Cardiac Magnetic Resonance Imaging in Pediatric Turner Syndrome

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Objective To compare the detection of cardiac lesions with the use of cardiac magnetic resonance imaging (CMR) and conventional echocardiography in children with Turner syndrome.

Study design Twenty-four girls with Turner syndrome, 8-18 years of age, were recruited through the Pediatric Endocrinology Program. Participants underwent CMR and echocardiography within a 2-year period, and discrepancies between the results of each modality were identified.

Results Fifteen of 24 (63%) girls had a cardiac lesion identified on CMR or echocardiography. Both modalities identified the same lesion in 10 of 15 (67%); however, 6 of 15 (40%) participants had a lesion identified on CMR but not echocardiography. Participants with a missed lesion had a trend towards greater body mass index. Aortic dilation and bicuspid aortic valve were the most commonly missed lesions by echocardiography.

Conclusions CMR identifies significant cardiac lesions missed by echocardiography in pediatric patients with Turner syndrome, particularly along the aorta. These findings support the current guidelines that recommend screening CMR in addition to echocardiogram. Early identification of cardiac abnormalities in patients with Turner syndrome will allow for a greater understanding of the natural history in these patients and potentially identify candidates for earlier intervention. *(J Pediatr 2016;175:111-5)*.

Turner syndrome arises from anomalies of the second X chromosome and phenotypically presents with premature ovarian failure, short stature, and multisystem involvement.[1] Congenital and acquired cardiac disease affect nearly one-half of patients with Turner syndrome. Commonly associated cardiac lesions include bicuspid aortic valve (BAV), coarctation of the aorta (CoA), aortic dilation (AoD), elongated transverse aorta, and partial anomalous pulmonary venous return (PAPVR).[2,3] Aortic dissection is the most serious complication; it occurs in 1%-2% of girls with Turner syndrome and accounts for 2%-8% of premature deaths.[4] Known risk factors for dissection include BAV, AoD, and hypertension.[3-8]

Echocardiography is currently the standard of care to assess the cardiac anatomy of girls with Turner syndrome and is sufficient in infants and young children[9]; however, assessment of the transverse and descending aorta can be limited by chest-wall abnormalities and poor acoustic windows in older children.[4,10,11] Also, the majority of dissections originate in the ascending aorta, but approximately one-third occur more distally,[4,10,12] which emphasizes the importance of evaluating the entire aortic anatomy. Studies in adult women with Turner syndrome have demonstrated that cardiac magnetic resonance imaging (CMR) identified lesions such as CoA and AoD that were missed on echocardiogram.[13,14] Guidelines by Bondy and the Turner Syndrome Study Group[9] have recommended screening CMR in all children with Turner syndrome at an age when it can be performed without sedation, even if no cardiac anomalies are detected on echocardiography. Even though these guidelines have been applied to children with Turner syndrome, their recommendations were based on studies in adults. Currently, no comparisons are available for CMR and echocardiography in children with Turner syndrome.

The objective of this study was to compare the number and types of cardiac lesions identified on echocardiogram vs CMR in children and adolescents with Turner syndrome. Determining the types of lesions that may be seen with CMR compared with echocardiography would lend support to the guidelines that suggest the complementary use of CMR for screening purposes.

Methods

Participants with Turner syndrome, 8-18 years of age, were recruited during routine visits to the pediatric endocrinology clinic between May 2013 and June 2015 at the Stollery Children's Hospital, University of Alberta, Edmonton, Canada. Included were those able to tolerate CMR without sedation; thus, participants <8 years of age were excluded because they typically require

AoD	Aortic dilation
BAV	Bicuspid aortic valve
BMI	Body mass index
CMR	Cardiac magnetic resonance imaging
CoA	Coarctation of the aorta
LSVC	Left superior vena cava
PAPVR	Partial anomalous pulmonary venous return

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sedation for CMR. Participants with the usual contraindications to magnetic resonance imaging (ie, pacemaker, claustrophobia) also were excluded. Written informed consent and assent were obtained from each caregiver and participant, respectively. The study was approved by the University of Alberta Human Research Ethics Board.

The clinical history of each patient was collected via electronic and paper chart review. Relevant clinical data, including the participant's age, anthropomorphic measurements, resting blood pressure, karyotype, presence of neck webbing, concurrent medical conditions, previous cardiac surgery, and ongoing medical therapies, were recorded (Table I).

