Cardiovascular abnormalities in patients with Turner syndrome according to karyotype

Own experience and literature review

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ABSTRACT

BACKGROUND  Cardiovascular diseases account for a threefold higher mortality in women with Turner syndrome (TS). It has also been suggested that the occurrence of these diseases is dependent on karyotype.

OBJECTIVES  To assess the cardiovascular system by clinical examination, echocardiography and electrocardiography in female patients with TS, depending on karyotype.

PATIENTS AND METHODS  Thirty-four women with TS, aged 7–58 (35.2 ±14.6) years, were evaluated. The patients were categorized into 3 groups according to karyotype: group 1 comprised 12 patients with monosomy X (45,X), group 2 comprised 19 women with mosaicism, and group 3 comprised 3 patients with structural aberrations of X chromosome. Echocardiography was performed using the Sonos 5500 machine, following the current standards.

RESULTS  Congenital cardiovascular malformations were detected in 21% of TS women. Valvular heart disease was present in 50% of the entire study population, including aortic valve diseases in 24% and mitral valve diseases in 21%. The patients with mosaicism, more often than those with monosomy X, were overweight and had a tendency to higher incidence of hypertension, as well as thicker interventricular septum, and larger left ventricular mass on echocardiography.

CONCLUSIONS  Congenital cardiovascular malformations are more common in TS patients compared to the general population. There were no differences in risk factors and cardiovascular abnormalities between various karyotypes except for higher incidence of overweight and tendency to higher blood pressure, thicker interventricular septum, and larger left ventricular mass observed in patients with mosaicism compared to those with monosomy X.

KEY WORDS  cardiovascular abnormalities, echocardiography, electrocardiography, karyotype, Turner syndrome

INTRODUCTION  At present, Turner syndrome (TS) (first descriptions by Ullrich in 1930¹ and Turner in 1938²; determination of etiology by Ford et al. in 1959³) is defined as a congenital disease caused by structural and/or functional aberrations of X chromosome⁴. It is characterized by short stature, gonadal dysgenesis, specific morphological phenotype (TS stigmata), inherited defects in internal organs, e.g. the bone, cardiovascular and urinary systems, as well as the unique phenotype of development and behavior.

Cardiovascular abnormalities in TS patients involve structural defects of the heart and large vessels along with the consequences of the presence of several cardiovascular risk factors including arterial hypertension, hyperlipidemia, obesity, and diabetes mellitus⁵,⁶. Congenital malformations are frequently observed in TS women (17–56% vs. ~2% in the general population).⁷,⁸ About threefold increase in mortality among patients with TS may result from cardiovascular complications, including fatal aortic dissection, ischemic heart disease...
(myocardial infarction), and stroke. Some authors have reported associations between phenotype and karyotype patterns in these individuals.10-13

The aim of our study was to assess the cardiovascular system by clinical examination, echocardiography and electrocardiography (ECG) in 34 patients with TS, depending on karyotypes.

**PATIENTS AND METHODS** Thirty-four women with TS, aged 7–58 years (mean ±SD, 35.2 ±14.6; median, 29 years) were recruited to the study from the Great Poland (Wielkopolska) branch of Turner Syndrome Support Society. Heart tests were performed in a cardiology outpatient clinic in patients who gave informed consent.

Patients were categorized into 3 groups according to karyotype. Group 1 comprised 12 women with classic X chromosome monosomy (45,X), aged 7–57 years (mean ±SD, 29.3 ±16.1; median, 24 years). Group 2 included 19 patients with mosaic karyotype, aged 24–58 years (40.5 ±12.8; median: 43 years). Finally, group 3 included 3 women with structural X chromosome aberrations (short or long X arm deletion), aged 23–28 years (26.0 ±2.6; median, 27 years). In patients with mosaicism, monosomy was accompanied by cellular line with normal female karyotype, isochromosome Xq, ring X chromosome, Y chromosome or trisomy X.

The study was approved by the local Ethical Committee. The patients gave informed consent and their anonymity was preserved.

