Myocardial Performance Index Combining Systolic and Diastolic Myocardial Performance in Doxorubicin-Treated Patients and Its Correlation to Conventional Echo/Doppler Indices

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Abstract. This study was designed to evaluate the utility of myocardial performance index (MPI) in anthracycline cardiotoxicity. The MPI measures the ratio of total time spent in isovolumic activity (isovolumetric contraction time and isovolumetric relaxation time) to the ejection time, thus giving a global index combining systolic and diastolic myocardial performance. In this study, MPI was measured in 35 doxorubicin-treated children (aged 108.5 ± 55.31 months, 23 males and 12 females) in sinus rhythm and 32 age-matched controls, and it was compared with conventional Doppler echocardiographic parameters. The isovolumetric contraction time was prolonged (38.37 ± 24.43 vs 26.37 ± 15.53, p < 0.02) and ejection time was shortened (231.91 ± 28.87 vs 256.21 ± 19.55, p < 0.001) in doxorubicin-treated patients compared to that in normal children. The isovolumetric relaxation time did not show significant difference between patients and control group (60.11 ± 10.92 vs 61.06 ± 12.12, p > 0.05). MPI was significantly increased in doxorubicin-treated patients compared with that in control groups (0.42 ± 0.07 vs 0.34 ± 0.06, p < 0.001), and significant correlation was observed between MPI and fractional shortening, ejection fraction, and left ventricular end diastolic and end systolic diameters (respectively, r = −0.508, p < 0.002; r = −0.532, p < 0.001; r = 0.467 p < 0.005; r = 0.606, p < 0.001). Also, a weak correlation was found between MPI and duration of the disease and patient ages (r = 0.393, p < 0.02; r = 0.379; p < 0.02). However, there was no correlation between MPI and cumulative doxorubicin dose (r = 0.311, p > 0.05) and diastolic Doppler parameters in doxorubicin-treated patients. We think that MPI may be a useful parameter in monitoring left ventricular dysfunction in anthracycline-treated patients.

Key words: Myocardial performance index — Anthracycline cardiotoxicity

Doxorubicin is an anthracycline antibiotic agent that is effective in the treatment of various solid tumors and hematologic malignancies. Unfortunately, its use is also associated with irreversible myocardial damage, the severity of which is proportional to the cumulative dose received [15]. Furthermore, because of marked individual variations in cardiotoxicity, there is a compelling need for a reliable and safe method for the early detection and monitoring of this cardiotoxicity [13].

Until recently, echocardiographic studies on doxorubicin cardiotoxicity were mainly focused on the systolic and diastolic function evaluation [13].

Recently, an easily measured index of myocardial performance, combining systolic and diastolic time intervals, was proposed [19]. This index has been reported to be simple, reproducible, and independent of heart rate and blood pressure and to correlate with severity of clinical congestive heart failure in patients with dilated cardiomyopathy [22]. The purpose of this study was to evaluate whether doxorubicin can alter left ventricular myocardial performance index (MPI) and to analyze how the MPI correlates with other echocardiographic systolic and diastolic function parameters.

Methods

The study group was selected from a cohort of patients admitted to the oncology department of our hospital for a treatment protocol that included doxorubicin. Most patients received the drug as intravenous infusion for 2 hours every 3 or 4 weeks. All patients were given doxorubicin in combination with cyclophosphamide, cisplatin, vinblastine, or vincristine. None of the patients we studied had received mediastinal irradiation or had overt cardiomyopathy. The site or etiology of primary neoplasm was lymphoma in 11 patients,
acute leukemia in 7, Hodgkin’s disease in 2, Wilms’ tumor in 5, osteosarcoma in 3, neuroblastoma in 2, rhabdomyosarcoma in 3, and Ewing’s sarcoma in 2. The study group consisted of 35 children (23 males and 12 females, mean age 108.5 ± 55.31 months). They had received a mean cumulative dose of 219.9 ± 144.37 mg/m² of body surface area of doxorubicin. Six patients had also received cerubidine (mean cumulative dose 208.0 ± 102.96 mg/m²). The mean duration of treatment was 11.6 ± 10.56 months. Each patient underwent echocardiographic examination once during doxorubicin treatment. No baseline study was performed. The results were compared with those in a control group of 32 healthy children matched for age (20 males and 12 females, mean age 106.6 ± 40.35 months).

