

Normative reference values of major thoracic arterial vasculature in Turkiye

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ABSTRACT

OBJECTIVE: The aim of this study was to determine normative reference values for major thoracic arterial vasculature in Turkiye and to evaluate differences according to age and gender.

METHODS: Low-dose unenhanced chest computerized tomography images acquired with pre-diagnosis of COVID-19 between March and June 2020 were evaluated retrospectively. Patients with known chronic lung parenchymal disease, pleural effusion, pneumothorax, chronic diseases such as diabetes, hypertension, obesity, and chronic heart diseases (coronary artery disease, atherosclerosis, congestive heart failure, valve replacement, and arrhythmia) were excluded from the study. The ascending aorta diameter (AAD), descending aorta diameter (DAD), aortic arch diameter (ARCAD), main pulmonary artery diameter (MPAD), right pulmonary artery diameter (RPAD), and the left pulmonary artery diameter (LPAD) were measured in the same sections by standardized methods. The variability of parameters according to age (<40 years; ≥40 years) and gender (male to female) was evaluated by statistical methods. The Student's t test was used to compare the normal distribution according to the given quantitative age and gender, while the data that did not fit the normal distribution were compared with the Mann-Whitney U test. The conformity of the data to the normal distribution was tested with the Kolmogorov-Smirnov, Shapiro-Wilk test, and graphical examinations.

RESULTS: Totally 777 cases between the ages of 18–96 (43.80±15.98) were included in the study. Among these, 52.8% (n=410) were male and 47.2% (n=367) were female. Mean diameters were 28.52±5.13 mm (12–48 mm in range) for AAD, 30.83±5.25 mm (12–52 mm in range) for ARCAD, DAD 21.27±3.57 mm (11–38 mm in range) for DAD; 23.27±4.03 mm (14–40 mm in range) for MPAD, 17.27±3.19 mm (10–30 mm in range) for RPAD, and 17.62±3.06 mm (10–37 mm in range) for LPAD. Statistically significantly higher values were obtained in all diameters for cases over 40 years of age. Similarly, higher values were obtained in all diameters for males compared to females.

CONCLUSION: The diameters of all thoracic main vascular structures are larger in men than in women and increase with age.

Keywords: Ascending aorta diameter; descending aorta diameter; left pulmonary artery; main pulmonary artery; right pulmonary artery.

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Major thoracic arterial vasculature consists of the thoracic aorta and the main pulmonary trunk as well as their branches. Acute and chronic pathologies involv-

ing this vasculature are of vital importance. The current literature generally focuses on evaluating the relationship between abdominal aorta and cardiovascular risk, and

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studies on thoracic aorta are relatively limited. Similarly, studies on the pulmonary artery (PA) normative diameters are scarce, with the highest number of cases reported by Framingham Heart Study which was conducted on different patient groups and healthy individuals (n=706) [1]. To fill this gap in the literature, we aimed to establish the reference values for the different parts of aorta (the ascending and descending parts as well as the aortic arch) and PA (the main artery as well as the left and right branches). We also evaluated differences in vessel diameters by age and gender. The high volume of chest computerized tomographs (CTs) performed in otherwise healthy adult population during the COVID-19 pandemic provided an adequate data source for this purpose.

MATERIALS AND METHODS

Study Population

Clinical documents of 1265 patients who underwent chest CT with suspected and/or clinical pre-diagnosis of COVID-19 in our hospital between March and June 2020 were evaluated in this study. Exclusion criteria were small airway diseases (emphysema, chronic bronchitis, chronic obstructive pulmonary disease [COPD], bronchiectasis), restrictive lung diseases, mass lesion in the lung, history of pulmonary thromboembolism (PTE), diabetes, hypertension (HT), chronic heart diseases (which can affect the diameter of the aorta), rhythm disturbances, generalized atherosclerosis, severe coronary artery disease, valvular diseases, congestive heart failure, and history of valve replacement and by-pass operations. In addition, patients with parenchymal infiltration (ground glass, crazy paving, and consolidation) affecting more than 25% of the lung parenchyma, pleural effusion and pneumothorax on chest CT were not included in the study. Apart from this, patients with Marfan syndrome and similar connective tissue diseases were not included in the study. Patients' demographic information, age, and gender were recorded. Local Institutional review board approval was obtained for this retrospective study (January 28, 2021, 2021-02/17).