At the time of examination, 32 women were receiving estrogen-progesterone replacement therapy, and 1 patient (26-years old) menstruated spontaneously. One patient had taken growth hormone therapy at the age of 7. Three more patients received growth hormone treatment in the past.

**TABLE 1** Age, height, weight, body mass index, congenital cardiovascular malformations, valvular heart disease, ischemic heart disease, and some coronary risk factors in Turner syndrome according to karyotype

<table>
<thead>
<tr>
<th></th>
<th>Group 1 monosomy n = 12</th>
<th>Group 2 mosaicism n = 19</th>
<th>Group 3 structural aberrations n = 3</th>
<th>Total n = 34</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (years), x ±SD</td>
<td>29.3 ±16.1</td>
<td>40.5 ±12.8a</td>
<td>26.0 ±2.6</td>
<td>35.2 ±14.6</td>
</tr>
<tr>
<td>height (cm), x ±SD</td>
<td>146.3 ±8.9</td>
<td>148.2 ±7.9</td>
<td>143.7 ±6.7</td>
<td>147.1 ±8.1</td>
</tr>
<tr>
<td>weight (kg), x ±SD</td>
<td>52.3 ±10.4</td>
<td>57.3 ±9.0</td>
<td>58.7 ±14.4</td>
<td>55.6 ±10.0</td>
</tr>
<tr>
<td>BMI (kg/m²), x ±SD</td>
<td>25.1 ±4.4</td>
<td>26.6 ±3.7</td>
<td>28.3 ±4.9</td>
<td>26.2 ±4.1</td>
</tr>
<tr>
<td>BMI &gt;25 ≤30 kg/m², n (%)</td>
<td>1 (8)</td>
<td>10 (53)a</td>
<td>1</td>
<td>12 (35)</td>
</tr>
<tr>
<td>BMI &gt;30 kg/m², n (%)</td>
<td>3 (24)</td>
<td>2 (11)</td>
<td>1</td>
<td>6 (18)</td>
</tr>
<tr>
<td>congenital cardiovascular malformations</td>
<td>4 (33)</td>
<td>2 (11)</td>
<td>1</td>
<td>7 (21)</td>
</tr>
<tr>
<td>bicuspid aortic valve, n (%)</td>
<td>2 (17)</td>
<td>–</td>
<td>–</td>
<td>2 (6)</td>
</tr>
<tr>
<td>VSD perimembranous, n (%)</td>
<td>–</td>
<td>1 (5)</td>
<td>1</td>
<td>2 (6)</td>
</tr>
<tr>
<td>aortic coarctation, n (%)</td>
<td>1 (8)</td>
<td>–</td>
<td>–</td>
<td>1 (3)</td>
</tr>
<tr>
<td>patent ductus arteriosus, n (%)</td>
<td>–</td>
<td>1 (5)</td>
<td>–</td>
<td>1 (3)</td>
</tr>
<tr>
<td>dilatation of the aorta, n (%)</td>
<td>1 (8)</td>
<td>–</td>
<td>–</td>
<td>1 (3)</td>
</tr>
<tr>
<td>valvular heart disease</td>
<td>8 (67)</td>
<td>7 (37)</td>
<td>2</td>
<td>17 (50)</td>
</tr>
<tr>
<td>mitral regurgitation, n (%)</td>
<td>2 (17)</td>
<td>3 (16)</td>
<td>1</td>
<td>6 (18)</td>
</tr>
<tr>
<td>aortic stenosis, n (%)</td>
<td>1 (8)</td>
<td>1 (5)</td>
<td>–</td>
<td>2 (6)</td>
</tr>
<tr>
<td>aortic regurgitation, n (%)</td>
<td>2 (17)</td>
<td>1 (5)</td>
<td>1</td>
<td>4 (12)</td>
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<tr>
<td>tricuspid regurgitation, n (%)</td>
<td>1 (8)</td>
<td>2 (11)</td>
<td>–</td>
<td>3 (9)</td>
</tr>
<tr>
<td>mitral prolapse, n (%)</td>
<td>1 (8)</td>
<td>–</td>
<td>–</td>
<td>1 (3)</td>
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<tr>
<td>tricuspid prolapse, n (%)</td>
<td>1 (8)</td>
<td>–</td>
<td>–</td>
<td>1 (3)</td>
</tr>
<tr>
<td>ischemic heart disease</td>
<td>–</td>
<td>3 (16)</td>
<td>–</td>
<td>3 (9)</td>
</tr>
<tr>
<td>angina pectoris, n (%)</td>
<td>–</td>
<td>2 (11)</td>
<td>–</td>
<td>2 (6)</td>
</tr>
<tr>
<td>previous MI, n (%)</td>
<td>–</td>
<td>1 (5)</td>
<td>–</td>
<td>1 (3)</td>
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<tr>
<td>selected coronary risk factors</td>
<td></td>
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<tr>
<td>hypercholesterolemia, n (%)</td>
<td>8 (67)</td>
<td>10 (53)</td>
<td>–</td>
<td>18 (53)</td>
</tr>
<tr>
<td>arterial hypertension, n (%)</td>
<td>3 (25)</td>
<td>9 (47)b</td>
<td>–</td>
<td>12 (35)</td>
</tr>
<tr>
<td>type 2 diabetes mellitus, n (%)</td>
<td>–</td>
<td>2 (11)</td>
<td>–</td>
<td>2 (6)</td>
</tr>
<tr>
<td>obesity</td>
<td>3 (24)</td>
<td>2 (11)</td>
<td>1</td>
<td>6 (18)</td>
</tr>
</tbody>
</table>