All enrolled participants underwent echocardiography to evaluate the intracardiac anatomy, systemic and pulmonary venous drainage, and the great vessels. If an echocardiogram had not been performed in the preceding 2 years, a repeat echocardiogram was performed either before or after the CMR. M-mode, 2-dimensional echocardiography and Doppler imaging were performed with a Philips iE33 system (Philips Medical Systems, Andover, Massachusetts) with the participant in the supine or left lateral decubitus position (Figure 1). Measurements of the aortic valve at the annulus, aortic root, ascending aorta at the level of the right pulmonary artery, proximal transverse arch, and descending aorta (luminal edge to luminal edge) were recorded and standardized to body surface area. All measurements were performed in end-systole.

CMR was performed on a 1.5-T Siemens Aera scanner (Siemens Medical Solutions, Erlangen, Germany) with a 32-channel body array coil with end-expiratory breath-holds from each participant. Standard balanced steady-state free precession cines of the heart and the aorta were obtained to evaluate the anatomy and volumetric function. Navigator, noncontrast 3-dimensional whole-heart magnetic resonance angiography was performed to evaluate the extracardiac anatomy and visualize the entire aorta in 3 dimensions (Figure 1). Dimensions (luminal edge to luminal edge) of the aortic valve, aortic root, sinotubular junction, and ascending aorta at the level of the right pulmonary artery were measured from the cine images, and the proximal transverse aorta, aortic isthmus, and descending aorta were measured from the multiplanar reformatted magnetic resonance angiography by the use of cmr[42] (Circle Cardiovascular Imaging, Calgary, Canada). Measurements were standardized by body surface area to determine z scores, and the aorta was considered dilated if a z score of greater than 2 was obtained. The aortic size index (cm/m^2) also was calculated. In addition to aortic measurements, the presence of BAV, CoA, PAPVR, and left superior vena cava (LSVC) was noted on both modalities.

A pediatric cardiologist or radiologist with training in interpretation of CMR assessed and reported the images. All previous echocardiograms also were reviewed. The principal investigator then read each report to see whether there were differences in the reported anatomical cardiac lesions (BAV, CoA, LSVC, PAPVR) or the presence of aortic dilatation (root, ascending, or descending aorta) between the imaging modalities.

Statistical Analyses

Descriptive statistics were used to analyze the data. Continuous data were expressed as medians with ranges. Z scores of body mass index (BMI), height, and blood pressures were calculated and represented as a mean. The frequency of observed cardiac lesions on both imaging modalities was analyzed, and any discrepancy between the echocardiogram and CMR findings was noted.

Results

All 26 patients who were approached agreed to participate in the study. One participant turned 18 years of age before both imaging modalities could be obtained, and a second participant was excluded because her imaging modalities were more than 3 years apart, leaving a total of 24 participants. All participants tolerated CMR without sedation or complication.

A mosaic genotype of Turner syndrome was found in 13 of 24 (54%) participants. Three participants had previous cardiac surgery for CoA repair. No participant had preexisting hypertension. The blood pressures obtained at the time of imaging revealed 6 participants with elevated systolic blood pressure. On review of the previous clinic visit, however, they were all normotensive. Sixteen of 24 participants (66%) had a BMI in the normal range, 4 of 24 (17%) were considered overweight, and 4 of 24 (17%) were obese.

The median time between imaging modalities was 74 days (0-739). Normal cardiac anatomy was identified in 9 of 24 (38%) participants on both echocardiogram and CMR. The remaining 15 of 24 (62%) had a cardiac lesion identified on either echocardiogram or CMR (Figure 2; available at www.jpeds.com). Of the 15 participants with a cardiac abnormality, only 9 of 15 (60%) had the same lesion(s) described on both echocardiography and CMR. These lesions included 5 BAV, 5 AoD, 3 LSVC, and 1 PAPVR. The 3 participants with more than 1 cardiac lesion had all

Table I. Clinical characteristics of study participants with Turner syndrome

Age at investigation, y	13.3 (9.0-17.9)*
Time between echocardiogram and CMR, d	74 (1-739)
BMI, z score	0.75 (+/− 1.07)
BSA, m^2	1.31 (0.83-1.90)
Height, z score	1.33 (+/− 1.23)
SBP, z score	1.03 (+/− 1.16)
DBP, z score	0.67 (+/− 1.02)
Previous cardiac surgery	3/24 (13%)
45 XO karyotype	11/24 (46%)
Neck webbing	12/24 (50%)
Growth hormone therapy	17/24 (71%)
Estrogen-replacement therapy	8/24 (34%)
Thyroid-replacement therapy	8/24 (34%)

BSA, body surface area; *DBP*, diastolic blood pressure; *SBP*, systolic blood pressure.
*Continuous variables are represented as medians (range); z scores are represented as means (SD); categorical variables are represented as frequencies.