Imaging Method and Image Analysis

All CT scans were performed with Siemens Somatom Sensation-Syngo CT 2009 device using a low-dose non-contrast CT protocol. Patients were scanned in the supine position during deep inspiration. The acquisition parameters were standardized as tube voltage: 140 kV, tube current: 40 mA, pitch: 1.4, FOV: 455 mm, slice thickness: 64×0.6 mm. Images were converted into 1 mm thin

Highlight key points

- The diameter of the vascular structures varies according to age and gender.
- It is possible to treat many thoracic vascular pathologies that may lead to life-threatening complications with endovascular methods.
- The variations and differentiation of the vascular structures must be taken into account in order to develop new instruments for interventional endovascular procedures.

reconstructions, and 8-mm maximum intensity projection images were also created in coronal, sagittal, and axial plans by post-processing procedures. The rules of isolation and disinfection during and after the scanning had complied.

All measurements of major thoracic arterial vascular structures were done by a single radiologist retrospectively on previously taken and reported images due to COVID-19.

Measurement Methods

The ascending aortic diameter (AAD), arcus aorta diameter (ARCAD), descending aortic diameter (DAD), main PA diameter (MPAD), right PA diameter (RPAD), and left PA diameter (LPAD) were measured.

Aortic diameters were measured from two different sections in the axial plane. Largest transverse diameter of the ascending and descending aorta was measured at the level of pulmonary bifurcation at the same level with MPAD measurement (Fig. 1A). The diameter of the arcus aorta was measured from the widest part of the lumen diameter on the axial section where the longest axis was observed (Fig. 1B) [1].

The widest diameter perpendicular to the long axis of the main PA was measured with computer calipers at the level of the PA bifurcation (Fig. 2A). The diameters of the right and left PAs were measured at the widest portion, nearly 2 cm before the branching of the lobar arteries (Fig. 2B, C) [2].

Statistical Analysis

The mean value (mean±standard deviations), age specific, and gender adjusted upper-lower normal limits of the vessels were calculated. The correlation analysis was done between AAD and MPAD and age-gender.

Number cruncher statistical system) program was used for statistical analysis. Descriptive statistical methods (average, standard deviation, frequency, ratio, minimum, and

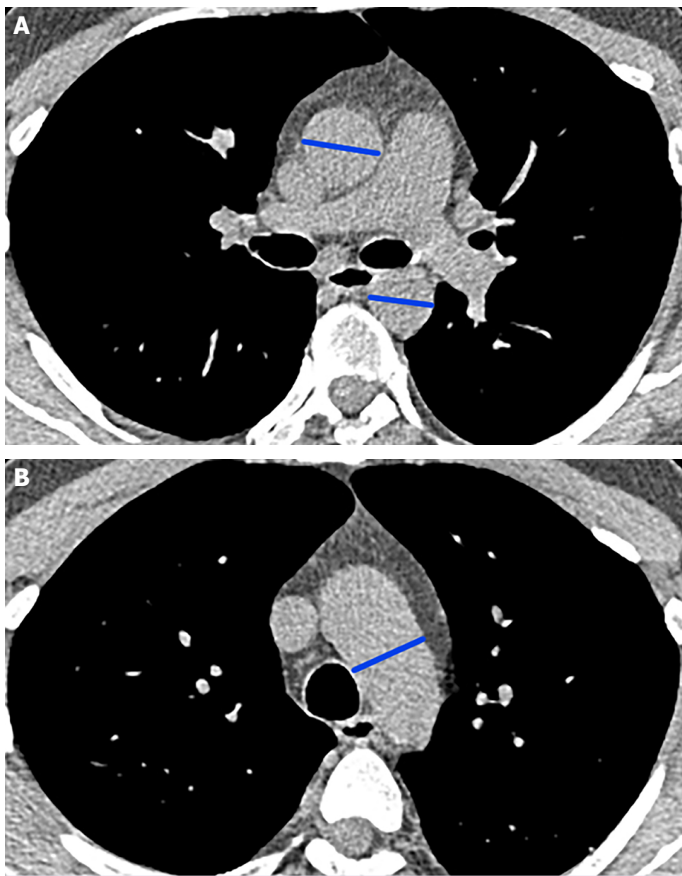


FIGURE 1. (A, B) Ascending-descending and arcus aorta measurement methods; Largest transverse diameter of the ascending and descending aorta were measured at the level of pulmonary bifurcation at the same level with main pulmonary artery diameter measurement. The diameter of the arcus aorta was measured from the widest part of the lumen diameter on the axial section where the longest axis was observed.

