VIA MEDICA

ORIGINAL ARTICLE

Folia Morphol.
Vol. 80, No. 3, pp. 583–589
DOI: 10.5603/FM.a2020.0100

ISSN 0015–5659
eISSN 1644–3284
journals.viamedica.pl

Which morphological abnormalities better define the elongation of transverse aortic arch: a magnetic resonance angiography study

H. Yiğit, E. Ergün, P.N. Koşar

Department of Radiology, University of Health Sciences, Faculty of Medicine, Ankara Health Practice and Research Centre, Ankara, Turkey

[Received: 19 June 2020; Accepted: 13 August 2020; Early publication date: 22 August 2020]

Background: *The aim of the study is to investigate the relation between morphological abnormalities that might indicate elongation of transverse aortic arch (ETA) and various aortic and thoracic measurements, and to determine which morphological criteria define the elongated transverse arch better.*

Materials and methods: *Patients under 40 years of age who underwent contrast enhanced thoracic magnetic resonance angiography were included in the study. Images were evaluated for the presence of morphological arch abnormalities such as late take off (LTO) of left subclavian artery (LSA), flattening of the arch, and kinking at the posterior or anterior contour of the lesser curvature. Various aortic and thoracic measurements, including the distance between the orifices of the left common carotid artery (LCCA) and LSA, were made. Statistical relation between morphological abnormalities and these measurements was analysed. The effect of morphological abnormalities and their combinations on the distance between LCCA and LSA orifices was evaluated by linear regression analysis.*

Results: *Ninety three cases were included in the study. All morphological abnormalities and most of their combinations show statistically significant relation with longer LCCA to LSA distance. The parameters that most affected this distance were combination of flattening with LTO of LSA, anterior kinking and combination of anterior kinking with both flattening and LTO, respectively.*

Conclusions: *Our study showed that the finding which best defines ETA is the combination of LTO and arch flattening. Therefore, we recommend using this combination in the diagnosis of ETA instead of the classical diagnostic criteria including combination of LTO and posterior kinking.* (Folia Morphol 2021; 80, 3: 583–589)

Key words: elongation of transverse aortic arch, cardiovascular abnormalities, anatomy, magnetic resonance angiography

INTRODUCTION

Elongation of transverse aortic arch (ETA) was first defined by Ho et al. [6]. It is the most common aortic abnormality seen in Turner syndrome with the reported frequency of 37–49%, and it is more common in adults than in younger patients [1, 4, 5, 7, 12]. ETA is not specific to Turner syndrome and can be seen in 1.1% of the population without Turner syndrome [3, 11].

Address for correspondence: H. Yiğit, MD, Associate Professor of Radiology Ankara Health Practice and Research Centre, Department of Radiology, Hacettepe Mh. Ulucanlar Cd. No: 89, TR-06280, Altındağ, Ankara, Turkey, tel; +903125953785, fax: +903123626400, e-mail: hasan.yigit@sbu.edu.tr; hayigit@hotmail.com

Ho et al. [6] defined typical characteristics of ETA as the increase in the distance between the origins of left common carotid artery (LCCA) and left subclavian artery (LSA) with flattening of transverse arch and kinking along its lesser curvature. Although their definition emphasis on the increase in the distance between the origins of LCCA and LSA it is not based on a study that directly measures this distance. Their definition of ETA included two morphological criteria: origin of LSA at a level posterior to the trachea on axial images and indentation or convex kinking in the inferior aortic contour along the course of the lesser curvature [6]. In their study and in others related to ETA, the definition of convex kinking points to the angulation in the posterior contour of the aortic arch, also known as aortic isthmus. This anomaly which is also named as "box-shaped" appearance may be associated with angulation in the anterior contour of the arch in addition to the posterior contour; however, kinking in the lesser curvature is defined as posterior kinking in the isthmic region [7]. Although Ho et al. [6] described flattening of the arch as a typical feature of ETA, they didn't add it to the two morphological criteria that they specified for the diagnosis of ETA. Similarly, except Ece et al.'s study [3], it is not clear whether flattening of the arch is used as a criterion of ETA by other studies conducted in the following years.

Mortensen et al. [8] investigated the relation between ETA and the distances between the origins of the arch branches. To the best of our knowledge their study is the only one investigating the relation between ETA and aortic measurements. In the present study we investigated the relation between each aortic morphological abnormality (and combinations of them) that may indicate ETA and various aortic measurements and thoracic diameters and we aimed to determine which morphological criteria define the elongated transverse arch better.