a p <0.05 vs. group 1, b p = 0.19 vs. group 1

Abbreviations: BMI – body mass index, MI – myocardial infarction, SD – standard deviation, VSD – ventricular septal defect
RESULTS

Age, height, weight, BMI, congenital cardiovascular malformations, valvular heart disease, ischemic heart disease, and selected coronary risk factors of the study population and of the karyotype subgroups are presented in Table 1. Cardiovascular abnormalities and selected risk factors in the entire study population, arranged according to the frequency of occurrence, are presented in the figure.

Congenital cardiovascular malformations (bicuspid aortic valve, ventricular septal defect perimembranous, aortic coarctation, patent ductus arteriosus, VSD – ventricular septal defect

All patients underwent clinical examination. Body weight and height were measured, and body mass index (BMI) was calculated as body weight divided by height squared (kg/m²). Arterial blood pressure measurements with mercury sphygmomanometer were taken repeatedly. Serum total cholesterol level was measured. Echocardiography, including M-mode, two-dimensional (2D), classical and color Doppler techniques, was performed using Sonos 5500 apparatus following current standards. The resting standard ECG was also done.

The karyotype was determined from peripheral blood lymphocytes. The preliminary analysis of metaphase chromosomes was followed by the analysis of prometaphase chromosomes using banding techniques (Q-bands by fluorescence using quinacrine, R-bands by bromodeoxyuridine (BrdU) using Giemsa, C-bands by barium hydroxide using Giemsa) and immunocytochemical detection BrdU. In selected cases, hybridization in situ and fluorescence in situ hybridization (FISH) were performed using biotin-labeled probes specific for Y chromosome and immunocytochemical reaction for probe detection at the hybridization site (Wojda et al.).

Statistical analysis

Statistical analysis was performed using Statistica 7.1 program (StatSoft Inc.). Data for the whole study population and separate groups were presented as numbers, percentages, means, medians, and standard deviations as appropriate. Differences between percentage values for the study subgroups were tested with exact Fisher’s test, whereas those between means for separate groups were calculated with Student’s t test. A p-value <0.05 (two-sided test) was considered statistically significant.
various valvular heart diseases coexisted: mitral and aortic regurgitation (1 patient), mitral and tricuspid regurgitation (1 patient), tricuspid prolapse and regurgitation (1 patient), and aortic stenosis plus aortic, mitral, and tricuspid regurgitation (1 patient).

