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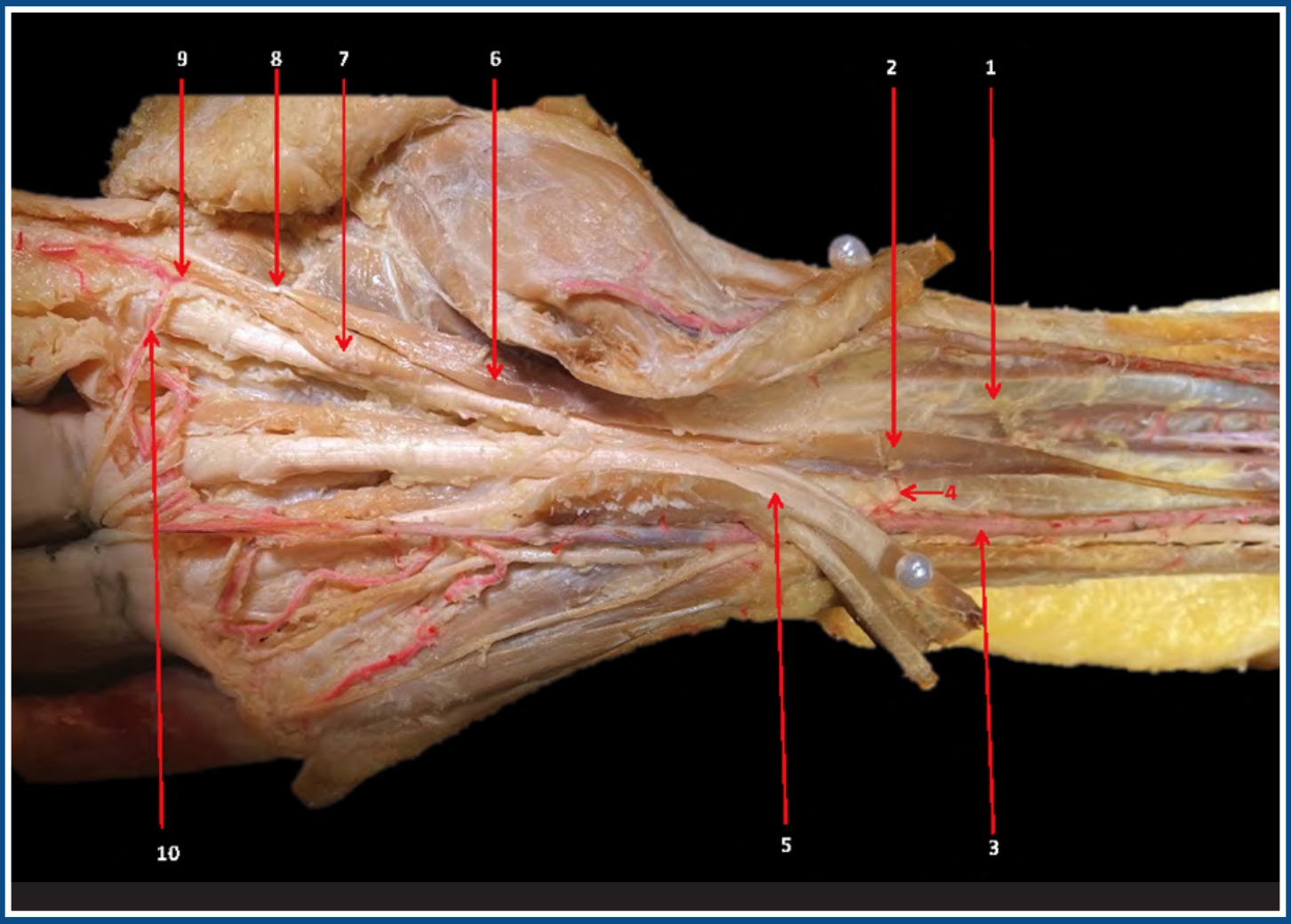

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Disparity in coronary artery dimensions in diabetic and non-diabetic population undergoing quantitative coronary angiography in South India: a 2-year prospective analysis

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SUMMARY

Diabetic subjects have higher prevalence as well as increased risk for coronary artery disease than non-diabetic counterparts. The study was aimed to seek the disparity of vessel diameters among diabetic and non-diabetic patients undergoing quantitative coronary angiography (QCA). The objectives were to compare coronary artery measurements (CAM) between diabetic and non-diabetic patients and also to find the respective segment of coronary artery affected greatest among diabetics by QCA. A cross sectional study was conducted in four cities of India after procuring the sanction for the same from the ethical committee of the pre-selected hospitals of four states in India. Informed consents were obtained. Post CABG, post PCI patients and patient being diabetic for ≥5 years were also excluded from the study.

Among total sample population, non-flow limiting coronaries were seen in 1100(27.5%) cases [167 in NFL diabetic and 933 in NFL non-diabetic group]. We had 2890 (72.2%) patients with diseased coronaries. Ten segments of the coronary arteries were taken for diameter measurements namely, LMCA, LAD (O, P), DIAG, LCx (O, P), OM, RCA (O, P), RAM. These coronary diameters were indexed to body surface area (BSA) (mean diameter mm/m^{2}BSA). For all arterial segments both indexed and non-indexed measurements of diabetic patients with NFL coronaries had significantly ($p<0.01$) smaller arterial segments except for RCA-o. Reduced dimensions after post balloon dilatations of PCI, diffused lesions can result in increased chances for in-stent restenosis among diabetics leading to poor outcome following PCI.

Key words: Coronary artery measurements – Diabetic patients – Specific variation – Gender differences – Multi-center study

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ABBREVIATIONS:

QCA - Quantitative coronary angiography

LMCA - Left main coronary artery

LAD (O, P) - Left anterior descending artery (Ostium, Proximal part)

DIAG - Diagonal

LCx (O, P) - Left circumflex coronary artery

OM - Obtuse Marginal

RCA (O, P) - Right coronary artery

RAM - Ramus

BSA - Body surface area

INTRODUCTION

The International Diabetes Federation (IDF) estimated that 415 million, i.e., 8.8% of the world's population have diabetes mellitus (DM). Among them, type 2 (T2DM) prevail of 91% and a rise to 642 million is predicted by 2040 (Atlas, 2015; Leon and Maddox, 2015). Coronary artery disease (CAD) is a major cause of death and disability among people with T2DM (Atlas, 2015, Hertzel et al., 2010). Diabetic subjects have higher prevalence as well as increased risk for CAD than non-diabetic counterparts (Singh et al., 2013; Haffner et al., 1998). Risk of CAD can be increased in T2DM patients along with associated risk factors, such as age, hypertension, dyslipidemia, obesity, physical inactivity, and stress (Kannel, 1987). Worldwide statistics of 2007 denoted 135 million people affected with diabetes. India had the leading statistics of 40.9 million people with diabetes (Sicree, 2006). T2DM is on the verge of becoming a pandemic in India (Wild et al., 2004). Statistic predictions denote that, by the year 2025, 80.9 million people will have diabetes in India, with evidence of increased prevalence of CAD among T2DM patients (Sicree, 2006; Reddy and Yusuf,1998).

