylsalicylic acid (ASA) for thromboembolic event prevention. The objectives of this study do not include any analysis of the influence of treatment on patient progress.

Statistical analysis was performed using Epi-Info 6.04 by the CDC (Centers for Disease Control & Prevention) and Statistica 6.0 by Statsoft Inc. Dichotomous data was evaluated using the χ² (chi-square) test and odds ratios (OR) were calculated when applicable with their 95% confidence intervals (CI95). Descriptive data was expressed as mean±standard deviation (SD) and value bands, and was analyzed with the Student t test. Continuous time-dependent variables were evaluated with analysis of variance (ANOVA) for unbalanced repeated measures and were grouped by outcome (survival vs. death) and by time since onset. Alpha was set as 0.05 and power at 80%.

Ethical Factors: Authorization was obtained from the Commission for Ethics in Research at the Instituto Nacional de Cardiologia in Laranjeiras and the Universidade do Estado do Rio de Janeiro for information contained in medical record to be used in the study.
Results

General Characteristics

Mean age at onset was 26.2±38.9 months (0 to 188 months – median = 8.7 months, 25/75% quartiles = 4.6 and 22.8) or 2.1±3.2 years (0 to 15.4 years – median = 0.71 years, 25/75% quartiles = 0.39 and 1.9). Mean follow-up time for the sample was 42.7±50.6 (median = 24.4 months, 25/75% quartiles = 7.3 and 57.4) months or 3.55±4.21 (median = 2.03 years, 25/75% quartiles = 0.60 and 4.78) years. At the end of the study 85 (51.5%) patients continued under observation, 10 (6.1%) had received medical discharges, 40 (24.2%) had died and the hospital had lost contact with 30 (18.2%), amongst which last the mean follow-up period had been 27.5 (0.1 to 94.9) months.

With respect of disease onset, there was an observed preference for the before two years old group (125 – 75.8% - CI95 = 68.5% to 82.1%; x = 0.67±0.50 years) in comparison with the group of patients with onset after 2 years (40 – 24.2% - CI95 = 17.9% to 31.5%; x = 6.77±3.63 years) (p < 0.0001). There was no observed difference in terms of sex – females: 92 (55.8% - CI95 = 6.77–3.63 years) (p < 0.0001). There was no observed preference for the before two years old group (125 – 75.8%, CI95 = 68.5% to 82.1%; x = 0.67–0.50 years) vs. age group at diagnosis (p = 0.94). A majority of the patients (103 – 62.4% - CI95 = 54.6% to 69.8%) did not have viral disease prior to IDCM (p = 0.0018), although, when it was present, respiratory virosis was part of the primary condition (53 – 85.5% - CI95 = 74.3% to 95.2%), followed by gastrointestinal infection (9 – 14.5% - CI95 = 4.8% to 25.7%) (p < 0.0001). There was no difference observed in mortality (p = 0.16) between the two groups. Previous viral disease was more common among those less than 2 years old (51/62 – 82.3% - CI95 = 70.5% to 90.8%) (p < 0.0001) (OR = 21.50 – CI95 = 7.86 to 60.97), with mean age of those with a viral condition being from 1.97±3.16 years (median = 0.60 years, 25/75% quartiles = 0.34 and 1.68), for the whole sample and by age group 0.69±0.53 years (median = 0.55 years, 25/75% quartiles = 0.33 and 0.93) for the under-two group and 7.92±3.48 years (median = 6.07 years, 25/75% quartiles = 4.04 and 9.60) for those over two.

A clinical diagnosis of myocarditis was made at disease onset for 65 patients (39.4% - CI95 = 31.9% to 47.3% p = 0.0001) and its presence did not affect mortality (p = 0.35). The period since onset was not influenced by a diagnosis of myocarditis: myocarditis present = 39.37±45.86 months (0 to 162 months – median = 23.2 months, 25/75% quartiles = 5.1 and 54.1) vs. myocarditis absent = 44.84±53.54 months (0.23 to 241.5 months – median = 25.4 months, 25/75% quartiles = 9.7 and 58.8) (p = 0.4984). There was a strong association between myocarditis and previous viral disease (p = 0.0005) (OR = 3.15 – CI95 = 1.55 to 6.44). Accompanying fever not explained by associated infectious bacterial disease was present in 38.5% of the children with myocarditis (p = 0.0058) (OR = 2.66 – CI95 = 1.24 to 5.74).