No significant differences were observed between the study groups regarding the incidence of congenital and valvular heart diseases.

Women from group 2 (with mosaicism) were significantly older and had more frequently BMI 25–30 kg/m² than group 1 (with monosomy) (p <0.05). Arterial hypertension was observed in 47% of women with mosaicism and in 25% with monosomy (p = 0.19). One case of myocardial infarction and 2 cases of angina pectoris were noted in group 2. Hypercholesterolemia, type 2 diabetes mellitus, and obesity were demonstrated with similar frequency in groups 1 and 2.

Echocardiography revealed a tendency to thicker interventricular septum (p = 0.06) and larger left ventricular mass (p = 0.14) in group 2 compared to group 1 (Table 2). The differences between the study groups regarding the dimensions of the left and right ventricles, left atrium and aortic ring, and left ventricular posterior wall thickness were nonsignificant (Table 2).

Changes in ECG were found in 62% of all study subjects (Table 3). Inverse T waves (18%), ST segment depression (15%), and right bundle branch block (12%) were most commonly observed. The incidence of ECG changes was similar in groups 1 and 2 (66 and 68%, respectively).

**DISCUSSION**

Out of internal organ abnormalities and concomitant diseases, cardiovascular changes are major causes of higher mortality among women with TS in comparison with the general population.15 In a large study by Sybert, conducted in women aged 0–80 years (mean: 18.4 ±13.7), cardiovascular abnormalities, including structural ones, hypertension, mitral valve prolapse, and conduction defects, were detected in 136 of 244 (56%) TS patients.7 Volkl et al. demonstrated that about every third female patient in Bavaria was affected by at least one structural cardiovascular anomaly.16

In our paper, congenital cardiovascular malformations were found in 21% of patients with TS. Bicuspid aortic valve and aorta defects (coarctation

### Table 2

<table>
<thead>
<tr>
<th>Echocardiographic parameters (2D image)</th>
<th>Group 1 monosity (n = 12)</th>
<th>Group 2 mosaicism (n = 19)</th>
<th>Group 3 structural aberrations (n = 3)</th>
<th>Total (n = 34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDD/mm² (mm²/m²), x ±SD</td>
<td>33.4 ± 4.8</td>
<td>33.4 ± 4.3</td>
<td>33.1 ± 3.4</td>
<td>33.4 ± 4.3</td>
</tr>
<tr>
<td>LA/mm² (mm²/m²), x ±SD</td>
<td>21.7 ± 3.4</td>
<td>22.2 ± 2.2</td>
<td>24.4 ± 0.5</td>
<td>22.2 ± 2.6</td>
</tr>
<tr>
<td>RV/mm² (mm²/m²), x ±SD</td>
<td>20.0 ± 4.0</td>
<td>21.0 ± 2.6</td>
<td>23.3 ± 2.9</td>
<td>20.8 ± 3.2</td>
</tr>
<tr>
<td>Ao/mm² (mm²/m²), x ±SD</td>
<td>14.4 ± 1.6</td>
<td>13.9 ± 2.1</td>
<td>16.2 ± 4.2</td>
<td>14.3 ± 2.2</td>
</tr>
<tr>
<td>IVS/mm² (mm²/m²), x ±SD</td>
<td>6.0 ± 0.9</td>
<td>6.6 ± 1.3²</td>
<td>5.4 ± 0.8</td>
<td>6.1 ± 1.2</td>
</tr>
<tr>
<td>TSLV/mm² (mm²/m²), x ±SD</td>
<td>5.4 ± 0.8</td>
<td>5.4 ± 1.2</td>
<td>6.2 ± 1.1</td>
<td>5.4 ± 1.1</td>
</tr>
<tr>
<td>LV mass/m² (g/m²), x ±SD</td>
<td>86.5 ± 20.9</td>
<td>103.4 ± 34.5²</td>
<td>90.6 ± 8.1</td>
<td>96.2 ± 29.1</td>
</tr>
</tbody>
</table>