It has been reported that the phenomenon of high prevalence of diabetes reported among migrant Asian Indians (Mckeigue et al., 1991) has a wide spread from urban India as well as to rural areas (Mohan et al.,2008). Increased prevalence of diabetes in urban Indians ranges from 2.1-16% from the year 1970-2006 (Ahuja, 1979; Ramachandran et al., 1988; Ramachandran et al., 2001; Mohan et al., 2006). Evidences of endothelial dysfunction, arterial stiffness and carotid intimal medial thickness (IMT) were found to be reduced in diabetes patients compared to age- and sex-matched non-diabetic subjects (Mohan et al., 2000; Ravikumar et al., 2002). An intimal medial thickness (IMT) value is a cut-off for defining carotid atherosclerosis, and studies indicated that diabetic subjects had more incidences for carotid atherosclerosis compared to non-diabetic subjects (Mohan et al., 2000).

The left main (LMCA) coronary artery and its branches were observed as narrower in diabetic patients than in non-diabetics when the diameters of both were compared using QCA. The comparisons were done after normalizing patient's BSA by Mosteller formula between two study groups to rule out the possible bias which may have an effect on coronary artery diameter (Adil et al., 2012). Marked angiographic evidence of narrowing of coronary artery segments and long segment lesions was found in diabetic patients with CAD (Stein et al., 1995). The major arteries supplying the heart are the right coronary artery (RCA) and LMCA, with left anterior descending (LAD) and circumflex artery (LCx) for LMCA as the main branches, and the right posterior descending artery (PDA) for RCA (Aricatt et al., 2022). Evidence of narrowing of lumen diameter of coronary arteries in patients with diabetes and several factors affecting the lumen diameters have been studied previously in different countries on different populations (Melidonis et al., 1999; Gui et al., 2009; Mosseri et al., 1998; Muhammad et al., 2012).

Coronary artery diameter is one of the most important factors that affect the procedure and outcome of percutaneous coronary angioplasty (PCI), as well as coronary bypass operations (CABG) (Saikrishna et al., 2006). Post angioplasty studies among diabetic patients marked an increased risk of progressive CAD and coronary artery re-stenosis after stent implantation. The predictors of in-stent re-stenosis were decreased dimensions of coronary arteries, long segment lesion, and decreased body mass index (Moses et al., 2004; West et al., 2004).

Currently, there is no other multi-center study with international recognition among South In-

dian population regarding the comparison between coronary dimensions between diabetic and non-diabetic population. The study was aimed to seek the disparity of vessel diameters among diabetic and non-diabetic patients undergoing quantitative coronary angiography (QCA). The objectives under consideration were to compare coronary artery dimensions between diabetic and non-diabetic patients and also to find the respective segment of coronary artery most greatly affected among diabetics by QCA.

MATERIALS AND METHODS

Study population

A cross-sectional study was conducted in four cities of India. Hospitals were purposely selected according to the number of cardiac patients identified by them. The age of the study subjects was given a cut-off at 75 years due to marginal benefits marked during the follow-ups. Hence, a conservative approach is proven to be appropriate for the above-mentioned age, which itself indicates a poor prognosis with an average yearly mortality rate of 33-35% (Azad and Lemay, 2014). The inclusion criteria were all patients who undergo percutaneous coronary angiographic procedure due to abnormalities in the normal cardiac parameters after obtaining their informed consent. We divided the study population into two groups. Patients who were known for more than five years diabetic or were taking oral hypoglycemic or insulin therapy were enrolled in diabetic group. In non-diabetic group patients had no previous history of diabetes mellitus or patients with a controlled (an ideal glycated hemoglobin levels (HbA1c) of 48 mmol/mol (6.5%) or below) diabetic history less than five years (Srinivasan et al., 2016). Diabetic history was confirmed when patient is taking oral anti hypoglycemic drugs, insulin or recent fasting blood sugar (FBS >126 mg/dl) on two consecutive occasions. Lipid levels were obtained from hospital laboratory.

Exclusion criteria were patients with a previous history of CABG and recanalized normal looking coronary arteries with or without in-stent restenosis coronary arteries as well as patients being diabetic for five or more than five years for assessing non flow limiting (NFL) coronary artery dimensions (Srinivasan et al., 2016). The sample size was estimated by consulting a statistician and using the statistical software G* Power 3.0.10 and a 1100 NFL patients among total sample population of 4000 consecutive patients were included in the study by convenience sampling [167 in NFL diabetic and 933 in NFL non-diabetic group]. All ethical principles for human research were followed and Ethical approval was obtained from the Institutional Ethics Committee of all the hospitals from which data were collected.

Database pooling and statistical analysis

i. LMCA and RCA along with its main branches were assessed for the vessel morphology at the ostium (o) and proximal (p) segment among normal cases by stenosis analysis program. Ten segments of the coronary arteries were taken for diameter measurements namely, LMCA, LAD (o, p), diagonal (DIAG), LCx (o, p), obtuse marginal (OM), RCA (O, P), ramus (RAM). This program had incorporated an automated coronary analysis package of the Innova 2100 IQ Cath at an AW4.4 workstation or of the Siemens QCA – Scientific coronary analysis. The gender-wise categorization of the data was done to denote the mean differences in the artery measurements.

ii. Patient's anthropometric measurements were done using the fore mentioned relevant equipments. Body mass index (BMI) and body surface area (BSA) were calculated. BMI was calculated by the relevant formula weight in kilograms divided by the square of height in meters. BSA was calculated from patient's height and weight measurements using Mosteller's formula. The diameters of the ten segments of coronary artery from angiogram study samples were indexed (adjusted) to BSA (mean diameter mm/m^2BSA).

Calibration assessments from QCA (Hermiller et al., 1992) systems were carried out by the same method in which the coronary catheter was employed for angiography procedure. This was used as calibrating the object by automated edge detection technique resulting in corresponding calibration factors (mm/pixel) and the vessel contour were detected by operator independent edge detection algorithms. Angiographic views were

selected for calibration assessment by minimizing the foreshortening of the coronary segments by separating them from adjacent intervening structures. Confounding variable was controlled by matching characteristic of the two groups such as age, gender, BMI and BSA. All QCA images were also reviewed by two cardiologists from each center for the definition of normal vessels and for the subsequent quantitative analysis by the double blinding method. Both the observers from each center were blinded regarding the patient identity, and interobserver variability was accounted during statistical analysis, and bias was controlled. All information was recorded on a standard proforma. All arterial dimensions were compared between the diabetic (N=167) and non-diabetic group (N=933) using Welch's t-test. Statistical analysis of the present study was done using GraphPad Prism v9.