MATERIALS AND METHODS

The study was performed retrospectively and was approved by the institutional review board (approval number 4322). Patients under the age of 40 who underwent contrast enhanced thoracic magnetic resonance (MR) angiography between 2009 and 2019 were retrieved from picture archiving and communication system and reassessed. Informed consent was obtained from all patients prior to MR imaging.

Two 1.5 tesla MR imaging systems (Signa HDi, GE Healthcare, Milwaukee, WI, USA) with 8 channel phased array torso surface coil and (Magnetom Aera, Siemens AG, Erlangen, Germany) 18 channel phased array torso surface coil were used. MR angiography examinations were performed as three-dimensional (3D) contrast enhanced angiography or four-dimensional (4D) high temporal resolution contrast enhanced MR angiography (TRICKS, time-resolved imaging of contrast kinetics or TWIST, time-resolved angiography with interleaved stochastic trajectories). Gadolinium based contrast agent was administered with a 0.1–0.2 mmol/kg dose at a rate of 1.8 mL/s via automatic injector which was followed by 20 mL of saline with the same injection protocol. For optimal scan timing automatic triggering or fluoroscopic triggering was used in 3D contrast enhanced MR angiography. High resolution angiography images were obtained as 10–19 temporal phases.

The inclusion criteria for the study cases were being under 40 years of age and having contrast-enhanced MR angiography examination with diagnostic image quality. Patients under the age of 40 were included to avoid the effect of atherosclerotic changes on the accurate diagnosis of ETA. The main exclusion criterion was having aortic abnormalities such as interrupted aortic arch, double aortic arch etc. that could significantly change the arch morphology and prevent the evaluation of ETA. Data corrected according to body surface area (BSA) were used therefore patients whose BSA could not be calculated due to lack of height and/or weight information were excluded from the study. The cases with insufficient image quality were also excluded.

The image analysis was performed by a radiologist that has 11 years of experience in cardiovascular imaging. In contrast enhanced MR angiography both maximum intensity projection and volume rendering images were evaluated for the presence of morphological abnormalities that might indicate ETA. Origin of LSA at a level posterior to the trachea on axial images (late take off sign: LTO), flattening of the arch (loss of typical upward convexity of the arch), kinking at the posterior or anterior contours of the lesser curvature of the aortic arch were the abnormalities searched for (Fig. 1). Then aortic measurements, including the distance between the orifices of LCCA and LSA, maximum distance between ascending and descending aorta at a level caudal to the aortic arch and ascending and descending aorta diameters at the level of pulmonary trunk, were made. Antero-posterior, right-left and supero-inferior diameters of thoracic cavity were

