Unreliability of aortic size index to predict risk of aortic dissection in a patient with Turner syndrome

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Abstract

Aortic size index (ASI) has been proposed as a reliable criterion to predict risk for aortic dissection in Turner syndrome with significant thresholds of 20-25 mm/m². We report a case of aortic arch dissection in a patient with Turner syndrome who, from the ASI thresholds proposed, was deemed to be at low risk of aortic dissection or rupture and was not eligible for prophylactic surgery. This case report strongly supports careful monitoring and surgical evaluation even when the ASI is < 20 mm/m² if other significant risk factors are present.

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Key words: Aortic dissection; Aortic aneurysm; Turner syndrome

Core tip: Aortic size index (ASI) has been proposed as a reliable criterion to predict risk of aortic dissection in Turner syndrome. This case report emphasizes the need for careful monitoring and surgical evaluation of the patients even when the ASI is < 20 mm/m² if other significant risk factors are present.

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INTRODUCTION

Turner syndrome (TS) is a relatively common chromosomal disorder, caused by complete or partial X monosomy in some or all cells[1]. This abnormality is denoted medically as the 45,X karyotype as opposed to the usual 46,XX female karyotype. Many TS patients are actually mosaic, meaning that they have cells with more than one karyotype and occasionally there is mosaicism for cells containing Y chromosome material (Table 1)[2-4]. Short stature and gonadal dysgenesis are two of the characteristic clinical features of the syndrome, although many organ systems and tissues may also be affected to a lesser or greater extent. However, approximately 50% of karyotypically-proven, asymptomatic women with TS have evidence of abnormal cardiovascular development and most patients die from cardiovascular defects mainly involving the left ventricular outflow tract, left heart and/or aortic hypoplasia. Common congenital defects in surviving girls and adults with TS include bicuspid aortic valve (30%), aortic coarctation (12%) and partial anomalous pulmonary connection (18%)[5,6]. Nonetheless, the occurrence of aortic dilatation, dissection or rupture is one of major concerns in TS[7]. The annual incidence of aortic dissection or rupture is 15 cases/100000 for individuals < 20 years of age, 73-78 cases/100000 for women 20-40 years...
Table 1  Chromosomal dissection pattern based on karyotyping of women with Turner syndrome

| Karyotype | Description | El-Mansoury et al.2007 (n = 126) | Gravolt et al.1996 (n = 304) | Hook et al.1983 (n = 1043) |
|-----------|-------------|--------------------------------|----------------------------|--------------------------|
| 45,X      | Monosomy X  | 48%                           | 56%                        | 56%                      |
| 45,X/46,XX| Monosomy X mosaic with normal female sex chromosome complement | 23% | 17% | 15% |
| 46,X,i(Xq)| isochromosome X | 13% | 11% | 15% |
| 46,X,del(X)| deletion chromosome X ring | - | 8% | 6% |
| 46,X,t(X)| chromosome X complement | 3% | 5% | 2% |
| 45,X/47,XXX| monosomy X mosaic with triple X chromosome complement | 3% | 3% | 4% |
| 45,X/46,XY| monosomy X mosaic with normal male sex chromosome complement | 10% | - | - |

Figure 1  2D Coronal reformatted image. Digital multiplane reformatted image of the aortic arch, depicting the double barrel-shaped contained rupture of the aortic arch, in-between the common brachial trunk (CBT) and the left carotid artery (LCA) (white arrowhead) and LCA and the left subclavian artery (LSA) (black arrowhead).

A 23-year-old woman with TS (45,X karyotype), Graves-Basedow disease and systemic arterial hypertension treated with β-blockers, presented to our hospital facility because of fever unresponsive to antibiotics. She had experienced chest pain 1 mo previously which regressed spontaneously. She had no pain at hospital admission. Blood pressure was 110/82 mmHg.

The patient’s height and weight were 160 cm and 82 kg, respectively, with a body surface area of 1.85 m². TS was diagnosed at the age of 14 years after an evaluation for short stature and delay of pubertal development. Since then, the patient underwent yearly computed tomography (CT) which showed any aortic dilatation (the diameter of the ascending aorta at the latest scan before admission was 26 mm).

