Progress in Pediatric Cardiology 52 (2019) 18–21

Contents lists available at ScienceDirect

Progress in Pediatric Cardiology

journal homepage: www.elsevier.com/locate/ppedcard

# Evaluation of cardiac MRI and ambulatory blood pressure monitoring in a pediatric Turner syndrome population

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ARTICLE INFO

*Keywords:*
Turner syndrome
Pediatric population
Ambulatory blood pressure monitoring
Cardiac MRI

ABSTRACT

*Background:* The benefits of cardiac MRI in the diagnosis of cardiac abnormalities in adults with Turner syndrome (TS) have been shown by several studies. High blood pressure frequently occurs in TS patients; therefore ambulatory blood pressure monitoring (ABPM) is routinely performed in adults with TS. However, potential benefits of either technique remain undetermined in the pediatric TS population.
*Aims:* To evaluate the potential benefits of cardiac MRI and ABPM in pediatric patients with TS.
*Methods:* A total of 19 girls with TS, aged between 9 and 18 years old, were prospectively included in a cross-sectional study from May 2015 to November 2015. We evaluated data from both cardiac MRI and ABPM by comparison with 2D echocardiography and instant measurement of blood pressure.
*Results:* Of the 16 cardiac MRI performed, 4 (25%) revealed anatomical abnormalities undiagnosed by echocardiography. Our analysis demonstrated a low correlation between echocardiography and cardiac MRI in measuring diameters of the aortic root. ABPM revealed 5 cases (29.5%) of moderate hypertension, 4 of which were previously unknown.
*Conclusions:* This study has shown an advantage of using cardiac MRI and ABPM for diagnosing cardiovascular abnormalities in pediatric TS patients, therefore we recommend the routine use of both examinations to improve overall care and ensure a better transition into adulthood.

## 1. Introduction

Turner syndrome (TS) is a rare genetic disorder caused by a complete or partial absence of the X chromosome. It affects one out of 2500 female neonates [1]. Congenital cardiovascular structural abnormalities affect approximately 50% of individuals with TS [2].

Congenital cardiac abnormalities have been reported in almost one third of TS patients, the most common of which are bicuspid aortic valve (BAV) and aortic coarctation [3]. Acquired abnormalities mainly include aortic root dilatation and high blood pressure (HBP).

Aortic dissection is the most severe cardiac abnormality and often occurs within the aortic root at an average age of 30 years old [4]. In cases of aortic dissection, there is typically a high prevalence of BAV and aortic coarctation, and 75% suffer from HBP [5]. According to several studies, HBP affects almost 50% of adult TS patients, although the cause and age of onset are not fully understood [6,7]. Therefore, ambulatory blood pressure monitoring (ABPM) is usually performed in the follow-up of TS adult patients.

Several studies have shown the benefits of cardiac MRI in the adult population of TS [8,9]. MRI brings an accurate anatomical diagnosis of certain cardiovascular anomalies such as BAV, distal aortic coarctation and horizontal aortic dilatation [10]. Although transthoracic echocardiography (TTE) is routinely used to detect most cardiac diseases, it can be limited, especially in patients with poor echogenicity. Therefore,

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https://doi.org/10.1016/j.ppedcard.2018.08.005
Received 25 December 2017; Received in revised form 5 August 2018; Accepted 27 August 2018
Available online 07 September 2018
1058-9813/ 

**Table 1**
Patients with abnormal ABPM results.

| Patients | | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|
| ♦ Age (year) | | 17.9 | 17 | 13.7 | 13.5 | 10.8 |
| ♦ History of cardiovascular diseases | | Yes[a] | No | Yes[b] | No | Yes[c] |
| ♦ History of high blood pressure | | No | No | Yes | No | No |
| ♦ Percentage of abnormal diurnal blood pressure measurements[d] (%) | Systolic | 82.4 | 35 | 38.5 | 30 | 64 |
| | Diastolic | 53 | < 30 | < 30 | < 30 | < 30 |
| ♦ Percentage of abnormal nocturnal blood pressure measurements[d] (%) | Systolic | 57.1 | 60 | 40 | 55.5 | 85.7 |
| | Diastolic | 57 | < 30 | < 30 | < 30 | 43 |
| ♦ Percentage of abnormal 24 h blood pressure measurements[d] (%) | Systolic | 75 | 43.3 | 38.5 | 38 | 69 |
| | Diastolic | 54.2 | < 30 | < 30 | < 30 | < 30 |
| ♦ Percentage of day and night blood pressures ≤ variation/dipping (%) | Systolic | 13.5 | 12.9 | 8.5 | 10.3 | 8.1 |
| | Diastolic | 16.1 | 23.7 | 12.6 | 12.7 | 11.5 |
| | Mean BP | 15.6 | 17.8 | 6.1 | 11.4 | 6.6 |