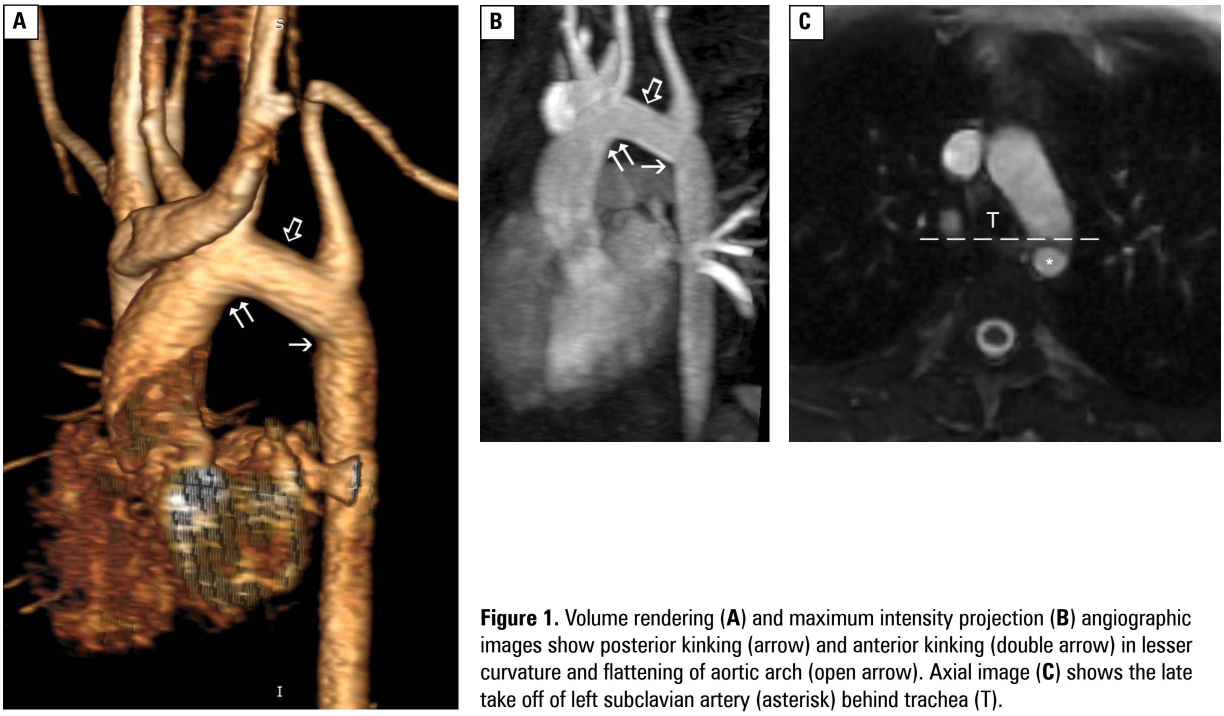

Figure 1. Volume rendering (**A**) and maximum intensity projection (**B**) angiographic images show posterior kinking (arrow) and anterior kinking (double arrow) in lesser curvature and flattening of aortic arch (open arrow). Axial image (**C**) shows the late take off of left subclavian artery (asterisk) behind trachea (T).

measured on three plane localizer images. All measurements were corrected according to BSA and this corrected data was used in statistical analysis. Mosteller formula taking into account the height and weight was used to calculate the BSA [9].

Statistical analysis

Student t test and Mann-Whitney U test were used to evaluate the relation between morphological abnormalities that indicate ETA (and their double, triple, or quadruple combinations) and aortic and thoracic measurements. We used Student t test for normally distributed variables and Mann-Whitney U test for the variables without normal distribution. Linear regression analysis of the morphological abnormalities (or their combinations) that are associated with statistically significant lengthening of the distance between LCCA and LSA orifices was performed to determine the abnormalities that most affected this distance. Statistical analysis was performed with SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, NY, USA).

RESULTS

One hundred forty-nine patients under the age of 40 who underwent thoracic aorta MR angiography were retrieved from picture archiving and communication system. Among them those who didn't have height and weight records and those who had abnormalities that significantly changed the aortic morphology and may prevent its evaluation for ETA were excluded from the study. The abnormalities found in the excluded group was as follows: double outlet right ventricle, aortopulmonary window, transposition of great arteries, coarctation or pseudocoarctation of the aorta, interrupted aortic arch, aortic aneurysm, aberrant right subclavian artery, pulmonary atresia, aortic hypoplasia, double aortic arch, aortic dissection, right sided aortic arch.

Ninety-three cases, 68 (73.1%) female and 25 (26.9%) male, aged 2–39 years were included in the study. Mean age was 17.18 ± 6.88 and median age was 16. Forty-five (48.4%) cases had Turner syndrome and 24 (25.8%) had surgically corrected tetralogy of Fallot. Thirteen (14%) cases had congenital anomalies that wouldn't interfere with the evaluation of ETA. These were situs inversus totalis, pulmonary stenosis, persistent left superior vena cava, partial anomalous pulmonary venous return, hypoplastic right ventricle, Ebstein anomaly and bicuspid aortic valve. Remaining 11 (11.8%) cases didn't have a congenital anomaly or an aortic abnormality.

The frequencies of morphological findings that indicate ETA are shown in Table 1. In Tables 2 and 3, results of the statistical analysis evaluating the relation between morphological findings of ETA with aortic measurements and thoracic diameters are given along with p values. $P < 0.05$ was considered as statistically significant. All measurements that had significant correlation with the morphologic findings were larger in those that had these morphologic findings.

When LTO or flattening or posterior kinking or any combination of them were present, the distance between LCCA and LSA was significantly longer ($p < 0.05$). In addition, there was significant association between each of these findings or any combination of them and ascending and/or descending aorta diameters ($p < 0.05$). Except posterior kinking, these morphological findings or any combination of them had significant association with one or more thoracic measurements. With anterior kinking or its combination with flattening and/or LTO, both the distance between LCCA and LSA and all thoracic diameters were significantly longer ($p < 0.05$). Some of the morphological findings were also significantly associated with the increase in the distance between ascending and descending aorta. They are also shown in Table 2.