* a p = 0.06 vs. group 1, b p = 0.14 vs. group 1

**Abbreviations:** Ao – aortic ring dimension, IVS – interventricular septum thickness, LA – left atrial dimension, LV – left ventricular, LVEDD – left ventricular end-diastolic diameter, RV – right ventricular dimension, SD – standard deviation, TSLV – left ventricular posterior wall thickness, 2D – two-dimensional

### Table 3

<table>
<thead>
<tr>
<th>Electrocardiographic changes</th>
<th>Group 1 monosity (n = 12)</th>
<th>Group 2 mosaicism (n = 19)</th>
<th>Group 3 structural aberrations (n = 3)</th>
<th>Total (n = 34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBBB, n (%)</td>
<td>1 (8)</td>
<td>3 (16)</td>
<td>–</td>
<td>4 (12)</td>
</tr>
<tr>
<td>LGL syndrome, n (%)</td>
<td>1 (8)</td>
<td>–</td>
<td>–</td>
<td>1 (3)</td>
</tr>
<tr>
<td>dextrogram, n (%)</td>
<td>1 (8)</td>
<td>–</td>
<td>–</td>
<td>1 (3)</td>
</tr>
<tr>
<td>LAH, n (%)</td>
<td>–</td>
<td>1 (5)</td>
<td>–</td>
<td>1 (3)</td>
</tr>
<tr>
<td>QS waves, n (%)</td>
<td>–</td>
<td>1 (5)</td>
<td>–</td>
<td>1 (3)</td>
</tr>
<tr>
<td>T wave inversion, n (%)</td>
<td>2 (17)</td>
<td>4 (21)</td>
<td>–</td>
<td>6 (18)</td>
</tr>
<tr>
<td>ST segment depression, n (%)</td>
<td>3 (25)</td>
<td>2 (11)</td>
<td>–</td>
<td>5 (15)</td>
</tr>
<tr>
<td>RV hypertrophy, n (%)</td>
<td>–</td>
<td>1 (5)</td>
<td>–</td>
<td>1 (3)</td>
</tr>
<tr>
<td>non-sustained VT, n (%)</td>
<td>–</td>
<td>1 (5)</td>
<td>–</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>

* Abbreviations: LAH – left anterior hemiblock, LGL – Lown-Ganong-Levine syndrome, RBBB – right bundle branch block, RV – right ventricular, VT – ventricular tachycardia
and dilatation) were most commonly detected. According to the data cited in this paper, congenital heart malformations are observed in 17–56% of TS patients compared to ~2% of the general population. Aortic valve disease (30–50% of heart malformations, presumably bicuspid aortic valve) and aortic coarctation (35%) are most commonly detected.\textsuperscript{1,17} Dilatation of the aortic root is rare (~5% of congenital abnormalities), but it is potentially dangerous – its perforation may lead to death.\textsuperscript{18} The risk of aortic dissection appears to be mainly a consequence of structural and hemodynamic abnormalities in the cardiovascular system (aortic coarctation, bicuspid aortic valve, arterial hypertension) rather than of abnormality in a connective tissue.\textsuperscript{7}

In our study we found cases of aortic coarctation and bicuspid aortic valve less often than in the available data. This may result from a small number of the study group rather than the smaller percentage of women with monosomy in our paper (35%) compared to the data based on classic genetic methods (>50%). However, recent investigations, which have employed molecular biology techniques, show lower incidence of monosomy (<50%).

According to Gravholt, there are differences in the appearance of congenital cardiovascular defects in TS depending on karyotype: defects were present in 30–39% of the patients with X chromosome monosomy, in 24% with mosaicism, and in 11–12% with structural aberrations.\textsuperscript{19,21} In a study by Landin-Wilhelmsen et al., the rate of monosomy X (45,X) was markedly higher (88%) in patients with congenital malformations.\textsuperscript{8} Most congenital defects were also found in patients with karyotype 45,X by Giano and et al. and Goetsche.\textsuperscript{22,23} As in other papers, congenital abnormalities correlated with karyotype.\textsuperscript{11-13}