maximum) were used to evaluate the study data. Normal distribution was tested using Shapiro-Wilk test and graphical analysis. Student's *t* test and Mann-Whitney *U* test were used for intergroup comparisons. The statistical significance level was accepted as $p < 0.05$. In addition, 5–95th percentile values, and *t* and *z* scores were calculated for all values.

RESULTS

The study cohort included 777 cases, of which 52.8% ($n=410$) were male and 47.2% ($n=367$) were female with a mean age of 43.80 ± 15.98 (18–96). In the whole study cohort, overall mean diameters were 28.52 ± 5.13 mm (12–48 mm in range) for AAD, 30.83 ± 5.25 mm (12–52 mm in range) for ARCAD, 21.27 ± 3.57 mm (11–38 mm in

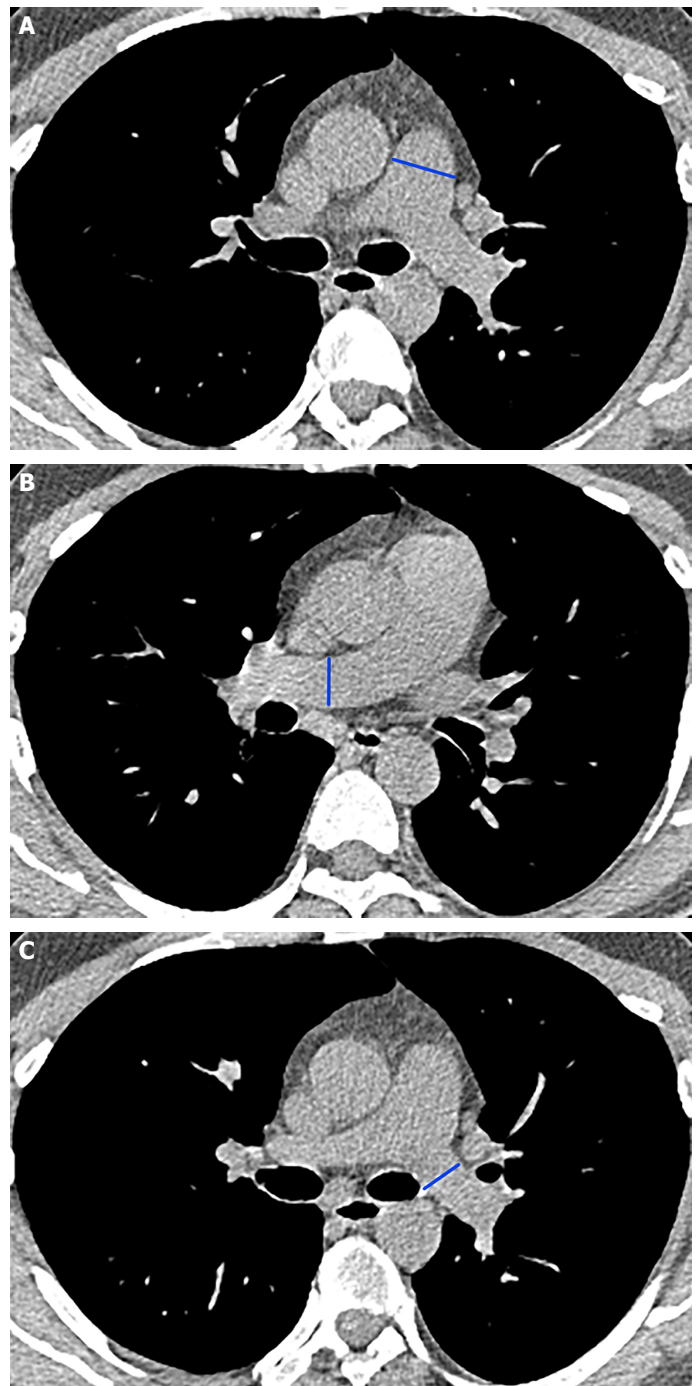


FIGURE 2. (A–C) Main pulmonary artery, right and left pulmonary artery measurement methods; the diameters of the right and left pulmonary artery were measured at the widest part, approximately 2 cm before the branching of the lobar arteries, at the bifurcation level in the main pulmonary artery axial sections.

