Introduction

Most of the clinical studies concerning anthracycline cardiotoxicity have investigated ‘late onset cardiotoxicity’ and focused on particularly the left ventricular systolic functions.

We aimed in this study to assess ‘early onset chronic progressive anthracycline cardiotoxicity’ in the left and right ventricular segments using tissue Doppler imaging (TDI) with increasing cumulative anthracycline doses.

Results

72 patients (38 girls, 34 boys) and 31 controls (18 girls, 13 boys) were enrolled in this study. The mean age was 8.2±4.5 years in patient group and 9.6±4.2 years in the control group (p=0.05).

While 31 of the patients (43%) were enrolled in the study before the first anthracycline dose and evaluated after each doxorubicin/dauorubicin treatment (newly diagnosed patients); 13 patients (18%) were enrolled when their chemotherapy was ongoing and 28 patients (39%) were enrolled when they had received the last anthracycline dose within one year.

Each echocardiographic data of the patients were classified into the treatment groups according to the instant cumulative anthracycline dose when they were examined as described above. Thus, while 46 patients took part in only one TG, 19 patients were included in two groups and 7 patients were included in three groups.

Consequently, distribution of the groups were as following: 31 healthy children in ‘control group’, 26 patients in ‘TG-I’, 39 patients in ‘TG-II’ and 40 patients in ‘TG-III’.

The comparison of control and TG-I groups revealed significant decreases in E’ velocities in tricuspid valve lateral annulus and right ventricular lateral wall segments (p<0.001 and p<0.05, respectively) and these findings continued in TG-II and III.

S’ velocity decreased in TG-I, II, and III at lateral mitral annulus. However, decrease in EF were statistically significant after TG-III (p<0.001).

While MPI was significantly increased in all treatment groups in both segments, it was primarily due to significant increases in IVRT at lateral tricuspid annulus and IVCT at lateral mitral annulus (Table 1).

Abnormalities in diastolic function in right ventricle and systolic function in left ventricle were observed even with a cumulative anthracycline dose of less than 120 mg/m² by TDI.

Conclusions

This study has shown us that children receiving cancer treatment have a significant risk for cardiac injury within the first year of anthracycline treatment.

We have demonstrated that TDI is superior to standard echocardiographic methods to detect subtle impairment in both systolic and diastolic functions.

Furthermore, while right ventricle is under increased risk of diastolic dysfunction even in a cumulative dose of less than 120 mg/m², left ventricle tends to lose systolic function that can be detected earlier by TDI.

Finally, all patients should be monitored carefully for late-onset cardiomyopathy because of the risk to develop further LV dysfunction with or without additional anthracycline doses.

Methods

The patient group included the patients who had been received doxorubicin and/or daunorubicin within a time period of between one week and one year when they were examined (mean 2.6±2.9 months, range: 0-31.15 months).

During TDI studies, apical 4-chamber view were obtained and diastolic and systolic parameters were measured at four different segments (lateral annulus of the mitral valve, middle part of left ventricular lateral wall, lateral annulus of the tricuspid valve and right ventricular lateral wall).

However, because of high amount of data and limited space in the poster page, we presented echocardiographic parameters from only two segments (lateral annulus of the mitral and tricuspid valves ) in Table 1.

The echocardiographic data of all examinations of 72 patients were classified into three groups according to instant cumulative anthracycline doses:

- Treatment group (TG-I) (< 120 mg/m²; n=26),
- TG-II (120-240 mg/m²; n=39),
- TG-III (> 240 mg/m²; n=40).

Standard echocardiographic and TDI parameters of the patients were compared with healthy controls.

Table 1

<table>
<thead>
<tr>
<th>Control</th>
<th>TG-I (&lt;120 mg/m²)</th>
<th>TG-II (120-240 mg/m²)</th>
<th>TG-III (&gt;240 mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF (%)</td>
<td>63.4±3.4</td>
<td>52.8±5.4</td>
<td>51.2±5.9</td>
</tr>
<tr>
<td>A' (cm/s)</td>
<td>2.6±0.3</td>
<td>2.0±0.3</td>
<td>1.8±0.5</td>
</tr>
<tr>
<td>E'/A'</td>
<td>1.4±0.5</td>
<td>1.2±0.5</td>
<td>1.0±0.5</td>
</tr>
<tr>
<td>DT (ms)</td>
<td>50.7±7.6</td>
<td>51.9±7.3</td>
<td>51.2±7.3</td>
</tr>
<tr>
<td>IVRT (ms)</td>
<td>6.2±1.1</td>
<td>5.8±1.1</td>
<td>5.5±1.1</td>
</tr>
<tr>
<td>MPI</td>
<td>0.37±0.05</td>
<td>0.41±0.05</td>
<td>0.41±0.07</td>
</tr>
</tbody>
</table>

> Tissue Doppler Imaging, TG treatment groups, EF ejection fraction, DT early diastolic Doppler peak flow velocity, A' early systolic Doppler peak flow velocity, E'/A' early-systolic to late-diastolic Doppler peak flow velocity ratio, DT duration of the isovolumic relaxation time, MPI Myocardial performance index, NS not significant.