According to multivariate linear regression analysis the parameters that most affected the distance between LCCA and LSA were a combination of flattening with LTO, anterior kinking and a combination of anterior kinking with both flattening and LTO, respectively [$F (3, 89) = 21.81$, $p = 0.00$, adjusted $R^2 = 0.40$].

Table 1. Morphological findings sorted according to frequency

Morphologic findings	Total (per cent)
PK	42 (45.2%)
LTO	39 (41.9%)
Flat.	33 (35.5%)
Flat. + LTO	23 (24.7%)
Flat. + PK	23 (24.7%)
PK + LTO	21 (22.6%)
LTO + Flat. + PK	17 (18.3%)
AK	12 (12.9%)
AK + LTO	8 (8.6%)
Flat. + AK	6 (6.5%)
PK + AK	6 (6.5%)
LTO + Flat. + AK	5 (5.4%)
Flat. + PK + AK	4 (4.3%)
LTO + PK + AK	3 (3.2%)
LTO + Flat. + PK + AK	3 (3.2%)

PK — posterior kinking; LTO — late take off; Flat. — flattening; AK — anterior kinking

DISCUSSION

To the best of our knowledge this is the first study that investigates the relation between each component of ETA (and their combinations) and thoracic diameters and various aortic measurements, including the distance between LCCA and LSA. This study also

Table 2. P values for the relation between morphological findings and measurements

Variables	LCCA to LSA distance	AA to DA distance	Thorax AP diameter	Thorax RL diameter	Thorax SI diameter	AA diameter	DA diameter
LTO	0.000*	0.196	0.057	0.029*	0.173	0.034*	0.079
Flat.	0.000*	0.037*	0.005*	0.036*	0.079	0.004*	0.005*
PK	0.025*	0.299	0.218	0.228	0.695	0.051	0.001*
AK	0.008*	0.663	0.035*	0.008*	0.036*	0.701	0.292
Flat. + LTO	0.000*	0.115	0.002*	0.004*	0.025*	0.001*	0.015*
PK + LTO	0.000*	0.009*	0.025*	0.024*	0.147	0.009*	0.012*
Flat. + PK	0.000*	0.029*	0.030*	0.049*	0.328	0.005*	0.007*
Flat. + AK	0.012*	0.373	0.047*	0.006*	0.033*	0.254	0.107
AK + LTO	0.009*	0.373	0.015*	0.002*	0.016*	0.480	0.150
PK + AK	0.133	0.975	0.200	0.122	0.326	0.467	0.164
LTO + Flat. + PK	0.000*	0.029*	0.003*	0.004*	0.037*	0.010*	0.006*
LTO + Flat. + AK	0.023*	0.283	0.046*	0.007*	0.012*	0.201	0.066
LTO + PK + AK	0.215	0232	0.134	0.050	0.263	0.373	0.170
Flat. + PK + AK	0.107	0.353	0.135	0.043*	0.440	0.443	0.256
LTO + Flat. + PK + AK	0.215	0.232	0.134	0.050	0.263	0.355	0.158

*Statistically significant relation; LCCA — left common carotid artery; LSA — left subclavian artery; AP — antero-posterior; RL — right-left; SI — supero-inferior; AA — ascending aorta; DA — descending aorta; PK — posterior kinking; LTO — late take off; Flat. — flattening; AK — anterior kinking

Table 3. Relation between morphological findings and left common carotid artery (LCCA) to left subclavian artery (LSA) distance measurements

Variables	LCCA to LSA distance [mm/m^2] (mean ± standard deviation)		
	Positive	Negative	P
LTO	10.83 ± 5.69	6.62 ± 3.27	0.000*
Flat.	11.99 ± 4.88	6.41 ± 3.62	0.000*
PK	9.61 ± 5.39	7.38 ± 4.23	0.025*
AK	11.39 ± 4.06	7.94 ± 4.87	0.008*
Flat. + LTO	13.58 ± 4.90	6.68 ± 3.51	0.000*
PK + LTO	12.24 ± 5.63	7.26 ± 4.05	0.000*
Flat. + PK	11.99 ± 5.38	7.20 ± 4.11	0.000*
Flat. + AK	12.72 ± 3.52	8.09 ± 4.84	0.012*
AK + LTO	12.58 ± 4.26	7.99 ± 4.78	0.009*
PK + AK	10.08 ± 2.93	8.27 ± 4.99	0.133
LTO + Flat. + PK	13.41 ± 5.45	7.26 ± 3.99	0.000*
LTO + Flat. + AK	12.88 ± 3.91	8.13 ± 4.83	0.023*
LTO + PK + AK	10.65 ± 3.40	8.31 ± 4.93	0.215
Flat. + PK + AK	10.97 ± 2.85	8.27 ± 4.94	0.107
LTO + Flat. + PK + AK	10.65 ± 3.40	8.31 ± 4.93	0.215

*Statistically significant relation; PK — posterior kinking; LTO — late take off; Flat. — flattening; AK — anterior kinking

evaluates the anterior kinking of aortic arch which wasn't mentioned in the previous studies.