We excluded patients with mitral regurgitation, systemic hypertension, cardiac disease, and significant anemia (hemoglobin level < 10 gr/dl). All patients were in a clinically stable condition at the time of the echocardiographic examinations and none developed clinical cardiac failure. The study was approved by the ethical committee of our hospital and informed consent was obtained from parents.

Echocardiographic examination was performed during the doxorubicin treatment protocol, immediately before the next intravenous bolus of doxorubicin. Two-dimensional, M-mode, and Doppler echocardiographic examination were performed to determine left ventricular systolic functions. Images were obtained on a HP SONOS 1000 echocardiogram with 3.5/2.7-MHz and 5.0/7.5-MHz transducer. Recordings were done with the subject in the supine position and breathing freely. M-mode tracings were obtained at the level of the tips of the mitral leaflets in the parasternal long-axis position and measurements were performed according to the American Society of Echocardiography recommendations [16]. We obtained interventricular septal thickness in diastole, interventricular septal thickness in systole (IVSs), left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), left ventricle posterior wall thickness in diastole, left ventricle posterior wall thickness in systole, and R-R interval. Left ventricular end diastolic volume, left ventricular end systolic volume, ejection fraction (EF), fractional shortening (FS), stroke volume, and cardiac output were calculated from these data using Teicholz’s method digitally and left ventricular mass was determined using Penn’s formula [6].

Pulsed Doppler was used to investigate left ventricular transmirtal flow by placing the Doppler cursor line parallel to flow and the sample volume between the tips of the mitral valve leaflets. The following variables were analyzed: the early peak velocity of mitral inflow (peak E), the late peak of mitral inflow (peak A), and the deceleration time of peak E velocity. Pulsed Doppler was also used to investigate pulmonary vein systolic and diastolic flow velocity and pulmonary vein a time of regurgitant flow [14]. Doppler signals were analyzed from three cardiac cycles to calculate a mean value for each variable. Isovolumic relaxation time was measured with the probe at the apical five-chamber position and the sample volume placed between the aorta and the mitral valve, where the recordings of both valves were taken simultaneously. The left ventricular outflow velocity pattern was recorded from the apical long-axis view with the pulsed-wave Doppler sample volume positioned just below the aortic valve. M-mode and Doppler tracing were recorded at a paper speed of 50 or 100 mm/sec. Doppler time intervals were measured from inflow and left ventricular outflow velocity time intervals. The interval a from the cessation to the onset of mitral inflow is equal to the sum of isovolumetric contraction time, ejection time, and isovolumetric relaxation time. Left ventricular ejection time b is the duration of left ventricular outflow velocity profile. The index of combined left ventricular systolic and diastolic function (the sum of isovolumetric contraction time and isovolumetric relaxation time divided by ejection time) was calculated as (a – b)/b (Fig. 1) [9, 22].

Data were expressed as mean ± standard deviation. Statistical analysis was performed using the Student’s t-test and correlation coefficient. Significance was established at p < 0.05.

Results

Some clinical characteristics and Doppler time intervals of the patients and control group are shown in Table 1, and echocardiographic and Doppler parameters are summarized in Table 2. Ejection fraction and fractional shortening were significantly decreased in the patient group compared with the those in normal children (61 ± 6.12 vs 68 ± 3.62, p < 0.001; 32 ± 4.32 vs 37 ± 2.91, p < 0.001), whereas left ventricular mass was significantly increased (71.43 ± 14.02 vs 63.66 ± 12.90, p < 0.02). The isovolumetric contraction time was significantly prolonged (38.37 ± 24.43 vs 26.37 ± 15.53, p < 0.02), whereas ejection time was significantly shortened (231.91 ± 28.87 vs 256.21 ± 19.55, p < 0.001) in the doxorubicin-treated patients compared with that in the control group. However, isovolumetric relaxation time was not different in the two groups (60.11 ± 10.92 vs 61.06 ± 12.12, p < 0.05). Thus, MPI combining these variables was significantly different in doxorubicin-treated patients and the control group (0.42 ± 0.07 vs 0.34 ± 0.06, p < 0.001). No significant correlation was observed in this study between the dose of doxorubicin and the extent of abnormalities in the Doppler echocardiographic parameters. Table 3 shows the correlation between MPI and echocardiographic/Doppler variables in the doxorubicin-treated patients. A significant correlation was observed between MPI and fractional shortening, ejection fraction, and left ventricular end diastolic and end