The NYHA functional class criteria were used to evaluate initial clinical status severity. There were 13 (7.9%) patients at FC I, 18 (10.9%) at FC II, 36 (21.8%) at FC III and 98 (59.4%) at FC IV. The majority of the patients (134 – 81.2% - CI95 = 74.4% to 86.9%) were, therefore, severe cases (FC III and IV) (p < 0.0001). All deaths occurred among patients classed as FC III/IV at first presentation (p = 0.0005).

Weight and nutritional status

Malnutrition was either present at presentation or occurred during clinical course in 84 of the patients in the sample studied (50.9% - CI95 = 43.0% to 58.8%). At initial evaluation malnutrition was presented by 57/165 (34.5% - CI95 = 27.3% to 42.3%), of whom 19/57 died (33.3% - CI95 = 21.4% to 47.1%). Death occurred in 21/98 (21.4% - CI95 = 13.8% to 30.9%) (p = 0.10) of those cases that had not presented malnutrition initially. Malnutrition occurred during the course of the disease in 27/98 children (27.5% - CI95 = 19% to 37.5%), who had not initially exhibited malnutrition, of whom 10 (37% - CI95 = 19.4% to 57.6%) died. Eleven of the 71 cases that did not develop malnutrition resulted in death (15.5% - CI95 = 8% to 26%) (p = 0.02) (OR = 3.21 – CI95 = 1.04 to 9.95).

There was no significant difference in terms of initial weight percentile between the survivors (x = 29.4±29.7) and those that died (x = 19.9±24.9) (p = 0.15). The same was true of z scores; survival = -0.82±1.15 vs. death = -1.32±1.30 (p = 0.14).

During the first 72 months the mean weight percentile for the whole sample was 29.4±31.8 (0.0 to 99.8 – median = 15.5 – 25/75% quartiles = 2.9 and 50.2), exhibiting a significant difference between the two outcome groups (p < 0.0001); 34.9±32.6 for the survival group and 8.6±16.0 for the death outcome group. The analysis of variance of the sample divided for outcome revealed a significant difference in the progress of weight percentiles between the two groups (p = 0.0417). Figure 1 shows the progress of weight percentiles for the two groups and their respective 95% confidence intervals.

During the first 72 months the mean z score for weight for the whole sample was -0.91±1.48 (-5.1 to 6.16 – median = -1.01 – 25/75% quartiles = -1.90 and 0.01), exhibiting a significant difference between the two outcome groups (p < 0.0001); -0.62±1.43 for survivors and -2.02±1.12 for those that died. The analysis of variance of the sample divided for outcome revealed a significant difference in the progress of z scores for weight between the two groups (p = 0.0005). Figure 2 shows the progress of z scores for weight for the two groups and their respective 95% confidence intervals.

Discussion

Mean age at presentation was 2.1 years in this series18 which is similar to the majority of published reports.10,11,19-21 although some authors have found higher averages.9,12,22,23 In the sample studied here, disease onset exhibited a preference for the under two years age group (75.8%), rather than the age ≥ 2 years.
Previous viral disease was more frequent among those under 2 years old. It could be speculated that this preference is due to this age group’s greater susceptibility to viral respiratory disease, which had a mean onset age of 0.68±0.51 year. It could be postulated that the differences in average age at IDCM onset to be found in published data could be related to differences in incidence and prevalence of viral diseases resulting in differences in the incidence and prevalence of myocarditis.

Patients with a clinical diagnosis of myocarditis were included in the study bearing in mind that the cause of dilated cardiomyopathy remains unknown even among patients with microscopic evidence of inflammation of the myocardium. A clinical hypothesis of myocarditis was indicated in 39.4% of the patients in this series. No endomyocardial biopsies (EMB) were performed for myocarditis diagnosis because EMB involves certain risks, especially for infants; the sample may be removed from a health area; there is no specific treatment for myocarditis or IDCM currently available. Endomyocardial biopsies are being replaced with success by myocardial scintigraphy with gallium 67, which offers a high level of correlation with EMB without the risks inherent in it. Immunosuppressor treatment was not given to patients diagnosed with myocarditis, there is controversy in published literature over its efficacy.