Ho et al. [6] hypothesized that there may be a disproportion between thoracic cage and great vessel development and this may be the cause of great vessel abnormalities in Turner syndrome; however, contrary to what they expected, they found several thoracic cavity dimensions corrected according to BSA to be higher in these patients when compared to the control group [6]. Their study demonstrated a significant association only between thoracic antero-posterior diameter and ETA; however, in our study we found statistically significant relation between morphological findings that classically define ETA (flattening is included or not) and all thoracic diameters. In addition, we observed a significant association between one or more thoracic diameters and each component of ETA mentioned in its definition by the present study. Anterior kinking, which was first defined by our study, and its combination with flattening and/or LTO were also found to be significantly associated with thoracic diameters. We also found an association between some of the findings of ETA (and their combinations) and the increase in distance between ascending and descending aorta.

Mortensen et al. [8] investigated the relation between ETA and the distance between LCCA and LSA and between innominate artery and LSA in adult Turner syndrome patients. They accepted a combination of posterior kinking and LTO as the diagnostic criteria of ETA. These distances which were not corrected according to BSA were found to be significantly higher in ETA patients when compared to the ones without ETA. Except ours this is the first and the only study which shows that the combination of posterior kinking and LTO indicate a transverse arch that is really elongated. In our study, in which morphological findings were detailed and each morphological finding and their various combinations were investigated separately, each morphological finding that might indicate ETA and most of their double or triple combinations were found to be associated with the increase in the distance between LCCA and LSA. Multiple regression analysis showed that a combination of LTO and flattening had the greatest association with the increase in this distance. Interestingly, posterior kinking and associated combinations which are among the diagnostic criteria of ETA had lesser association with this distance. Instead of posterior kinking, anterior kinking and its combination with flattening and LTO had greater association with the increase in distance between LCCA and LSA. However, in our study group anterior kinking was much less common than the other three main findings, and this may have affected the results of the statistical analysis of anterior kinking and related combinations. Since the combination of LTO and flattening has the greatest association with the increase in the distance between LCCA and LSA, we think that the combination of LTO and flattening should be evaluated instead of the combination of posterior kinking and LTO when investigating ETA.

In the present study we also evaluated the relation between aortic measurements and morphological findings of ETA. Morphological findings and most of their combinations were significantly associated with increased ascending and descending aortic diameters. In the previous studies conducted on patients with Turner syndrome association of ETA with aortic dilatation has been mentioned; however, those studies do not directly evaluate the relation between ETA and aortic diameters [5]. In line with our study, Mortensen et al. [8] reported significant association between the diameter of descending aorta and ETA; however, they didn't use aortic measurements that were corrected according to BSA. They reported that the distance between innominate artery and LSA showed a positive correlation with ascending and descending aorta diameters in adult patients with Turner syndrome, but this correlation was not observed in the control group. In Kim et al.'s study [7] the diameter of aortic sinus and descending aorta were found to be higher in patients with ETA; however, they didn't find a relation between standardised Z-scores of aortic diameters and ETA [7]. Although we did not include patients with aortic aneurysms in our study group, it should be taken into consideration that in our heterogeneous study group there may be different factors affecting aortic diameters which may hinder the evaluation of the relationship between aortic diameters and presence of ETA.

The clinical significance of ETA which is the most frequent aortic abnormality observed in Turner syndrome is controversial. It is thought that the presence of ETA alone does not have a clinical significance but may be an indicator for an abnormal wall structure prone to dilatation and maybe dissection [1, 5]. The studies investigating the effects of aortic abnormalities on blood flow revealed changes in flow characteristics of the arch in patients with ETA [2, 10]. Systolic and diastolic blood pressures in patients with ETA are also reported to be significantly higher when compared to the ones without ETA [6].