[a] Bicuspid aortic valve.
[b] Coarctation of the aorta in follow-up after surgical repair.
[c] Isolated aortic dilatation.
[d] Arterial pressure was considered abnormal when it exceeded the upper limit of the standard values in > 30% of ABPM measurements.

it is possible that certain congenital or acquired heart diseases in TS patients may go undiagnosed or are insufficiently described by echocardiography as coarctation of distal aorta, anomalies of the aortic arch, BAV, aortic root dilatation etc. However, accuracy in the diagnosis of congenital cardiovascular diseases is increased by combining echocardiography with MRI [3], therefore cardiac MRI is routinely performed in the follow-up of adult TS patients.

In the pediatric TS population, a potential benefit of ABPM and cardiac MRI has not yet been studied and neither of these two examinations is currently recommended in routine follow-up.

The main objective of this study was to evaluate cardiac MRI and ABPM for diagnosing cardiovascular diseases in children with TS by comparing data with echocardiography and clinical measurements of blood pressure (BP).

## 2. Methods

This prospective cross-sectional study was carried out between May and November 2015 (6 months) in the tertiary care pediatric and congenital cardiology department at Montpellier University Hospital in France. A total of 19 girls with TS aged between 9 and 18 years old were prospectively recruited during their annual pediatric endocrinology or cardiology outpatient visit. Routine follow-up included a physical examination with measurement of arm blood pressure, an electrocardiogram and echocardiography. Cardiac MRI and ABPM were performed on TS patients participating in the study. All cardiac MRI were carried out without general anaesthesia 2 to 4 weeks after echocardiography. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. Informed consent was obtained from all patients' parents.

### 2.1. Standards used and statistical analyses

The standards of Gautier et al. and American Society of Echocardiography (ASE) guidelines were followed to measure the diameter of the aortic root by echocardiography [11]. For ABPM, arterial pressure was considered abnormally high if the 24-hour mean arterial pressure exceeded the upper limit of the standard values in > 30% of ABPM measurements [12]. The standard values of 1997 ABPM were used in this study [13]. Non-dippers were defined as having < 10% nocturnal BP reduction. The ABPM was carried out using the SpaceLabs 90,217 brand machine with an adapted pediatric cuff. Individuals were asked to complete the activity log as instructed by the clinician.

The study population was described using means and standard deviations (SD) for quantitative variables and frequencies for qualitative variables. Quantitative variables were compared with the parametric Student's *t*-test. Echocardiography and cardiac MRI data were analyzed in a double-blind fashion. The measurements of the aorta were made by the radiologist and then confirmed by a pediatric cardiologist who made the same measurements using echocardiography as well.

The reproducibility between MRI and echocardiography in measuring the diameter of the aortic root was analyzed by intra-class correlation coefficient (ICC) and Bland-Altman graphic representation. The Bland-Altman method describe and quantify agreement between two quantitative measurements by constructing limits of agreement and using the mean and the standard deviation(s) of the differences between two measurements.

The two-sided significance level was set at 0.05 and SAS version 9 (SAS institute, Cary, NC, USA) was used for the analyses.

## 3. Results

With their parents' consent, 19 girls with TS agreed to participate in this study during their follow-up within the study period. Population characteristics showed an average age of 15 years old (SD: 2.4), average height of 146 cm (SD: 12) and average body mass index of 23 $kg/m^2$ (SD: 3.7). Of the 19 patients, 3 patients had BAV with aortic dilatation diagnosed by echocardiography, one patient had an operated coarctation of the aorta and 3 patients received beta-blockers for treatment of HBP (one case) and aortic dilatation (2 cases).