In our study, no statistical differences between congenital cardiovascular malformations by a karyotype were observed. They were detected in 33%, 10% and in 1 of 3 patients with monosomy, mosaicism and structural aberrations, respectively. After the study by Sybert, there have been insufficient data to allow to draw any conclusions on phenotype-karyotype correlations in terms of congenital cardiovascular abnormalities in TS, because of a small number of individuals with less common karyotypes (too small for a meaningful analysis).\textsuperscript{7} We found only 3 cases of TS with structural aberrations of X chromosome. Other authors did not demonstrate any correlations between karyotype and congenital defects of different internal organs, including cardiovascular abnormalities (bicuspid aortic valve, aortic coarctation).\textsuperscript{24}

According to the available data, aortic coarctation is detected in 4–14% of TS women. It occurs more often in patients with monosomy X.\textsuperscript{19} Lymphatic circulation disturbances in the fetal period are regarded as one of the causes of aortic coarctation. They manifest as generalized edema in the fetal period or edema of feet and hands at birth. This anomaly may lead to aortic dilatation and dissection as well as to the rupture of an aortic aneurysm. The loss of p1.4–21.1 region, with localization of a putative lymphogenic gene, predisposes circulatory and lymphatic system defects, e.g. webbed neck.\textsuperscript{25,24} In our investigation, aortic coarctation was detected in 1 woman (3%), who underwent surgery at the age of 2. Arterial hypertension was not observed in this patient, although it occurs even after a successful operation.

Dilatation, aneurysm, and dissection of the aorta occur in 3–8% of TS patients.\textsuperscript{5} Elsheikh et al. reported dilatation of the ascending aorta in 16 of 38 (42%) patients on echocardiography (M-mode and 2D).\textsuperscript{9} We demonstrated that dilatation of the ascending aorta occurred in 3% of the patients. Clinically overt anomaly may occur at every age. Connective tissue defects and hemodynamic disturbances, secondary to structural abnormalities of the heart and large vessels, are regarded as the causes of aortic dilatation and dissection.\textsuperscript{15} The recommended additional tests to diagnose these abnormalities are echocardiography, especially transesophageal echocardiogram, computer tomography and magnetic resonance imaging (MRI). An early diagnosis enables to schedule surgical removal and replacement of the diseased segment of the aorta.\textsuperscript{28-30} According to Matura et al., dilated ascending aorta defined as the aortic size index >2.0 cm/m\textsuperscript{2} requires close cardiovascular monitoring in women with TS.\textsuperscript{31}

Other malformations in TS include partial anomalous pulmonary venous connection in 3.8–13% of patients, patent ductus arteriosus in ~3.8%, left main superior vena cava anomalies in ~13%, and others.\textsuperscript{32-36} In our study 1 case of patent ductus arteriosus was observed in the mosaicism group.

Atrial and ventricular septal defects, as well as partial or complete atrio-ventricular canal have been rarely detected. We diagnosed membranous ventricular septal defect in 6% of patients (1 case in the group with mosaicism and 1 in the group with structural X chromosome aberrations).

Some authors emphasize coexistence of heart malformations and lymphedema, or the so-called webbed neck in particular.\textsuperscript{25} Our observations showed the presence of webbed neck in all the patients with cardiac anomalies.

In our study, valvular heart disease was relatively common – it was present in 50% of the patients. Mild-to-moderate mitral, aortic and tricuspid insufficiency was most frequently detected, aortic stenosis was less and mitral and tricuspid prolapse were the least common. Aortic valve disease (including bicuspid valve) was noted in 24% and mitral valve disease in 21% of the patients. So far, valvular heart disease have not led to clinical manifestations, cardiac dysfunction or other complications in our patients. High incidence of mild mitral regurgitation (I’) might result from congenital abnormalities of the connective tissue.
In another analysis, valvular heart disease was found in 10 of 100 women with TS. One patient underwent surgery for mitral regurgitation, and in the other 9 patients moderate aortic regurgitation and stenosis, bicuspid aortic valve and tricuspid regurgitation were detected. One woman with moderate aortic insufficiency and arterial hypertension died from acute aortic dissection at the age of 28. It has been estimated that arterial hypertension occurs in 7–17% of girls, and in 24–40% of adult women with TS. In over 30% of girls, 24-hour ambulatory monitoring showed moderate hypertension. Half of them had altered 24-hour blood pressure profile, with smaller night pressure drop than in healthy persons. These individuals showed hypertrophy of left ventricle, which might predict future cardiovascular events, including higher mortality. Hypertension was diagnosed in 35% of the analyzed patients with TS; every hypertensive subject was regularly treated with oral estrogens.