Limitations of the study

The present study has some limitations. First, morphological findings, especially flattening of the arch, were determined based on a subjective assessment. Second, evaluation was performed by only one observer; therefore, interobserver variability was not calculated. Third, majority of paediatric and young adult patients who underwent thoracic MR angiography at our centre had Turner syndrome, hence the frequency of morphological abnormalities in the aortic arch cannot be adapted to the general population. However, being frequency of ETA high in the present study population enabled us to evaluate the morphological findings indicating ETA in detail. Although our study group has cases with normal MR angiography findings, it is a limitation that we do not have a control group consisting entirely of healthy volunteers. There may be unpredictable factors that may affect aortic and thoracic diameters in these patients even if they didn't have ETA or morphological findings indicating ETA.

CONCLUSIONS

Although classical diagnostic criteria of ETA include LTO of LSA and kinking at the posterior contour of aortic arch, our study showed that the finding which has the greatest association with ETA is the combination of LTO and arch flattening. Posterior kinking and associated combinations are associated with the increase in distance between LCCA and LSA less than anterior kinking and associated combinations. Therefore, we recommend using the combination of LTO and arch flattening in the diagnosis of ETA instead of the classical diagnostic criteria including the combination of LTO and posterior kinking.

Conflict of interest: None declared

REFERENCES

1. Bondy CA. Turner Syndrome Study Group. Care of girls and women with Turner syndrome: a guideline of the Turner Syndrome Study Group. J Clin Endocrinol Metab. 2007; 92(1): 10–25, doi: 10.1210/jc.2006-1374, indexed in Pubmed: 17047017.
2. Chen J, Gutmark E, Mylavarapu G, et al. Numerical investigation of mass transport through patient-specific deformed aortae. J Biomech. 2014; 47(2): 544–552, doi: 10.1016/j.jbiomech.2013.10.031, indexed in Pubmed: 24210472.
3. Ece B, Yiğit H, Ergün E, et al. Elongated transverse aortic arch in subjects without turner syndrome: A preliminary comput-

ed tomography study. Clin Anat. 2018; 31(6): 887–890, doi: 10.1002/ca.23209, indexed in Pubmed: 29770485.

4. Granger A, Zurada A, Zurada-Zielińska A, et al. Anatomy of turner syndrome. Clin Anat. 2016; 29(5): 638–642, doi: 10.1002/ca.22727, indexed in Pubmed: 27087450.
5. Gutmark-Little I, Backeljauw PF, Gutmark-Little I, et al. Partial anomalous pulmonary venous return is common in Turner syndrome. J Pediatr Endocrinol Metab. 2012; 25(5-6): 435–440, doi: 10.1515/jpem-2012-0046, indexed in Pubmed: 22876535.
6. Ho VB, Bakalov VK, Cooley M, et al. Major vascular anomalies in Turner syndrome: prevalence and magnetic resonance angiographic features. Circulation. 2004; 110(12): 1694–1700, doi: 10.1161/01.CIR.0000142290.35842.B0, indexed in Pubmed: 15353492.
7. Kim HK, Gottliebson W, Hor K, et al. Cardiovascular anomalies in Turner syndrome: spectrum, prevalence, and cardiac MRI findings in a pediatric and young adult population. Am J Roentgenol. 2011; 196(2): 454–460, doi: 10.2214/AJR.10.4973, indexed in Pubmed: 21257900.
8. Mortensen KH, Hjerrild BE, Andersen NH, et al. Abnormalities of the major intrathoracic arteries in Turner syndrome as revealed by magnetic resonance imaging. Cardiol Young. 2010; 20(2): 191–200, doi: 10.1017/S1047951110000041, indexed in Pubmed: 20307329.
9. Mosteller RD. Simplified calculation of body-surface area. N Engl J Med. 1987; 317(17): 1098, doi: 10.1056/NEJM198710223171717, indexed in Pubmed: 3657876.
10. Prahl Wittberg L, van Wyk S, Fuchs L, et al. Effects of aortic irregularities on blood flow. Biomech Model Mechanobiol. 2016; 15(2): 345–360, doi: 10.1007/s10237-015-0692-y, indexed in Pubmed: 26104133.
11. Yiğit H, Ergün E. Elongation of transverse aortic arch; not specific for Turner Syndrome. Clin Anat. 2017; 30(5): 555––556, doi: 10.1002/ca.22816, indexed in Pubmed: 27935115.
12. Yiğit H, Önder A, Özgür S, et al. Cardiac MRI and 3D contrast-enhanced MR angiography in pediatric and young adult patients with Turner syndrome. Turk J Med Sci. 2017; 47(1): 127–133, doi: 10.3906/sag-1511-3, indexed in Pubmed: 28263479.