RESULTS

Based on QCA analysis, among total sample population, NFL coronaries were seen in 1100 (27.5%) cases (167 in NFL diabetic and 933 in NFL non-diabetic group). We had 2890 (72.2%) patients with diseased coronaries. Physical and demographic parameters were assessed. The mean age of the patients was 54.50 ± 5.5 vs. 55.9 ± 7.7 years (range 30-75 years) between the diabetic and non-diabetic groups. BMI and BSA of the samples were calculated. Mean BMI in diabetic and non-diabetic groups was 26.9±2.5 vs. 25.2±3.5 kg/m^2 (range 33.30-21.26 kg/m^2). Mean body surface area (BSA) was 2 ± 0.09 m^2 vs. 1.82 ± 0.13 m^2 (range 2.1-1.42 m^2) in diabetic and non-diabetic groups.

For all arterial segments, both indexed and non-indexed measurements of diabetic patients with NFL coronaries had significantly ($p<0.01$) smaller arterial segments compared to the non-diabetic group with NFL coronaries except

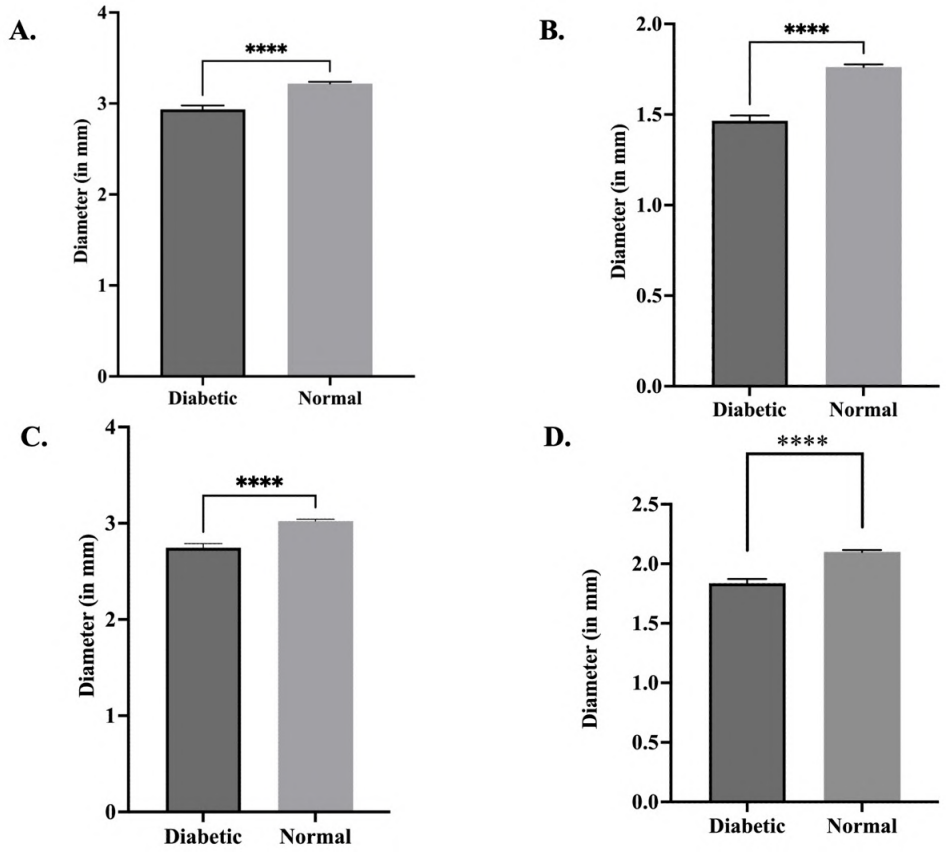

Fig. 2.- Difference in arterial dimensions between diabetic and non-diabetic patients. **A**: Difference in diameter for LAD-p. **B**: Difference in diameter for DIAG. **C**: Difference in diameter of LCX-p. **D**: Difference in diameter of OM.

Welch's t-test was performed between the between diabetic and non-diabetic patients and *p*-value<0.05 was considered significant. **** designates *p*-value <0.0001

Table 1. Differences in non-indexed coronary arterial dimensions between diabetic and non-diabetic patients.

Sl.no.	CAS	Mean diameter among NFL diabetic patients (N=167)		Mean diameter among NFL non-diabetic patients (N=933)		MD +/- SEM	Welch's-t-value	p-value
		n	CAM (mm)	n	CAM (mm)			
1.	**LMCA**	167	3.97± 0.64	927	4.16 ± 0.69	0.19 ± 0.05	3.55	0.0005
2.	**LAD-o**	167	2.95± 0.59	930	3.18 ± 0.62	0.22 ± 0.05	4.53	<0.0001
3.	**LAD-p**	167	2.94 ± 0.56	929	3.22 ± 0.59	0.28 ± 0.04	6.02	<0.0001
4.	**DIAG**	167	1.46± 0.39	912	1.76 ± 0.44	0.29 ± 0.03	8.91	<0.0001
5.	**LCX-o**	167	2.88 ± 0.67	933	3.04 ± 0.62	0.16 ± 0.05	3.02	0.0028
6.	**LCX-p**	167	2.75 ± 0.55	931	3.02 ± 0.62	0.27 ± 0.04	5.84	<0.0001
7.	**OM**	166	1.84 ± 0.46	915	2.10 ± 0.50	0.26 ± 0.03	6.64	<0.0001
8.	**RCA-o**	167	3.02± 0.75	917	3.15 ± 0.66	0.12 ± 0.06	1.97	0.0492
9.	**RCA-p**	167	2.78 ± 0.67	926	3.05 ± 0.65	0.27 ± 0.05	4.93	<0.0001
10.	**RAM**	----	----	102	2.25 ± 0.49	----	----	----

The CAM's been taken based on QCA reports and is represented as mean difference± Standard error mean of the diabetic and non-diabetic patient samples.
Statistical test used: *Welch's-t test.* $p<0.001^{***}$indicates very highly significant difference, $p<0.01^{**}$indicates highly significant difference, $p<0.05^{*}$indicates significant difference, p>0.05 indicates no significant difference between non- indexed NFL CAM of diabetic and non-diabetic patients.
Abbreviations: CAS – Coronary artery segments, N- samples, n- number of samples were CAM was measurable out of total N, CAM – Coronary artery measurements, LMCA - Left main coronary artery, LAD (O, P) - Left anterior descending artery (Ostium, Proximal part), DIAG - Diagonal branch of LAD, LCx (O, P) - Left circumflex coronary artery (Ostium, Proximal part), OM - Obtuse Marginal branch of LCx, RCA (O, P) - Right coronary artery (Ostium, Proximal part), RAM – Ramus branch of coronary artery, QCA- Quantitative coronary angiography.

for RCA-o, where the mean difference between the two groups was not statistically significant (Table 1).The most striking difference between the two groups were observed for LAD-p (mean difference=0.28 mm, t= 6.023, P<0.0001, Fig. 2A), DIAG (mean difference=0.3 mm, t= 8.906, P<0.0001, Fig. 2B), LCX-p (mean difference=0.28 mm, t= 5.849, P<0.0001, Fig. 2C), and obtuse marginal (mean difference=0.26 mm, t= 6.641, P<0.0001, Fig. 2D).