It has been demonstrated that suitable and systematic estrogen substitution significantly decreases diastolic blood pressure in 24-hour monitoring, and decreases systolic blood pressure during the day. This effect may be due to the influence of estrogens on vascular reactivity as a result of interaction with vascular smooth muscle cells, stimulation of nitric oxide secretion by endothelial cells, inhibition of platelet aggregation, monocyte adhesion, and smooth muscle hypertrophy.

Initial observations did not show higher incidence of coronary artery disease in TS women despite increased cholesterol levels, blood pressure and cardiac defects. However, Danish investigators have shown that ischemic heart disease is a frequent cause of death in TS compared to the general population. Ischemic heart disease may occur in TS women at a young age. Estrogen therapy decreases the risk of coronary artery disease. We diagnosed ischemic heart disease (myocardial infarction, angina pectoris) in 9% of TS patients in the mosaicism group. It might have been associated with older age and higher proportion of overweight subjects in this group. Other authors did not observe higher incidence of ischemic heart disease and cardiovascular risk factors in TS women. These discrepancies may result from age differences in the study populations. To decrease the risk of ischemic heart disease in patients with TS, effective control and regular treatment of hypertension, overweight, and hyperlipidemia are needed.

Women with TS demonstrate increased tendency to develop metabolic syndrome (arterial hypertension, lipid disorders, diabetes mellitus, obesity, hyperinsulinemia, hyperuricemia). 53% of our patients with TS had hypercholesterolemia, 35% had hypertension, 18% had obesity, and 6% had type 2 diabetes. According to Ross et al., higher cholesterol levels in untreated adolescent individuals with TS were independent of age, BMI, and karyotype. However, Van et al. demonstrated that women with karyotype 45,X and ovarian failure showed more atherogenic lipid profile than those with karyotype 46,XX and gonadal insufficiency. Similarly to Landin-Wilhelmsen et al., we observed that hypertension and diabetes did not correlate with the karyotype. Echocardiography demonstrated a tendency to thicker interventricular septum and larger left ventricular mass in patients with TS and mosaicism compared to the monosomy group. It might be associated with older age, higher rate of overweight and higher incidence of hypertension in patients with mosaicism. Besides, the cases of ischemic heart disease were observed only in TS women with mosaicism.

In the majority of our patients with TS (62%), ECG changes were detected. There were mostly T wave inversions, ST segment depression, and right bundle branch block. ECG abnormalities were demonstrated in groups 1 and 2 with similar frequency. They were caused by left ventricular hypertrophy, myocardial infarction, previous myocardial infarction, and congenital cardiac malformations. In another study, ECG abnormalities were noted in 2% of TS patients (one case of atrial fibrillation, and one case of right bundle branch block). The limitation of our study was the inclusion of a 7-year-old child into the analysis, which disturbed homogeneity of the study population and might have affected some mean values, particularly body mass and echocardiographic parameters. However, we consider this limitation to be of minor importance. The inclusion of one child into our series did not have a significant influence on the parameters. According to the available data, our own experience and available recommendations, it should be highlighted that every patient with TS should undergo cardiological assessment, including echocardiography. Blood pressure measurement should be performed at every check-up on a lifelong basis, at least twice a year. Tight control and efficient treatment of hypertension are particularly important for TS patients, due to a higher risk of aortic rupture (higher incidence of aortic dissection and coarctation). If aortic dissection or dilatation occur and transesophageal echocardiography is of low quality, transesophageal echocardiography, computed tomography and/or MRI should be performed. In patients with aortic dilatation these examinations should also be repeated. Even if cardiovascular abnormality was not detected in childhood, physical examination and echocardiography should be repeated during adolescence (12–15 years), and again every 3–5 years in adulthood. Particular attention should be paid to the aorta of the women who plan pregnancy using assisted reproductive technology, or in selected women during natural pregnancy.