Silva et al. found clinical criteria for myocarditis in 47.4% of their sample, confirming this by means of EMB in three children more than 2 years old. In series in which EMB was performed, a diagnosis of myocarditis was established in between 19.5% and 72.7%. There was no observed difference in mortality, which finding is identical to published observations, although Arola et al. found that, in a Finnish population, mortality was greater among those less than one year old with endocardial fibroelastosis and among male adolescents, while other authors have found elevated mortality among those older than two years.

There was no observed difference in incidence according to sex, which is in agreement with published data. Sex did not influence mortality in this series, which is in agreement with other authors.

Previous viral disease had been present in 37.6% of patients, with viral infection rates in published literature being between 4.8% and 54.2%. Taliercio et al. relate lower mortality among a group that presented prior virosis, an observation that has not been repeated in other series.

At the time of initial diagnosis, a majority (81.2%) of cases were considered severe (FC III and IV) and all deaths occurred in this group of patients. In a Polish study there was no difference in severity distribution (p = 0.0417) and in a Brazilian one there was a predominance of less serious cases, i.e. FC I and II. The age group at time of diagnosis did not affect mortality, which finding is identical to published observations, although Arola et al. found that, in a Finnish population, mortality was greater among those less than one year old with endocardial fibroelastosis and among male adolescents, while other authors have found elevated mortality among those older than two years.

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septal and posterior LV walls, and did not rule out the possibility that these findings were precursors of cardiomyopathy.

Cameron et al. assessed malnutrition in 160 children hospitalized with congenital heart disease for one year. They observed that acute malnutrition occurred in 33% and chronic in 64% of these children, although incidence, of both acute and chronic, increased to 70% for children with heart failure.

Anker et al. studied 171 adult patients aged 60±11 years and questioned the relationship between poor prognosis and wasting syndrome/cachexia. They compared ergometrically tested maximum O2 consumption (VO2 max.) (< 14 vs. ≥ 14 ml/kg/min) with FC (NYHA), serum sodium and ejection fraction evaluated by nuclear medicine, in addition to assessing weight loss of more than 7.5% of pre-disease weight. Twenty-eight patients (17.4%) were classed as having cachexia (loss of 9 to 36% ± 6.37 kg), characterized as being older patients with lower capacity for exercise and low serum sodium. The Cox method demonstrated that all these were predictive factors for death; with an 18-month survival rate for those with cachexia of 50%. When cachexia was associated with VO2 < 14 ml/kg/min, the survival rate was 23%, compared with 93% when neither factor was present. Fifty percent of those that died had cachexia.

Initial observed malnutrition was at 34.5% of the sample studied and malnutrition developed in 27.5% of patients. Malnutrition at onset did not affect death, but those children that developed malnutrition during the clinical course died in greater proportions with an OR of 3.21.

When initial weight percentile and z score for weight were analyzed no relationship was observed with death. The analysis of variance by death demonstrated significant differences between outcomes for: weight percentile – p = 0.0417 and z score for weight – p = 0.0005. A progressive increase in weight percentiles and z scores for weight was observed among surviving patients allowing patients who ought to survive to be separated at one month after diagnosis from those who run the risk of dying, using a 95% confidence interval

Mechanisms that could possibly cause malnutrition in IDCM are: malabsorption of nutrients because of intestinal edema; dietary deficiency and loss of nutrients via urinary and gastrointestinal losses. Digoxin provokes nausea in elevated doses and its levels should be carefully monitored in serum. It has been demonstrated in adults that a thiamin deficiency occurs with patients suffering from IDCM, possibly resulting from the use of loop diuretics (furosemide), since selenium and copper levels do not exhibit differences between groups. In the therapeutic follow-up of patients with IDCM, nutritional support with protein and vitamin supplementation is fundamental, especially thiamin since a deficiency worsens HF by mechanisms that are similar to what happens in beriberi.

Nutritional status evaluation is easily performed without a routine part of the follow-up of patients with chronic heart failure.

References


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