### 3.1. ABPM results

Among the 17 ABPM that have been performed, 5 patients (29.4%) exhibited abnormal ABPM results. Among these 5 cases, only one correlated to a high BP measured in the clinic before ABPM (Table 1). The circadian rhythm of systolic BP appeared abnormal in 53% of cases with no significant decrease in night systolic BP (non-dipper patient).

### 3.2. MRI results

Importantly, cardiac MRI revealed 3 cases of BAV which were previously undiagnosed and analysis showed an association with aortic root dilatation in two of these patients (Z-scores = 1.84 and 2). Cardiac MRI also diagnosed 4 previously unknown cases of aortic root dilatation (Z-score: 1.81, 1.84, 2.27 and 2.34), two of which showed no presence of BAV.

In the same child, MRI detected two anatomical anomalies associated with TS, also previously unknown: a retroesophageal right subclavian artery and a pseudo-coarctation with an elongated aortic arch. In the cases of BAV, MRI measured a significant dilatation of the aortic root. Three cardiac MRI could not be performed following a parental

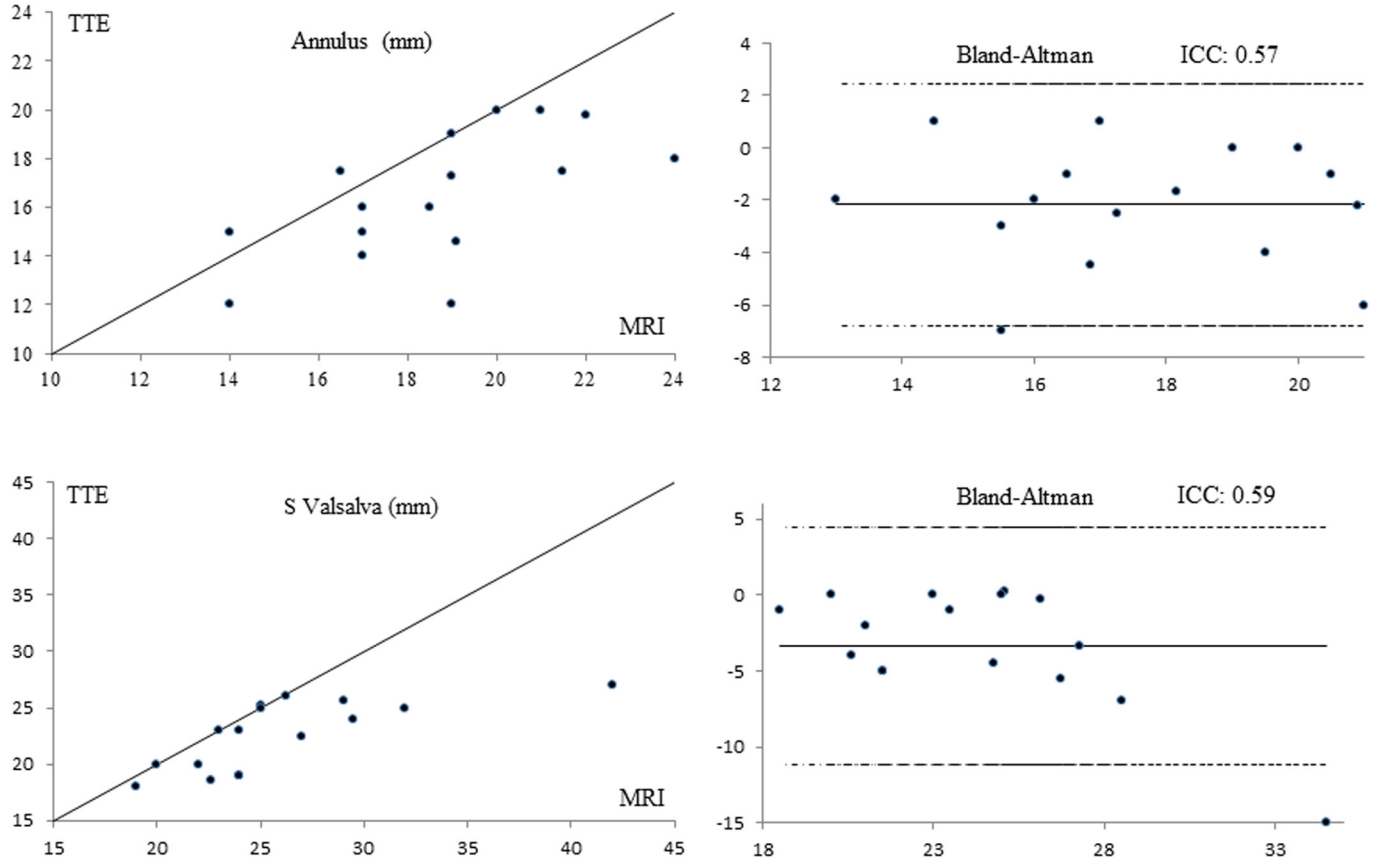


**Fig. 1.** Correlation between cardiac MRI and TTE for aortic diameters: annulus and sinus of Valsalva.
The aortic root diameter measured by TTE was smaller compared to MRI by 2.2 mm for annulus and 3.5 mm for sinus of Valsalva.
ICC: intra-class correlation coefficient.
Y-axis = difference between the values of the two methods. X-axis = average of paired values from each method.

refusal.

Our analysis revealed a low correlation between echocardiography and cardiac MRI for aortic root diameters (annulus, sinus of Valsalva, sinotubular junction and ascending aorta), particularly for the aortic annulus and sinus of Valsalva diameters. Echocardiography underestimated measurements compared to MRI. A comparison of aortic root diameters using the Bland-Altman representation revealed a smaller diameter measured by TTE compared to MRI by: 2.2 mm for annulus; 3.5 mm for sinus of Valsalva (S.Valsalva); 1.8 mm for sinotubular junction (STJ); 1 mm for ascending aorta (Asc aorta) (Figs. 1 and 2).