range) for DAD; 23.27 ± 4.03 mm (14–40 mm in range) for MPAD, 17.27 ± 3.19 mm (10–30 mm in range) for RPAD, and 17.62 ± 3.06 mm (10–37 mm in range) for LPAD.

TABLE 1. Aorta and pulmonary artery diameters by age and gender

	Gender			Age			Total
	Female	Male	p	40≥age	40<age	p	
Aorta							
AAD							
Min-max (median)	13-48 (26)	12-47 (30)	t:9.010	13-48 (30)	12-44 (26)	t:-14.081	12-48 (28)
Mean±SD	26.86±4.86	30.01±4.9	^a 0.001 *	30.67±4.89	26.07±4.21	^a 0.001 *	28.52±5.13
5p-95p	20-35	23-39		23-40	20-33		21-38
ARCAD							
Min-max (median)	12-52 (30)	15-52 (32)	t:8.555	17-52 (32)	12-46 (28)	t:-13.505	12-52 (30)
Mean±SD	29.2±5.04	32.29±5.01	^a 0.001 *	32.96±5.02	28.4±4.39	^a 0.001 *	30.83±5.25
5p-95p	22-38	25-42		25-42	22-35		23-40
DAD							
Min-max (median)	12-30 (20)	11-38 (23)	t:13.865	13-38 (23)	11-32 (20)	t:-12.877	11-38 (21)
Mean±SD	19.59±3	22.77±3.38	^a 0.001 *	22.66±3.52	19.68±2.91	^a 0.001 *	21.27±3.57
5p-95p	15-25	18-29		17-29	15-25		16-27
Pulmonary artery							
MPAD							
Min-max (median)	14-40 (22)	15-40 (24)	t:6.130	15-40 (24)	14-40 (22)	t:-5.403	14-40 (23)
Mean±SD	22.35±4.11	24.09±3.79	^a 0.001 *	23.98±3.94	22.44±3.99	^a 0.001 *	23.27±4.03
5p-95p	17-29	19-30		18-32	17-30		18-30
RPAD							
Min-max (median)	10-30 (16)	11-30 (18)	Z:-7.197	10-30 (18)	10-30 (16)	Z:-6.59	10-30 (17)
Mean±SD	16.47±3.05	17.98±3.13	^b 0.001 *	17.94±3.34	16.49±2.81	^b 0.001 *	17.27±3.19
5p-95p	12-22	13-23		13-24	12-21		12-22
LPAD							
Min-max (median)	10-37 (17)	11-37 (18)	Z:-6.420	11-37 (18)	10-37 (17)	Z:-6.747	10-37 (17)
Mean±SD	16.94±2.95	18.24±3.03	^b 0.001 *	18.27±3.14	16.89±2.79	^b 0.001 *	17.62±3.06
5p-95p	13-22	14.5-24		14-24	13-21		13-23

AAD: Ascending aorta diameter; ARCAD: Aortic arch diameter; DAD: Descending aorta diameter; MPAD: Main pulmonary artery diameter; RPAD: Right pulmonary artery diameter; LPAD: Left pulmonary artery diameter; SD: Standard deviation; a: Student-t test; b: Mann Whitney U test; *: P<0.01.

The study cohort was separated into two groups based on age (40 years of age was chosen as a cutoff). Patients aged 40 and over (n=414) had significantly larger vessel diameters (AAD: 30.67±4.89 mm (13-48 mm in range), ARCAD: 32.96±5.02 mm (17-52 mm in range), DAD: 22.66±3.52 mm (13-38 mm in range), MPAD: 23.98±3.94 mm (15-40 mm in range), RPAD: 17.94±3.34 mm (10-30 mm in range), LPAD: 18.27±3.14 mm (11-37 mm in range) compared to cases below 40 years of age (AAD: 26.07±4.21 mm (12-44 mm in range), ARCAD: 28.4±4.39 mm (12-46 mm in range), DAD: 19.68±2.91 mm (11-32 mm in range), MPAD: 22.44±3.99 mm (14-40 mm in range),

RPAD: 16.49±2.81 mm (10-30 mm in range), and LPAD: 16.89±2.79 mm (10-37 mm in range).