Gender-wise analysis of coronary artery dimensions in the present study showed that, except for the OM branch of LCx and RAM branch of LCA, all other eight segments taken for analysis had significant differences between the coronary artery measurements (CAM) among males and females in both diabetic and non-diabetic groups. The differences were highly significant (p < 0.001). Consistent with the previous studies, we found that men are highly significantly more prone to diabetes than women (Fig. 1). However, this difference disappeared when diameters were indexed to BSA in both groups. The diameters of the normal non-indexed CAS were not measurable in certain segments due to anatomical peculiarities.

DISCUSSION

Diabetic subjects have higher prevalence, as well as increased risk for CAD than non-diabetic counterparts (Singh et al., 2013; Haffner et al., 1998). Low control of diabetes and hypertension has been reported in a study in India (Shashank et al., 2008). The improved awareness and enhanced treatment can control cardiovascular risk factors in participants with known diabetes (Brown, 2013; Gupta, 2014).

CAD in diabetic patients is found to be more severe and follow a more diffused pattern than non-diabetics (Melidonis et al., 1999; Gui et al., 2009). This could be accounted for in various pathophysiological mechanisms in diabetic patients such as hyperglycemia, hyperinsulinism and insulin resistance (Melidonis et al., 1999). In addition, narrowing of coronary artery should also be viewed as an important factor for the increased prevalence of CAD among diabetics. Although a

number of prior studies have concluded that the disparity in coronary artery diameters between diabetics are non-diabetics is significant, there have been contradictory opinions regarding this concept as well. In the present study, there was no significant difference in the mean ages, BMI and BSA between the diabetic and non-diabetic groups. This is similar to the studies of Melidonis et al.(1999), and Gui et al (2009).

Angiographic comparison of different segments of the coronary artery revealed a tendency towards narrowing of artery diameters among diabetic patients with CAD (Stein et al., 1995). In the present study, all arterial segments of diabetic patients have significantly (P<0.01) smaller arterial segments compared to the NFL non-diabetic group, except RCA-o segment, where the mean difference between the two groups was not statistically significant. This contradicts the postulated theory that the predominance of stenosis in RCA can be due to the sluggish blood flow which coexists in RCA in comparison to other vessels, and the increased plasma viscosity among diabetics. The present study reports the severity of stenosis is the same for both left and right systems of coronary in patients with diabetes. In contrast, few authors from different countries have found the RCA to be significantly more frequently involved towards narrowing of artery diameters among diabetic patients with CAD (Adil et al., 2012; Melidonis et al., 1999; Gui et al., 2009; Mosseri et al., 1998; Kabir et al., 2017).

There is also evidence of smaller luminal diameter of the LAD among diabetics (Adil et al., 2012; Gui et al., 2009; Mosseri et al., 1998; Muhammad et al., 2012; Kabir et al., 2017) and distal LCx (Adil et al., 2012). The present study also indicates that the most striking differences in artery dimensions between the NFL diabetic and NFL non-diabetic group were observed for LAD-p (mean difference=0.28 mm, P<0.0001) with its DIAG branch (mean difference=0.3 mm, P<0.0001). In contrast, however, in a Greek Caucasian population, no statistically significant difference in vessel diameters between diabetics and non-diabetics for all segments of LAD was found (Melidonis et al., 1999). We had differences in artery dimensions between the NFL diabetic and NFL non-diabetic group of LCX-p (mean difference=0.28 mm, P<0.0001). However, some studies indicated the proximal LCx dimensions in diabetics and non-diabetics had no statistically significant difference between

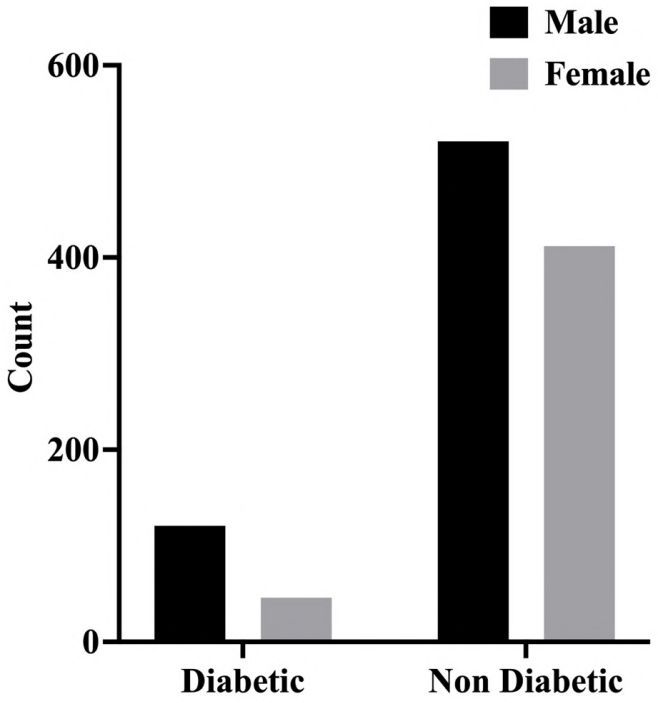

Fig. 1.- Gender specific difference in coronary arterial dimensions between diabetic and non-diabetic patients.

the two groups (Melidonis et al., 1999; Muhammad et al., 2012; Pajunen et al., 1997).

Gender-wise analysis of coronary artery dimensions in the present study showed that except for the OM branch of LCx and RAM branch of LCA, all other eight segments taken for analysis had significant difference between the CAM among males and females in both diabetic and non-diabetic groups. In general, the CAM of the male patients was greater than females in both LCA and RCA systems. However, this difference disappeared when diameters were indexed to BSA in both diabetic and non-diabetic groups. Similarly, an important observation of most QCA procedures involving coronary artery dimension analysis has revealed that women have smaller CAM compared to men (Yang et al., 2006; Raut et al., 2017).