Women with TS require screening of the cardiovascular system to identify a number...
of abnormalities in asymptomatic individuals. Except for higher rates of overweight and a tendency to higher incidence of arterial hypertension, thicker interventricular septum, and larger left ventricular mass in patients with mosaicism compared to the monosomy group, no other differences in risk factors and abnormalities of the cardiovascular system between various karyotypes were found. Every woman with TS should undergo repeated heart tests and transthoracic echocardiography. If the quality of transthoracic image is low and potentially dangerous cardiovascular malformations and complications (aortic dilatation or dissection) occur, transesophageal echocardiography, computed tomography, and/or MRI should be performed. In patients with dilatation of the aorta these tests should also be repeated. It is crucially important to detect, monitor and treat arterial hypertension, overweight and hyperlipidemia on a lifelong basis to prevent ischemic heart disease.

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REFERENCES

43 Van PL, Bakalov VK, Bondy CA. Monosomy for the X-chromosome is associated with an atherogenic lipid profile. J Clin Endocrinol Metab. 2006; 91: 2867-2870.
ARTYKUŁ ORYGINALNY

Zmiany sercowo-naczyniowe u pacjentek z zespołem Turnera w zależności od kariotypu

Badania własne i przegląd piśmiennictwa

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SŁOWA KLUCZOWE
echokardiografia, elektrokardiografia, kariotyp, zespół Turnera, zmiany układu sercowo-naczyniowego

STRESZCZENIE

WPROWADZENIE Choroby układu sercowo-naczyniowego powodują trzykrotnie większą śmiertelność wśród kobiet z zespołem Turnera (ZT). Sugieruje się również, że ich występowanie jest zależne od kariotypu.

CELE Ocena układu krążenia na podstawie badania klinicznego, badania echokardiograficznego (ECHO) i elektrokardiograficznego (EKG) u pacjentek z ZT, z uwzględnieniem kariotypu.

PACJENCI I METODY Badaniu poddano 34 kobiety z ZT w wieku 7–58 lat (35,2 ±14,6). W zależności od kariotypu pacjentki podzielono na 3 grupy: I grupę stanowiło 12 osób z monosomią chromosomu X (45,X), II grupę – 19 kobiet z kariotypem mozaikowym, III grupę – 3 pacjentki z aberracjami strukturalnymi chromosomu X. Badanie ECHO wykonano aparatem Sonos 5500, z uwzględnieniem obowiązujących standardów.

WYNIKI Wrodzone wady układu sercowo-naczyniowego stwierdzono u 21% pacjentek z ZT. Zastawkowe wady serca wykryto u 50% osób badanych, w tym wady zastawki aortalnej u 24%, a zastawki mitralnej u 21%. U pacjentek z kariotypem mozaikowym częściej niż u osób z monosomią stwierdzano nadwagę i tendencję do wzrostu ciśnienia tętniczego, a w badaniu ECHO – tendencję do występowania grubszej przegrody międzykomorowej oraz większej masy lewej komory.

WINIOŚKI Wrodzone wady układu sercowo-naczyniowego występują częściej w ZT niż w populacji ogólnej. Z wyjątkiem częstszego występowania nadwagi, tendencji do naciśnienia tętniczego, pogrubienia przegrody międzykomorowej oraz wzrostu masy lewej komory u pacjentek z kariotypem mozaikowym, w porównaniu z pacjentkami z monosomią, nie stwierdzono innych różnic w występowaniu czynników ryzyka i odchyleń układu sercowo-naczyniowego pomiędzy różnymi kariotypami.