Similarly, male patients (AAD: 30.01±4.9 mm, ARCAD: 32.29±5.01 mm, DAD: 22.77±3.38 mm, MPAD: 24.09±3.79 mm, RPAD: 17.98±3.13 mm and LPAD: 18.24±3.03 mm) had significantly larger vessel diameters compared to females (AAD: 26.86±4.86 mm (13-48 mm in range), ARCAD: 29.2±5.04 mm (12-52 mm in range), DAD: 19.59±3 mm (12-30 mm in range), MPAD: 22.35±4.11 mm (14-40 mm in range), RPAD: 16.47±3.05 mm (10-30 mm in range), and LPAD: 16.94±2.95 mm (10-37 mm in range)). Vessel diameters by age and gender are shown in detail in Table 1.

DISCUSSION

The aorta, an elastic artery with a three-layer wall structure (tunica intima, tunica media, and tunica adventitia) has to stand high luminal pressures [3]. The pulmonary arteries, on the other hand, have lower luminal pressure (2–15 mmHg) and a thin wall consisting of less elastic fibers [4]. Increased age is an important risk factor for cardiovascular diseases since degeneration occurs in the vasculature and the intimal structure of the arterial structures, vessel wall thickness, and diameter becomes affected as a result. Disruption of the intimal structure triggers thrombotic activity and subendothelial proliferation. The increase in wall thickness results in reduced elasticity and more rigid vessel [5, 6]. Thus, structural and functional changes occur in arterial structures as a result of aging [7].

The relationship between increasing diameter of the ascending aorta and mortality has been the subject of many studies [8–12]. According to the Jackson Heart study conducted on black population, the diameter of the proximal aortic diameter increased in proportion to age, weight and body surface area (BSA) in both genders, and the increase in aortic diameter was associated with mortality [11]. The international multicenter study the normal reference ranges for echocardiography-European Association of Cardiovascular Imaging evaluated 704 healthy volunteers (394 women, 310 men) with echocardiography and established the reference values for the proximal aortic diameter based on different variables. In this study, BSA, age, and gender have been shown to be the major factors affecting the diameter of the aorta, while glycaemia, cholesterolemia, and blood pressure, did not correlate with aortic dimensions in the healthy individuals [13]. Proximal aortic diameter is also affected by medications and diseases that change the stroke volume and blood pressure like heart failure, valve anomalies (aortic valve stenosis, aortic coarctation, and mitral valve disorders), HT, beta-blockers, and Digoxin [14–19]. However, small proximal aortic diameter has also been shown to be associated with mortality in patients with heart failure [10].

In the study of Hartley et al. [20], which was conducted on 1000 cases with contrast-enhanced chest CT showed a significant relationship between age and aortic diameter, while no relationship was found between gender, race, diabetes mellitus, HT, COPD, smoking, and aortic diameter. According to this study, the mean diameters of the thoracic aorta in male: 27.1 versus female: 26.0, $p=0.87$, <40 years: 22.92 mm and ≥ 40 years: 27.09 mm ($p<0.001$). On the contrary, in the study of Ja-

hangir et al. [21], with 18782 patients over 65 years old, smoking was defined as the major risk factor for abdominal aortic aneurysms. In another study conducted with CT aortogram on 120 adult Asians, mean AAD and DAD were 39.4 ± 6.7 , 34.5 ± 7.9 mm, respectively [22]. In the multi-ethnic study of atherosclerosis study conducted by Turkbey et al. [23], with 3573 cases assessed with magnetic resonance imaging (MRI), the mean ascending aorta lumen diameter was 33.4 mm in male and 30.5 mm in female. In our study, which was performed with non-enhanced chest CT on otherwise healthy individuals without cardiovascular risk factors, mean AAD and DAD were 28.52 mm and 21.27 mm, respectively, and values were higher in males than females. Our reference ranges are lower compared to the available literature. The underlying reason for the differences in reference values in our study compared to the literature might be overall lower mean age of our study cohort and absence of chronic diseases or other cardiovascular risk factors. However, performing the studies with different imaging modalities (ultrasound, echocardiography, Doppler sonography, CT, angiography, MRI), and different ethnicities might be an important reason for this difference. Except for the ascending aorta, the relationship of diameter of the aortic arch/descending aorta to age and gender has been evaluated in many studies [20, 22, 24].