## 4. Discussion

The TS cardiovascular mortality rate remains high, with complications often discovered in adulthood. Although dissection and rupture of the aorta are rare in the pediatric population, a few cases have been reported in the literature [5,14,15]. Hypertension affects up to 25% of adolescents with TS and a higher percentage of adults (40–60%) [16,17], although it is often isolated from heart disease. Despite the low number of patients in our study, we successfully detected 5 abnormalities from the 17 ABPM performed. The cases of hypertension detected by ABPM currently require no medical treatment; however, these patients' diagnosis will adapt their level of cardiovascular monitoring.

Although systematic cardiac MRI for pediatric TS patients is not recommended in all centers in France, it is often performed in cases requiring further investigation of a particular abnormality detected by echocardiography. This study has shown a clear advantage of cardiac MRI for detecting certain cardiovascular anomalies previously undiagnosed by echocardiography.

Many adult patients with TS begin consultation again in specialized centers to address important issues, such as the ability to do sport or assisted reproduction, often due to a decline in follow-up visits since childhood. This break in transition to adulthood is well-known and the subject of recent recommendations in congenital cardiology [18]. It is therefore essential to thoroughly evaluate all possible complications of pediatric TS patients, such as hypertension or an anatomical abnormality, before transition to adulthood.

The main limitations of this monocentric study were the small number of subjects and measurement bias. In addition, the measurement of aortic root diameters by both echocardiography and cardiac MRI did not include a second reading.

## 5. Conclusions

HBP can occur in pediatric TS patients even in asymptomatic cases with no congenital heart disease. On this basis, we recommend ABPM from childhood in TS patients in addition to clinical BP measurements. Echocardiography remains the first line examination for diagnosis and monitoring, yet our data have shown a clear benefit of cardiac MRI which is essential to confirm and complete the results of echocardiography. Accurate cardiovascular monitoring is vital to detect any predisposing factors of aortic dissection. Ultimately, both examinations will improve the overall care of pediatric TS patients, ensuring a better transition into adulthood. Indeed, our study has shown a diagnostic benefit of both cardiac MRI and ABPM; however it is important to confirm this finding in a study with larger patient numbers.