A CT scan at admission revealed a contained rupture of a dissected aortic arch with two false aneurysms between the common brachial trunk (CBT) and the left carotid artery (LCA), and between the LCA and left subclavian artery (LSA) (Figure 1). A peri-aortic hematoma (Figure 2) originating from the arch was present around the anterior aspect of the ascending aorta. The diameters of the aorta were as follows: ascending aorta 26 mm, arch 30 mm and proximal descending aorta 19 mm. The ascending aortic size index was 14 mm/m². Echocardiography confirmed the diagnosis and revealed the presence of a bicuspide aortic valve and slight valve insufficiency.

A cardio-circulatory arrest with deep hypothermia was planned. After cannulation of the femoral vessels and the axillary artery trough a 10-mm graft (Vascutek, Terumo Ltd, Egham, United Kingdom) surgical access was gained through median sternotomy. The ascending aorta was resected and the arch inspected: a rupture was detected between the CBT and the LCA with the tear extending towards the LSA. Because of the hematoma, the CBT could not be encircled or clamped and antegrade cerebral perfusion was conducted via the LCA, until the CBT was reconstructed, after which selective antegrade cerebral perfusion via the axillary artery was added. Two 12-mm grafts (Gelsoft, Terumo Ltd, Egham, United Kingdom) were anastomosed to the LCA and LSA and a 14-mm graft (Gelsoft, Terumo Ltd, Egham, United Kingdom) was anastomosed to the CBT. A 28-mm graft
Figure 2  Axial plane computed tomography image of the ascending aorta. Axial image of the ascending aorta at the level of the pulmonary artery bifurcation. The ascending aorta is compressed in an oval shape due to the sub-adjvential spreading hematoma. AA: Ascending aorta.

(Gelweave Terumo Ltd, Egham United Kingdom) was anastomosed to the distal arch. Afterwards, the prosthesis was clamped and the distal body perfusion resumed through the femoral artery. The aortic valve was a “true” bicuspid valve with no raphe and 180° commissural orientation. The aortic root was normal and the effective height of the aortic valve was 9 mm. Therefore, there was no indication for valve and root replacement. After the proximal anastomosis was completed, the supra-aortic vessels were reimplanted on the ascending aorta prosthesis. Cardiopulmonary bypass time was 440 min, aortic cross-clamp time was 180 min and circulatory body arrest time was 20 min. The operation was routinely completed. After an uneventful course, the patient was discharged to the referring hospital on postoperative day 8. Pathologic examination of the aorta revealed very limited myxoid degeneration with no evidence of either fragmentation or separation of the elastic fibers.

DISCUSSION

In TS, it remains unclear whether aortic dissection is preceded by progressive dilatation as it is in connective disorders, and whether the thresholds employed in MS can be safely employed for TS. Nevertheless, a large proportion of these patients are small women and, for this reason, it is not correct to use standards derived from adult men in the general population and, for instance, an ascending aortic diameter even < 5 cm may represent, in these patients, a significant dilatation.

To overcome the body size issue, the ASI has been introduced which adjusts the aortic diameter to body surface area\(^{[10]}\). Davies et al.\(^{[1]}\) showed that patients with thoracic aortic aneurysms with ASI < 27.5 mm/m\(^2\) are at low risk (approximately 4% per year), those with ASI between 27.5 and 42.4 mm/m\(^2\) are at moderate risk (approximately 8% per year), and those above 42.5 mm/m\(^2\) are at high risk (approximately 20% per year) of rupture, dissection, and death. Matura et al.\(^{[8]}\) employed this index in patients with TS demonstrating that subjects with ASI > 20 mm/m\(^2\) require close cardiovascular surveillance and those with ASI \(\geq 25\) mm/m\(^2\) are at highest risk of aortic dissection.

We presented a case of a 23-year-old TS female with contained rupture of a dissected aortic arch. The ASI in our patient was 14 mm/m\(^2\) at the level of the ascending aorta. Therefore, following current indications, there was no indication either for surgery or for close surveillance in this patient since the ASI was well below accepted thresholds. Hence, although recent studies\(^{[9]}\) have confirmed that body surface area normalization is the most appropriate approach for determining aortic dilation in TS, in our experience ASI was unable to predict impending aortic dissection and rupture.