The extensibility of aorta decreases with age due to structural changes such as intimal atherosclerosis, calcium accumulation, and increase in collagen content [5–7]. These atherosclerotic risk factors are strongly associated with male gender, age, smoking, and HT. While these mentioned factors are mostly risk factors for ascending aortic aneurysm (AAA), genetic predisposition plays a greater role in development of descending aortic aneurysm [25]. AAA can be fatal due to dissection or rupture [26]. Approximately 50% of patients with acute untreated ascending aortic dissection die within 48 hours, whereas mortality rates are about 15–26% in those who undergo emergency surgery [27, 28]. Elective surgery reduces mortality drastically to levels around 3–5% [29]. Likewise, the 5-year survival rate is 56% in patients with thoracic aortic aneurysm larger than 6 cm and who opted for surveillance. While the 5-year survival rate is 37% in patients undergoing emergency surgery, the 5-year survival rate is around 85% in patients who undergo elective surgical repair [30]. Therefore, early diagnosis of ascending and thoracic aortic aneurysms and elective aneurysm surgery is very important in reducing morbidity and mortality from aortic dissections or ruptures.

Although aortic diameter over 95%, based on the reference values according to age and gender, is considered aneurysm, in practice enlargement of the aortic diameter exceeding 50% of the normal range is considered ectasia, and enlargement more than 50%, that is, 1.5 times the normal diameter, is considered aneurysm [31]. Apart from age and gender, aortic diameter may differ among different races. Therefore, different cutoff values emerge in different populations for diagnosing AAA. According to our study, a 38 mm thickness, which corresponds to the 95th percentile of the diameter of the ascending aorta, can be accepted as the cutoff value for the diagnosis of AAA in Turkish population even though the generally accepted value is 50 mm [32]. According to these values, it can be concluded that aortic vessel diameters are narrower in Turkish population than in other races. Similarly, a 40 mm diameter in the arcus aorta and a 27 mm diameter (or larger) in the descending aorta can be considered as an aneurysmatic enlargement.

While generally a significant relationship is found between age and aortic diameter in the literature, the relationship between age and MPAD is controversial [1, 11, 33, 34]. In our study, we found a statistically significant relationship between not only MPAD but also left and RPAD and age ($p < 0.001$). Again, the relationship between gender and PA varies according to different studies in the literature. Akay et al. [35] showed that thoracic vascular structure dimensions are associated with age. We also found a significant relationship between age and diameter in our study ($p < 0.001$). Kuriyama et al. [36] found no significant difference in their study comparing PA diameters according to gender. However, in Edwards et al. and Karazincir et al. [33, 34] studies, MPAD has been shown to be wider in males than females. Similarly, in our study, MPAD and RPAD-LPADs were wider in males than females with a statistically significant difference (female: 22.35 mm, 16.47 mm, 16.94 mm; male: 24.09 mm, 17.98 mm, 18.24 mm; respectively, $p < 0.001$).

The upper limit of MPAD in adults is 29 mm [37]. PA aneurysm (PAA) is defined as MPAD over 40 mm [37]. PAA is another rare but deadly entity that increases MPAD. Congenital causes are the main cause of PAA and congenital heart diseases account more than half of these cases [37]. Vasculitis (Behçet's disease), connective tissue diseases (Marfan, Ehlers Danlos), and infectious diseases (syphilis, tuberculosis) are other etiological causes [37]. Early diagnosis is crucial in terms of treatment, since the majority of the cases are seen in otherwise asymptomatic young patients [38].

