SCIENTIFIC LETTER

Subclinical left ventricular dysfunction in normotensive women with Turner's syndrome

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Women with Turner's syndrome (TS) are at risk of not only congenital cardiovascular malformations but also hypertension and ischaemic heart disease,¹ risk factors that may all interact and reduce left ventricular (LV) performance. Conventional echocardiography, however, has not been able to identify LV dysfunction in TS,² but the techniques used may well have been insufficient to detect subtle alterations in cardiac function.

To confirm our hypothesis of impaired LV function in women with TS, we therefore used tissue and conventional Doppler echocardiography to evaluate systolic long-axis function and diastolic filling in a group of asymptomatic, normotensive women with TS.

METHODS

We studied 33 women with TS. Exclusion criteria were cardiac malformations (bicuspid aortic valve not included), LV ejection fraction < 55%, hypertension, impaired insulin sensitivity, and diabetes. All participants were not taking any drugs other than hormone replacement therapy (HRT). Three had previously received growth hormone. Thirty-three age-matched healthy female volunteers served as controls.

To address the metabolic state of the women with TS, fasting blood samples were drawn between 09 00 and 10 00. Insulin sensitivity (homeostasis model assessment (HOMA) -S) and β cell function (HOMA-B) were assessed by the HOMA model.

All echocardiographic examinations were performed by NHA on a GE Vivid Five (GE Medical Systems, Horten, Norway) equipped with a 2.5 MHz transducer.

Assessment of LV diastolic properties was based on mitral inflow and colour M mode velocity flow propagation (Vp) and classified as follows: (1) normal filling: E deceleration time (DT) $\geq$ 140 and < 240 ms, E:A ratio between 1 and 2 with Vp > 45 cm/s; (2) abnormal relaxation: DT > 240 ms and E:A ratio < 1; or (3) pseudonormal filling: DT $\geq$ 140 and < 240 ms with Vp < 45 cm/s.

Tissue Doppler imaging was obtained from the apical views during end-expiratory apnoea. Peak myocardial systolic strain rate (SR) was measured (mean of three consecutive cardiac cycles) in the basal one third of each of 16 myocardial segments used for wall motion scoring. Negative SR values represent contraction, with more negative values representing enhanced contraction. The peak systolic SR in each segment was assessed as the lowest value between the R wave on the ECG and end systole.

The intraobserver variability of the SR measurements in the laboratory was 9 (7)%, and the standard deviation of the absolute difference in SR was 0.08/s.

Student's two-tailed unpaired t test or the Mann-Whitney two-tailed test was used as appropriate. Pearson correlation was used to examine the relationship between estimates of LV function, systolic and diastolic function, and measures of body composition and glucose homeostasis. Results are

Table 1 Echocardiographic measurements in women with Turner's syndrome and in controls

	Turner's syndrome (n = 33)	Controls (n = 33)
Age (years)	37 (10)	41 (12)
Heart rate (beats/min)	80 (12)*	69 (7)
Body mass index (kg/m ²)	25 (4)*	22 (2)
Left atrial diameter (cm)	3.4 (0.4)	3.6 (0.4)
Left atrial diameter/m ² (cm)	2.3 (0.3)*	2.1 (0.2)
LV diastolic diameter (cm)	4.4 (0.5)	4.6 (0.6)
LV systolic diameter (cm)	2.7 (0.6)	3.0 (0.6)
Septal wall thickness (cm)	0.9 (0.2)	0.8 (0.2)
Posterior wall thickness (cm)	0.9 (0.2)	0.8 (0.2)
LV mass index (g/m ^{2.7})	39 (7)	33 (9)
LV ejection fraction (%)	60 (4)	61 (3)
Mitral E wave velocity (cm/s)	97 (22)*	78 (12)
Mitral A wave velocity (cm/s)	76 (20)*	58 (11)
E:A ratio	1.4 (0.4)	1.4 (0.3)
Deceleration time (ms)	150 (40)	170 (20)
Velocity flow propagation (cm/s)	54 (10)*	68 (9)

Data are presented as mean (SD).