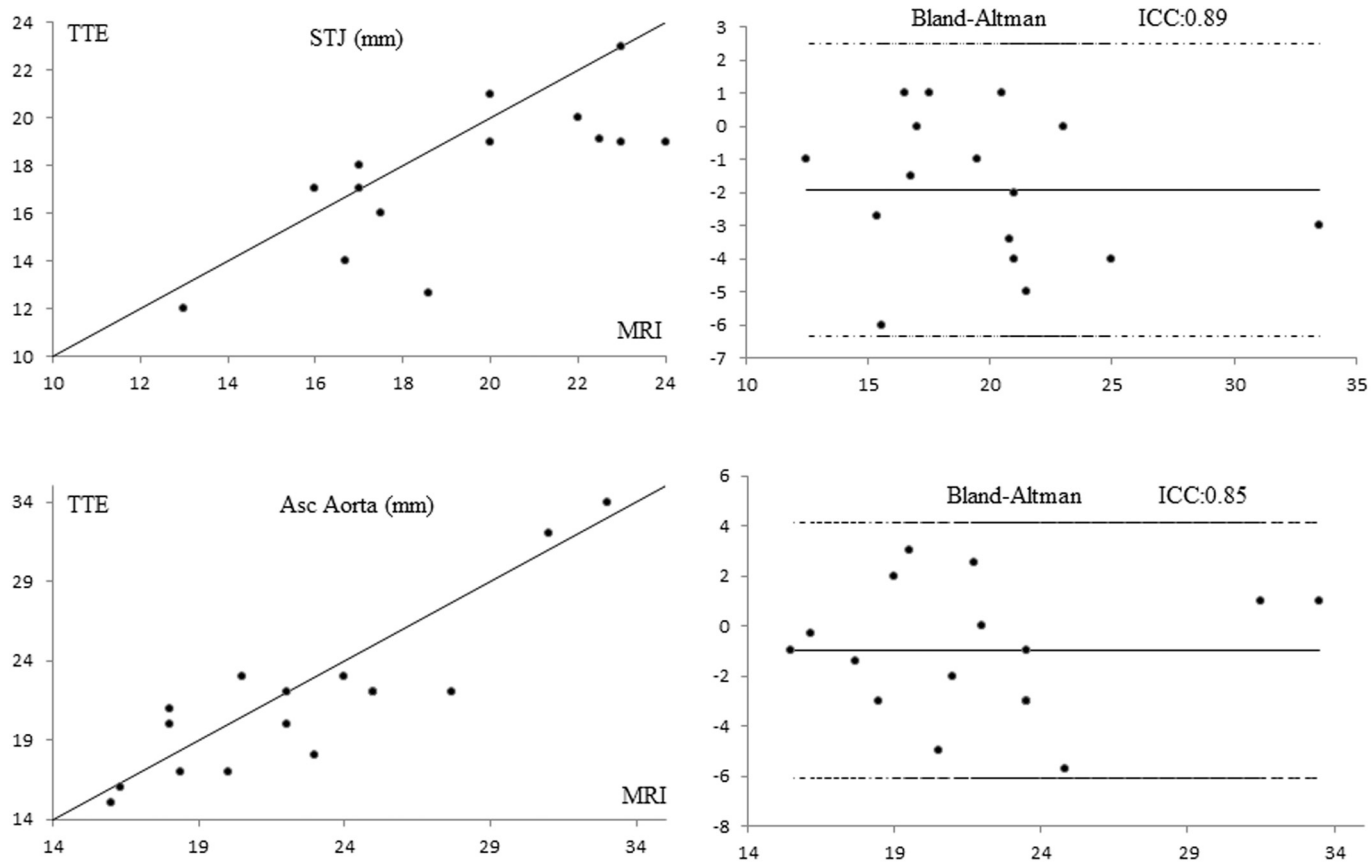


**Fig. 2.** Correlation between cardiac MRI and TTE for aortic diameters: STJ and Asc aorta.
The aortic root diameter measured by TTE was smaller compared to MRI by 1.8 mm for STJ and 1 mm for Asc aorta.
ICC: intra-class correlation coefficient.
Y-axis = difference between the values of the two methods. X-axis = average of paired values from each method.