Coronary dimensions vary throughout its length giving rise to different vessel diameters, a reference data could not be applied for comparison totally. Thus, the reduced CAM projects on its therapeutic implications, especially during revascularization procedures like CABG and PCI in diabetic patients. Reduced dimensions after post balloon dilatations of PCI, diffused lesions and prerequisite of longer stents can result in increased chances for in-stent re-stenosis and enhanced frequency of CAD among diabetics leading to poor outcome following PCI (West et al., 2004; Pajunen et al., 1997; Alonso, 2002; Fallow and Singh, 2004; Aronson and Edelman, 2010).

CONCLUSION

For all arterial segments, both indexed and non-indexed measurements of diabetic patients with NFL coronaries had significantly smaller arterial segments compared to the non-diabetic group with NFL coronaries except for RCA-o, where the mean difference between the two groups was not statistically significant.

Limitations: We could not correct the CAM of the present study for the presence of left ventricular hypertrophy, which would have enhanced the study results.

AUTHOR CONTRIBUTIONS

All authors hereby declare that their contribution was equal towards the formation of the manuscript.

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Flatfoot in the neglected age group of adolescents

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SUMMARY

The foot arches in humans are the complex musculo-skeletal-ligamentous structure that helps in shock absorption because of the elasticity and provides stability while transmitting the muscle force for walking. Primarily we observed the prevalence of flatfoot among adolescents going to college. Thereafter we determined the correlation of flatfoot with the body mass index and gender of the adolescents being studied. Footprint analysis of undergraduate students was obtained based on Harris – the Beath mat principle. Clarke's angle, Chippaux-Smirak index, and Staheli arch index were observed in the footprints. Subsequently, the correlation between the flatfoot, body mass index, and gender of the participants was assessed. The prevalence of flatfoot in college-going adolescents was 18.28% by footprint analysis, presenting a female predilection (20% of the footprint analysis) for the condition. The most valid and reliable plantar arch index for diagnosing flatfoot was the Staheli arch index, followed by the Chippaux-Smirak index having a moderate to strong correlation ($R = 0.7, 0.95$; $p < 0.05$). Only 1.1% of females and up to 2.2% of males were observed to have flatfoot and were obese. Eighteen out of a hundred (approximately one–fifth) adolescents in the studied group had flatfoot. The gender predilection for females was observed. Contradictory to the findings of the previous study, obesity was not observed as a foot arch-altering factor in adolescents.

Key words: Flatfoot – Adolescents – Body mass index – Gender – Prevalence

INTRODUCTION

The foot arches in humans are the complex musculo-skeletal-ligamentous structure that helps in shock absorption because of the elasticity and provides stability while transmitting the muscle force for walking (Aenumulapalli et al., 2017). The medial longitudinal arch (MLA) is the most prominent of all the foot arches, the height of which, when lowered, leads to flatfoot or pes planus. One of the most typical foot deformities, flatfoot, is characterized by medial rotation and plantar flexion of the talus, eversion of the calcaneus, collapsed medial longitudinal arch, and forefoot abduction (Ezema et al., 2014; Neeraj et al., 2020).

In infants, the flatfoot is observed because of the plantar pad of fat, which disappears between 2-10 years of age, and subsequently, the arch becomes prominent (Gould et al., 1989). The flatfoot in children is mostly of flexible form, which appears on

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weight bearing, while in adults, the condition is of the rigid type, which is present irrespective of the weight (Benvenuti et al., 1995; Atamturk, 2009; Medina-Alcantara et al., 2019).

The prevalence of flatfoot in children varies inversely with age (Pauk et al., 2012). As per literature, this variation is based on factors such as age, gender, weight, family history, body mass index (BMI), type of footwear, physical activity, and population being studied, and is associated with hypermobility, heel valgus, and genu valgum. The prevalence of flatfoot varies between 21% and 77% in children until six years of age, whereas in primary school children, the same decreases to 13.4-27.6% (Pfeiffer et al., 2006; Chen et al., 2009, 2011; Chang et al., 2010; Ezema et al., 2014; Pourghasem et al., 2016).

In adults, the prevalence of the pathological entity was observed to vary between 13.6% to 26.62% (Benvenuti et al., 1995; Pita-Fernández et al., 2015). The literature on flatfoot presents a bias of bimodal age group representation.

Adolescence traverses the age of biological growth period to the one with an active social role. The World Health Organization (WHO) mentions adolescence as the age group of 10-19 years, which also includes a few years of *a child* (as adopted by the Convention on the *Rights of the Child*), a few of the *youth* (15-24 years), and much of the *young people* (10-24 years) (WHO, 2014). While the beginning of adolescence has been shifted to an early age due to early puberty, the end of the same has continued into the third decade of life as per the paradigm shift in the perception regarding the beginning of adulthood based on the elongation of the education period and delayed marriage. Thus, redefining the age of adolescence as 10-24 years of age (Sawyer et al., 2018).

The literature rarely presented data on flatfoot in adolescents before the second decade of the 21st Century. The present study aims to fill this gap by observing the prevalence of flatfoot in adolescent-aged individuals and the association of BMI and gender with flatfoot in this age group, as many orthopedic deformities are often associated with obesity (Pauk et al., 2012; Rivera-Saldívar et al., 2012; Woźniacka et al., 2015).

MATERIALS AND METHODS

The participants for this cross-sectional study were undergraduate students of the medical institute. After approval by the institutional ethics committee, the study was conducted in the Department of Anatomy between July 2021 to February 2022. Only students who gave their written agreement after being informed about the procedures and had no history of foot fractures, orthopedic procedures, congenital foot abnormalities, or neuromuscular problems were permitted to participate.

Out of 257 students fitting the age criteria and consenting to participate, a sample size of 175 (85 females, 90 males) in the age group of 17-21 years (as per the redefined adolescent age group by Sawyer et al., 2018) were included in the study as per the criteria. The demographic characteristics noted for these participants were age, sex, height, and weight.

Calculation of the plantar arch index

The footprint of all participants was taken using Harris and Beath's footprinting mat. The participants were asked to stand on the apparatus's hydrophobic mat, which transferred the image of the footprint onto the white sheet present underneath it.

As a universal definition of flatfoot is not present, we accepted the clinical diagnosis of the condition as per Pfeiffer et al. (2006) to be the gold standard.

Thereafter, Staheli's planter arch index (SAI), Chippaux-Smirak index (CSI), and Clarke's angle (CA) of each participant's footprint (Fig. 1) were calculated by two different investigators as per Chen et al. (2011).

Staheli Plantar arch index (SAI) = minimum support width of center of the arch (j)/ maximum support width of heel region (h); SAI = j/h×100%.

Chippaux-Smirak index (CSI) = minimum support width of center of the arch (j)/Maximum support width of the metatarsals (r); CSI = j/r×100%.