*p < 0.01 v controls.

LV, left ventricular.

expressed as mean (SD). A value of p < 0.05 was considered significant.

RESULTS

Blood pressure was similar in the two groups (systolic/diastolic: 119 (7)/71 (8) v 121 (10)/74 (8) mm Hg, NS). Patients were insulin sensitive (HOMA-S: 0.69 (0.40) v 1 (expected in a reference population), p < 0.001) but had diminished β cell function (HOMA-B: 75 (24)% v 100%, (expected in a reference population), p < 0.001). All had structurally normal hearts without LV hypertrophy (table 1).

Mitral E and A wave velocities were significantly higher in women with TS, whereas E:A ratio and DT were similar in both groups. Measures of global LV compliance (Vp and left atrial size index) were significantly different in patients with TS (table 1).

Nine women with TS (27%) had evidence of diastolic dysfunction: five abnormal relaxation and four pseudonormal filling. These women also had significantly higher heart rate than did women with TS and normal diastolic function (87 (12) v 77 (12) beats/min, p < 0.05). Resting heart rate correlated significantly with the E:A ratio (r = -0.56, p < 0.01) but not with Vp or left atrial size.

There was a significant correlation between Vp and mean systolic SR (r = -0.42, p < 0.01) (fig 1) and a trend

Abbreviations: DT, deceleration time; HOMA, homeostasis model assessment; HRT, hormone replacement therapy; LV, left ventricular; SR, strain rate; TS, Turner's syndrome; Vp, velocity flow propagation

Figure 1 Correlation between systolic strain rate and velocity flow propagation in women with Turner's syndrome.

towards a similar correlation with the E:A ratio ($r = 0.30$, $p = 0.1$).

The mean systolic SR of all 16 segments was significantly less negative in women with TS (-1.38 (0.32) v -1.57 (0.31)/s, $p < 0.05$). Systolic SR was not correlated with age, blood pressure, LV mass, HOMA-S or HOMA-B.

DISCUSSION

This study shows that diastolic dysfunction is present in more than a quarter of young asymptomatic normotensive, non-obese and insulin-sensitive women with TS who were not taking any drugs other than HRT. The presence of diastolic dysfunction in a group of young women with no predisposing conditions is remarkable and, possibly, may be explained as a syndromic trait.

Interestingly, we found a relatively high number of patients with pseudonormal filling, which is a more severe form of diastolic impairment, who would have remained unidentified if diastolic performance had been assessed only by Doppler-derived mitral inflow. The presence of diastolic dysfunction was closely related to the increased heart rate seen in TS, possibly associated with some degree of autonomic cardiac neuropathy.³

To avoid the extreme hypo-oestrogenism associated with TS, all patients received combined HRT. Whereas the impact of HRT on cardiac performance in premature menopausal women is unknown, beneficial effects on blood pressure and aortic compliance have been seen in TS.⁴

Systolic dysfunction, defined as decreased SR, was present in the TS group as a whole and was closely related to the impaired diastolic function.

The coexistence of impaired relaxation and decreased systolic performance has previously been found in hypertensive patients and in patients with diabetes mellitus, irrespective of blood pressure levels. In such cases, the

presence of increased LV mass concomitant with poorer metabolic control seems explanatory.⁵ However, in this population of normotensive women with TS, metabolic control and LV function were not clearly related. This may relate to the narrow range of normal insulin sensitivity in the study group. In contrast, LV global stiffening was reflected in both diastolic and systolic performance, determined by two different modalities. Myocardial stiffening in women with TS may be due to an intrinsic myocardial component, possibly a primary defect in TS leading to LV inadequacy over time. In addition, longstanding subclinical diastolic dysfunction with increased left atrial volume and pressure may explain the increased stroke risk in patients with TS.¹

In conclusion, diastolic dysfunction, decreased LV long-axis function, increased resting heart rate and left atrial enlargement are common findings in normotensive women with TS.

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