## Ethical standards

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from the child's parents included in the study.

## Disclosure of interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and publication of this article.

The authors received no financial support for the research, authorship, and/or publication of this article.

## References

[1] Nielsen J, Wohlert M. Sex chromosome abnormalities found among 34,910 newborn children: results from a 13-year incidence study in Arhus, Denmark. Birth Defects Orig Artic Ser 1990;26:209–23.
[2] Bondy CA. Heart disease in Turner syndrome. Minerva Endocrinol 2007;32:245–61.
[3] Bondy CA. Congenital cardiovascular disease in Turner syndrome. Congenit Heart Dis 2008;3:2–15.
[4] Gravholt C, Landin-Wilhelmsen K, Stochholm K, Hjerrild BE, Ledet T, Djurhuus CB, et al. Clinical and epidemiological description of aortic dissection in Turner's syndrome. Cardiol Young 2006;16:430–6.
[5] Carlson M, Silberbach M. Two cases and review of 85 cases in the literature. Dissection of the aorta in turner syndrome. J Med Genet 2007;44:745–9.
[6] Nathwani NC, Unwin R, Brook CG, Hindmarsh PC. Blood pressure and Turner syndrome. Clin Endocrinol 2000;52(3):363–70.
[7] Gravholt CH, Juul S, Naeraa RW, Hansen J. Morbidity in Turner syndrome. J Clin Epidemiol 1998;51(2):147–58.
[8] Sachdev V, Matura LA, Sidenko S, Ho VB, Arai AE, Rosing DR, et al. Aortic valve disease in Turner syndrome. J Am Coll Cardiol 2008;51(19):1904–9.
[9] Ho VB, Bakalov VK, Cooley M, Van PL, Hood MN, Burklow TR, et al. Major vascular anomalies in Turner syndrome: prevalence and magnetic resonance angiographic features. Circulation 2004;110(12):1694–700.
[10] Lopez L, Arheart KL, Colan SD, Stein NS, Lopez-Mitnik G, Lin AE, et al. Turner syndrome is an independent risk factor for aortic dilation in the young. Pediatrics 2008;121:1622–7.
[11] Gautier M, Detaint D, Fermanian C, Aegerter P, Delorme G, Arnoult F, et al. Nomograms for aortic root diameters in children using two dimensional echocardiography. Am J Cardiol 2010;105:888–94.
[12] White WB, Dey HM, Schulman P. Assessment of the daily blood pressure load as a determinant of cardiac function in patients with mild-to-moderate hypertension. Am Heart J 1989;118(4):782–95.
[13] Soergel M, Kirschstein M, Busch C, Danne T, Gellermann J, Holl R. Oscillometric twenty-four-hour ambulatory blood pressure values in healthy children and adolescents. A multicenter trial including 1141 subjects. J Pediatr 1997;130:178–84.
[14] Pleskacova J, Rucklova K, Popelova J, Cerny S, Syrucek M, Snajderova M, et al. Aortic dissection and rupture in a 16-year-old girl with Turner syndrome following previous progression of aortic dilation. Eur J Pediatr 2010;169:1283–6.
[15] Lacombre M, Lesèche G. G. Atteintes cardiovasculaires du ST. A propos d'un cas d'anévrysme artériel sous-clavier. é-mémoires de l'Academie National de. Chirurgie 2005;4:46–9.
[16] Elsheikh M, Casadei B, Conway GS, Wass JA. Hypertension is a major risk factor for aortic root dilatation in women with Turner's syndrome. Clin Endocrinol 2001;54:69–73.
[17] Gravholt CH, Hjerrild B. Hypertension and ischemic cardiovascular disease in Turner's syndrome. Int Congr Ser 2006;1298:174–9.
[18] Sable C, Foster E, Uzark K, Bjornsen K, Canobbio MM, Connolly HM, et al. Best practices in managing transition to adulthood for adolescents with congenital heart disease: the transition process and medical and psychosocial issues: a scientific statement from the American Heart Association. Circulation 2011;123:1454–85.