Clarke's angle (CA) = Defined as the angle obtained by a tangent line joining the medial edges of the first metatarsal head and the heel, and

the second line that connects the first metatarsal head to the acme of the medial longitudinal arch concavity.

The validity of the above footprint parameters compared to the clinical diagnosis had been previously documented (Zuil-Escobar et al., 2018).

For measuring the weight, participants were asked to stand on a digital weighing machine (make - Philips device, Netherlands, sensitive to 100 g) without shoes and minimal formal clothing.

For measuring height, participants were asked to stand in an erect position under a stadiometer (make - Mowell, India; sensitive to 1 mm) without shoes and with the head in the Frankfurt plane.

Standard stationery was utilized to measure the lengths and angles of the footprint. To ensure the reliability of the measurements, the investigators took footprints of ten subjects (not participating in the study) of the same age group. They measured the parameters twice on two different days. The inter- and intra-class correlation coefficient values ranged from 0.77-0.94 and 0.81-0.93, respectively. Thus, a strong correlation confirmed the reproducibility of the measurements.

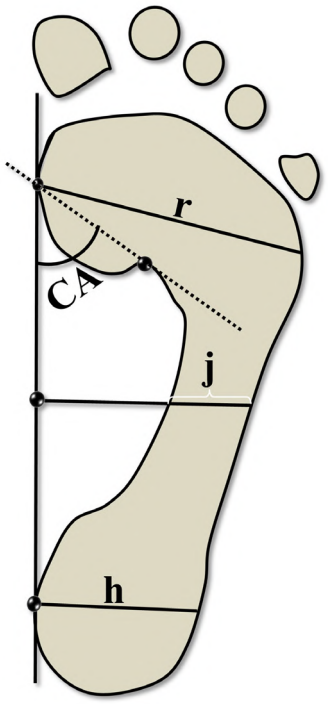

Fig. 1.- Schematic presentation of the footprint and the parameters measured. r = maximum support width of the metatarsals, j = minimum support width of center of the arch, h = maximum support width of the heel region, CA = Clarke's angle.

The data were entered in Microsoft Excel 2019 package and then transferred to Statistical Package for Social Sciences- SPSS 26.0 version for analysis. Mean and standard deviation was calculated for quantitative values, while categorical values were presented as percentages. Student paired t-test was applied to determine the p-value of the measurements on either foot. Thereafter, correlation coefficients were determined using bivariate analysis, and regression analysis was done to derive the regression equation between the pair of factors compared (y=mx + c, where m= slope, c= interception on 'y' constant).

RESULTS

The mean age of the study population was 19.37 ± 0.87 years in males and 19.21 ± 0.69 years in females (Table 1).

Table 1. The mean (± standard deviation, SD) age and BMI of the study population.

Parameters	Total (n = 175) Mean ± SD	Males (n = 90) Mean ± SD	Females (n = 85) Mean ± SD
Age	19.29 ± 0.79	19.37 ± 0.87	19.21 ± 0.69
BMI (Kg/m^2)	22.42 ± 4.11	22.52 ± 4.11	22.32 ± 4.11

The frequency of flatfoot was observed as 18.28% (n = 32) by clinical diagnosis and later by comparing the same with their footprints. The gender distribution for flatfoots was slightly more prevalent in females, with a frequency of 20% (n = 17), while that in males was 16.6% (n = 15).

As per Clarke's angle, flatfoot was observed on the left side in 8.57% (n=15, female = 9, male = 6) participants, while that on the right side was observed in 6.28% (n=11, female = 7, male = 4). For CSI, flat left foot was observed in 23.42% (n=41, female = 25, male = 16), and on the right foot the observed value was 18.85% (n=33, female = 19, male = 14). Finally, SAI presented with a flatfoot frequency of 18.29% (n = 32, female = 17, male = 15), the same as that observed clinically in the present cohort. The plantar arch indices and an-

gle had statistically significant differences concerning either foot, but gender-wise distribution was observed to be significant only for SAI (Table 2).

The Pearson's correlation coefficient (PCC) presented with significant but weak negative correlation between BMI and CA on either foots (PCC for left = -0.26, right = -0.13; p = 0.004, 0.02), while significant and weak positive correlation of BMI was observed with CSI (PCC for left and right = 0.26, p = 0.0003, 0.001) and SAI (PCC for left = 0.16 and right = 0.29, p = 0.02, 0.003) values of either foot irrespective of gender. The correlation coefficient was moderately positive for CSI and SAI on left side (PCC = 0.75, $p < 0.001$) and strongly positive for right side (PCC = 0.95, $p < 0.001$). The linear regression equation (y=mx+c) where m= slope, c= interception on 'y' constant was derived to assess the effect of SAI on CSI of both sides as the linearity could be observed between the two in the scatter plot shown in Fig. 2a, 2b. There was homoscedasticity and normality of the residuals on either side analysis. A few outliers were not significant and were included for analysis.

The present study population had 4.57% obese individuals (Table 3). When flatfoot was observed as per the BMI of the participants for the different plantar arch indexes and angles, the frequency was minimal for obese individuals (Table 4). For obese females, the frequency for flatfoot was 1.17% (n = 1) for CSI, SAI, and CA, whereas obese males had a frequency ranging from 1.1-2.2% (n = 1-2) concerning the parameters mentioned above. Comparatively, normal-weighed males (as high as 11.1%) and females (as high as 16.4%) suffered the most from flatfoot.

DISCUSSION

Prevalence of flatfoot in pediatric age-group

Flatfoot is a prevalent condition in pediatric (birth to 17 years) (Staheli et al., 1987; Gould et al., 1989; Echarri and Forriol, 2003; Pfeiffer et al., 2006; Chen et al., 2009, 2011; Coughlin and Kaz, 2009; Chang et al., 2010, 2012, 2014; Abolarin et al., 2011; Pauk et al., 2012; Rivera- Saldívar et al., 2012; Umar and Tafida, 2013; Ezema et al., 2014; Woźniacka et al., 2015; Pourghasem et al., 2016; Tong and Kong, 2016; Aenumulapalli et al., 2017; Banwell et al., 2018; Medina-Alcantara et al., 2019) and old (>40 years) age population [4,5,29]. In the age group of 3-6 years, Ecchari and Forriol (2003) reported a high flatfoot prevalence of 70%, while that observed by Pfeiffer et al. (2006) was 44%. The prevalence rate of flatfoot in the age group of 5-8 years was reported as 40% by Ecchari and Forriol (2003) and 78% by Gould et al. (1989). The high prevalence rate at a young age

Table 2. The mean (± standard deviation, SD) of different plantar arch index and angle on either foot.