Pulmonary HT (pHT) is a progressive vascular disease characterized by abnormally high pressure in the pulmonary circulation and diffuse vascular proliferation [39]. While the most common cause is left heart failure, pHT can be secondary to congenital heart disease, valve disease (mitral stenosis), obstructive (COPD, emphysema, bronchiectasis) and restrictive (interstitial lung diseases) lung disease, chronic thromboembolic disease, veno-occlusive disease, and idiopathic arteritis like Nauser [40, 41]. Patients are usually asymptomatic and without treatment, pHT usually leads to mortality secondary to the right ventricular failure within 3 years after diagnosis [40]. In this aspect, timely diagnosis before clinical symptoms appear is important to reduce mortality. Although the most widely used diagnostic method is echocardiography, the gold standard method is direct measurement of pressures with the right heart catheterization. Enlargement of the PA diameter is also an indicator of increased pulmonary pressure [42]. The relationship between PA diameter and pHT has been well demonstrated by literature studies. MPAD increases with pHT and PA diameter greater than 30 mm indicates pulmonary pressures higher than 20 mmHg [36]. With chest CT images, the diameter of the main PA at the bifurcation level of 29 mm or more has a 97% positive predictivity with 89% specificity and 87% sensitivity for the diagnosis of pHT [43]. However, it is important to emphasize that diameters < 29 mm do not exclude pHT. The study by Terpenning et al. [44] which compared patients with pHT and cases with normal PA pressure using a main PA cutoff as ≥ 31.5 mm, found no relationship between MPAD and patient-dependent factors such as age, gender, body mass index, BSA, and showed that right or left PA measurement did not increase diagnostic accuracy. The study of Sanal et al. [45], showed that MPAD ≥ 28.6 mm in diagnosis of pHT had 75% sensitivity and specificity, 52% positive predictive value; whereas MPAD/AAD ratio of ≥ 1 had 59% sensitivity, 82% specificity, and 55% positive predictive value.

Increase in PA diameter is also a predictive parameter for diagnosis of PTE and is also associated with severity of the clinical status and mortality [46, 47]. At present, CT pulmonary angiography has become the preferred imaging method in the diagnosis of PTE and the gold standard diagnostic method [48]. Measurement of PA diameters in CT, which is easily accessible and frequently used in routine practice, plays a key role in diagnosis of PTE [48].

Studies on PA diameter in the literature have generally been examined in small populations and the largest cohort was the Framingham heart study which included non-contrast chest CT of 706 healthy subjects. In this aspect, our study has the highest number of healthy patients among similar studies in the literature in which different aortic and PA parameters were evaluated extensively. Considering that thousands of normal people, not only in our country but all over the world, have had chest CT with the suspicion of COVID-19 during the pandemic process that has affected the whole world since the end of 2019, it is possible to expand this cohort many times. Nevertheless, the biggest limitation of our study is absence of intravenous contrast agent. However, most of the similar studies in the literature have been done also on non-contrast CTs. As in all other CT studies without electrocardiography-gating, motion artifact secondary to cardiac pulsation and the effect of partial volume may cause vessel diameters larger than normal. This can be counted among the limitations of the study. Although there is a very heterogeneous population, cases with all pathologies-abnormalities-diseases that may affect the configuration and calibration of the heart, lung and therefore, the main vascular structures were excluded in these cases where detailed physical examination, laboratory analysis, and imaging were performed due to COVID-19.

Conclusion

In this CT study, average diameters of thoracic aorta sections and main PA and its branches are presented in an otherwise healthy Turkish population based on age and gender. This study can be used as a reference guide by radiologists and clinicians in terms of early diagnosis of vital major vascular pathologies such as aortic aneurysm and pHT-pulmonary embolism. In addition, the results of this study provide descriptive information to manufacturers in terms of tools used in endovascular treatments and prosthetic vessels.

Ethics Committee Approval: The Acibadem University Clinical Research Ethics Committee granted approval for this study (date: 28.01.2021, number: 2021-02/17).

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Authorship Contributions: Concept – DETS, ANS, OY; Design – DETS, ANS, OY; Supervision – DY, DETS, EE; Fundings – DETS, ANS, EE, OY; Materials – DETS, EE, OY; Data collection and/or processing – EE, DETS, ANS; Analysis and/or interpretation – DETS, ANS, OY, EE; Literature review – DETS, EE, OY; Writing – DETS, EE, OY, ANS; Critical review – DY.

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