A recent study employing mathematical models of aortic disease in TS\(^{[11]}\), showed that growth of the thoracic aorta is dynamic over time and risk factors such as aortic coarctation, bicuspid aortic valves, age, diastolic blood pressure, body surface area and antihypertensive treatment preferentially accelerated growth of the ascending aorta. Unfortunately, this model was not linked to aortic dissection and rupture. However, other papers\(^{[12-18]}\) report that bicuspid aortic valve, karyotype 45X, age 20-45 years, and hypertension are factors that confer an increased risk of dissection. All these features were present in the case reported therefore, in our opinion, when one or more of these factors are present, the risk of dissection should be taken into account even with ASI < 20 mm/m\(^2\), and a close surveillance by a multidisciplinary team (cardiologists, radiologists, cardiac surgeons) should be recommended.

Although a CT scan with contrast is the most widely used diagnostic procedure, recent studies\(^{[12-13]}\) have demonstrated that cardiac magnetic resonance imaging (CMRI) is an important tool for clinical care and it improves risk stratification of TS patients. Indeed, CMRI is outstanding for detection of the degree of aortic dilatation and coarctation that are not visible on echocardiography\(^{[13-14]}\), but is limited by its high cost and poor tolerability due to claustrophobia and anxiety in some TS patients. Meanwhile, fast scan seeds, low radiation dose and increased anatomic coverage are improving the image quality of cardiac multidetector CT (MDCT) and reducing patient risks in children. Cardiac MDCT is also considered to effectively bridge the gaps among echocardiography and cardiac MRI in children with congenital heart disease. In addition, cardiac MDCT has better cost benefit compared with CMRI.

In conclusion, our experience emphasizes the need for careful monitoring and surgical evaluation of TS patients even when the ASI is small if other significant risk factors are present. Even though this is only a case report, it provides the idea and sounds the alarm that using only an ASI is not sufficient for risk stratification for aortic dissection in patients with TS.

Large prospective studies are needed for risk stratification for aortic dissection in TS in order to identify reliable thresholds to identify patients who may require referral for surgery before life-threatening complications occur.
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COMMENTS
Case characteristics
A 23-year-old woman with Turner syndrome (TS).
Clinical diagnosis
Fever unresponsive to antibiotics, and chest pain.
Differential diagnosis
Other causes of chest pain, thoracic back pain.
Laboratory diagnosis
Blood, metabolic panel and liver function tests were within normal limits.
Imaging diagnosis
A computed tomography-scan at admission revealed a contained rupture of a dissected aortic arch with two aneurysms between the common brachial trunk and the left carotid artery and the left carotid artery and the left subclavian artery, respectively. The diameters of the aorta were as follows: ascending aorta 26 mm, arch 30 mm and proximal descending aorta 19 mm. The ascending aortic size index was 14 mm/m².
Pathological diagnosis
Pathologic examination of the aorta revealed very limited myxoid degeneration with no evidence of either fragmentation or separation of the elastic fibers.
Treatmen
The patient underwent aortic arch replacement and common brachial trunk, left carotid artery, and left subclavian artery replacement.
Related reports
Aortic root enlargement increases the risk of dissection in Turner syndrome but it is unclear whether aortic dissection is always preceded by progressive dilatation as occurs in Marfan syndrome. Nevertheless, a large proportion of these patients are small women, and for this reason, it is not correct to use standards derived from adult men in the general population and, for instance, an ascending aortic diameter even < 5 cm may represent, in these patients, a significant dilatation.
Term explanation
Aortic size index, which adjusts the aortic diameter to the body surface area, has been recently introduced as a reliable criterion to predict risk for aortic dissection in TS patients but its usefulness in this clinical entity is still a matter of debate.
Experiences and lessons
This case report emphasizes the need for careful monitoring and surgical evaluation of the patients even when the aortic size index is < 20 mm/m² if other significant risk factors are present.
Peer review
This is a potentially interesting case study that describes the limitation in using aortic size index to assess risk of aortic dissection in patients with Turner’s syndrome.

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