Flatfoot indices and angle		Total (n = 175) Mean ± SD	t-test	Males (n = 90) Mean ± SD	Females (n = 85) Mean ± SD	t-test
Clarke's angle (CA)	Left	45.45 ± 11.42	p = 0.002	46.21 ± 10.78	44.64 ± 12.02	p = 0.33
	Right	47.05 ± 10.58		47.83 ± 9.91	46.21 ± 11.18	p = 0.34
Chippaux-Smirak index (CSI)	Left	38.11 ± 14.23	p = 0.03	36.92 ± 12.81	39.36 ± 15.49	p = 0.05
	Right	35.97 ± 13.53		36.33 ± 11.51	35.59 ± 15.37	p = 0.45
Staheli's plantar arch index (SAI)	Left	67.87 ± 24.47	p = 0.01	66.87 ± 25.32	68.94 ± 25.58	p = 0.17
	Right	65.51 ± 25.26		66.75 ± 21.92	64.21 ± 28.31	p=0.035

Table 3. The frequency (percentage, %) distribution of BMI categories.

BMI categories	Total n (%)	Males n (%)	Females n (%)
Underweight (<18.5Kg/m^2)	29 (16.57)	15 (16.6)	14 (16.47)
Normal weight (18.5-25 Kg/m^2)	106 (60.57)	52 (57.7)	54 (63.52)
Overweight (25-<30 Kg/m^2)	32 (18.28)	20 (22.2)	12 (14.11)
Obese (≥30 Kg/m^2)	8 (4.57)	3 (3.33)	5 (5.88)

Table 4. Frequency of flatfoot as per BMI of the participants with respect to the different plantar arch index and angle.

Arch Parameters	Gender (n;F= 85, M= 90)		Underweight (<18.5 Kg/m²) [n (%)]	Normal weight (18.5-25 Kg/m²) [n (%)]	Overweight (25-<30 Kg/m²) [n(%)]	Obese (≥30 Kg/m²) [n(%)]	Total no. of flat foot
CSI	Female	Left	5 (5.8)	14 (16.4)	5 (5.8)	1 (1.17)	25
		Right	3 (3.5)	12 (14.1)	3 (3.5)	1 (1.17)	19
	Male	Left	3 (3.3)	10 (11.1)	1 (1.1)	2 (2.2)	16
		Right	3 (3.3)	9 (10)	0	2 (2.2)	14
SAI	Female	Left	4 (4.7)	9 (10.6)	3 (3.5)	1 (1.17)	17
		Right	4 (4.7)	9 (10.6)	3 (3.5)	1 (1.17)	17
	Male	Left	4 (4.4)	6 (6.6)	3 (3.3)	2 (2.2)	15
		Right	4 (4.4)	6 (6.6)	3 (3.3)	2 (2.2)	15
CA	Female	Left	0	5 (5.9)	3 (3.5)	1 (1.17)	9
		Right	0	4 (4.7)	3 (3.5)	0	7
	Male	Left	0	3 (3.3)	1 (1.1)	2 (2.2)	6
		Right	0	3 (3.3)	0	1 (1.1)	4

is attributed to the arch developing by six years, so estimating the prevalence in such age groups merely exaggerates the issue (Rose et al., 1985; Ezema et al., 2014). In addition, previous literature cites numerous reports regarding the decline in the prevalence of flatfoot with advancing age (Echarri and Forriol, 2003; Abolarin et al., 2011; Pauk et al., 2012; Ezema et al., 2014). Also, flatfoot in the pediatric age group is rarely reported to be associated with symptoms compromising the quality of life (Mosca, 2010).

As flatfoot prevalence is said to rise with age beyond age 40, it is anticipated that the elderly population would experience a reduced quality of life due to the condition. (Benvenuti et al., 1995; Pita-Fernández et al., 2015). Though the quality of life is not affected by the arch height (López-López et al., 2018), symptomatic presentation leading to

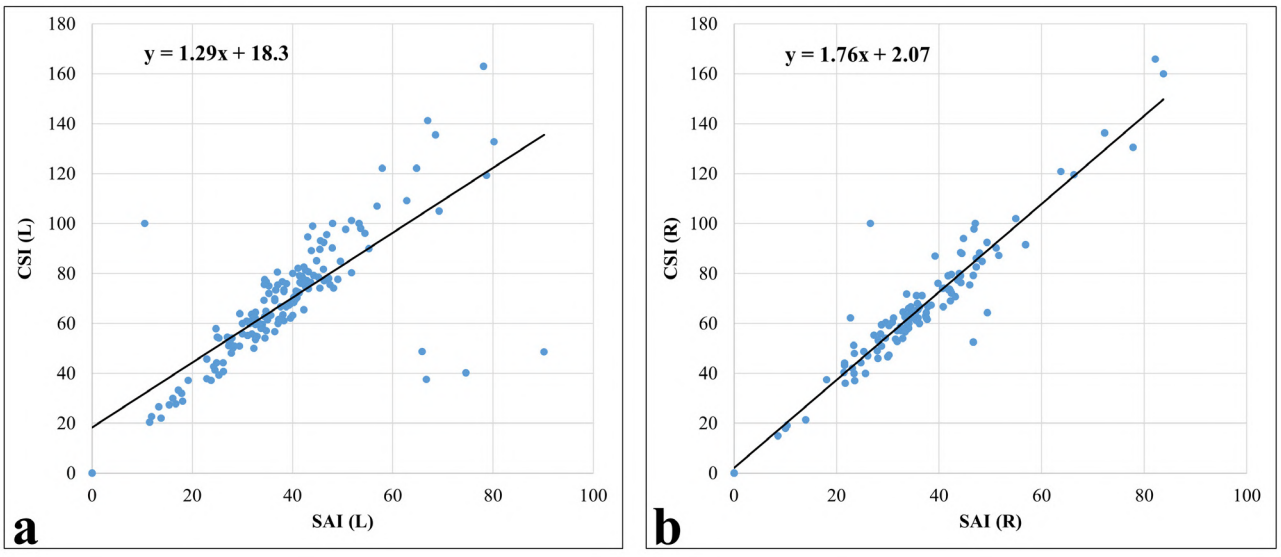

Fig. 2.- a, b - Graphs showing Linear regression correlation line derived from equation: y = mx + c, where y is CSI (L/R), m = 1.29 for a & 1.79 for b, x is SAI (L/R), and c = 18.3 for a & 2.07 for b.

discomfort due to flatfoot is often reported (Benvenuti et al., 1995).

The above explanations report the biased bimodal representation of variation in prevalence and association of flatfoot in pediatric (<17 years) and old age (<40 years) groups. This bias could be elucidated based on the fact that the arch is in the developing phase in the pediatric age, so the flatness is prominently visible as an abnormal feature, whereas in old age, the pathological effects of the condition highlight the situation (Ezema et al., 2014). Therefore, in light of the facts mentioned, it becomes necessary to study the prevalence of the condition in the adolescent age group.

Prevalence of flatfoot in adolescents

Accounts of data explaining the above findings and numerous others associated with flatfoot in the pediatric and old age groups could be found in previous literature. However, the absence of flatfoot data for adolescents (17-21 years) has had deleterious effects on the knowledge, awareness, and attitude of the masses regarding the condition (Aenumulapalli et al., 2017). The adolescents, though expected to have developed the plantar arches due to skeletal maturity, do suffer from flatfoot in considerable numbers (Tenenbaum et al., 2013). Apart from having aesthetic effects, this condition also hinders their professional prospect in security services. Lack of knowledge and awareness about flatfoot in adolescents leads to a torpid attitude to corrective attention, which could have a symptomatic presentation in old age (Ukoha et al., 2012; Tenenbaum et al., 2013).

The present study observed a flatfoot prevalence of 18.28% in adolescents 17-21 years which is much higher than that reported by previous literature in this age group, which ranges from 4.1-13.9% (Abdel Fattah et al., 2006; Atamturk, 2009; Ukoha et al., 2012; Bhoir et al., 2014; Aenumulapalli et al., 2017).

Prevalence in adolescents based on gender

The gender-based difference reported have contradictory evidence in the literature. Previous literature presents a predilection of flatfoot in males (Echarri and Forriol, 2003; Atamturk, 2009; Pauk et al., 2012; Woźniacka et al., 2015; Tong and Kong, 2016; Aenumulapalli et al., 2017). The present study observed statistically significant female predilection for flatfoot, which was previously mentioned by Umar and Tafida (2013). At the same time, the gender-based difference reported by Atamturk (2009) and Aenumullapalli et al. (2017) was statistically insignificant.

Sensitivity of various parameters for evaluation of flatfoot in all age-groups

For decades, footprints have been used to evaluate and diagnose flatfoot in all age groups. Banwell et al. (Banwell et al., 2018) reviewed articles using these parameters to evaluate flatfoot in children and observed that CSI and SAI were the only reliable and valid measurements for flatfoot estimation. The present study also observed CSI, SAI, and CA on footprints and deduced a moderate to strong positive correlation between CSI and SAI. The sensitivity was maximum for SAI, followed by CSI, and least for CA in predicting flatfoot in the studied age group. Chen et al. (2009) reported CSI as the most sensitive, followed by SAI and CA as the least.

Association of flatfoot and BMI in adolescents

While presenting the conundrum of the association between flatfoot and age, the literature also presented contradicting evidence regarding the association of flatfoot with BMI. The evidentiary support leans toward the positive correlation between flatfoot and BMI on many accounts (Pfeiffer et al., 2006; Chen et al., 2009; Chang et al., 2010, 2012; Tenenbaum et al., 2013; Ezema et al., 2014; Pita-Fernández et al., 2015; Woźniacka et al., 2015; Pourghasem et al., 2016; Gonzalez-Martin et al., 2017). Nonetheless, a study from the Turkish population reported no relationship between the two (Atamturk, 2009), while Wearing et al. (2012) mentioned that obesity has no effects on the bony alignment of the foot but distorts the reading of footprint-based arch indices and angle. The present study, too, observed the minimal impact of obesity on the plantar arch of adolescents. Most of the studies had reported the effect of obesity on children's foot without considering the pad of fat, which persists in these children and affect

the footprint readings. In adults, obesity does play a part in foot deformity as the bones are weakened and ligaments are loosened. However, in adolescents, the ligaments are taut, and bones are strong; therefore, obesity cannot impose on the arch integrity (Wearing et al., 2012).

The variations related to the prevalence of flatfoot have been associated with numerous demographic and parametric features. Age group-related studies regarding flatfoots are necessary to differentiate between those requiring corrective measures or not. Non-invasive corrective techniques must be used at the right age to be effective. Data on the conditions' contributing elements and diagnostic characteristics are needed to comprehend the time-based therapeutic application (Mosca, 2010). The lack of data for adolescents regarding flatfoot deprives the derivation of specific and valuable information for diagnosing and treating the condition, like the diagnostic information extracted by Banwell et al. (2018) for the pediatric flatfoot.

The limited knowledge of flatfoot in adolescents calls for more research into the various variables that might impact the plantar arch height. The present study's findings have to be seen in the light of the meager sample size of obese adolescent individuals, which limits the appropriate derivation of the related facts. Further, a prospective comparative study between the footprint and radiological data of participants from the adolescent age group would provide more clinically relevant observations.

CONCLUSION

The present study helps us to understand that flatfoot in adolescents requires attention and that the findings of the pediatric and old age flatfoot reports should not be extrapolated to adolescents. The findings explain that approximately one-fifth (18.28% in the footprint study) of the adolescent population suffers from flatfoot. The gender-based analysis points out the female predisposition for the condition. The decade-old fact that obese individuals are more prone to flatfoot does not hold the ground for adolescents. We observed a moderate to strong positive correlation between CSI and SAI. The sensitivity was maximum for SAI, followed by CSI, and least for CA in predicting flatfoot in the studied age group.

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Variations in branching pattern of middle cerebral artery using CT angiography in South Indian population

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SUMMARY

Middle cerebral artery (MCA) variants are rare compared to that of the other two cerebral arteries. Incidence of variations like duplication, fenestration, accessory vessel and early branching ranges from 0.17 to 4%. However, the literature describing MCA variations using CT Angiography (CTA) is limited, so this study was planned to determine the incidence of MCA branching pattern in Indian population using CTA. Datasets of CTA of 578 MCA from 289 patients (180 males and 109 females), with average age of 49.29±16.16 years (range of 11 to 85 years), from a tertiary care hospital were systematically reviewed for variations in branching pattern. Cases involving aneurysms and infarcts were excluded from the study.

Four branching patterns of MCA were seen. Pattern I: single trunk in 0.17% (1/578) cases, on left side. Pattern II: early bifurcation in 0.52% (2/578) cases, two cases on right and one on left side. Pattern III: bifurcation, in 97.75%, (565/578) cases, 46.15% (6/13) cases on right and 53.84% (7/13) on left side. Pattern IV: trifurcation, in 1% (6/578), two cases on right and four on left side. Duplicated MCA seen in 0.34% (2/578) cases, both on the right side. The fenestration of MCA seen in 0.17% (1/578), on the left side. No case of accessory MCA was seen. Awareness of these anatomical variations in the branching pattern of MCA is valuable for clinicians and surgeons handling cases of intracranial aneurysms and infarcts. Thus, data from this study would help surgeons minimize errors and provide the best possible outcome to the patients.

Key words: Middle cerebral artery – CT angiography – Anatomical variations

INTRODUCTION

The middle cerebral artery (MCA) emerges from the internal carotid artery (ICA) in the interpeduncular fossa, at the lateral angle of the Willis circle (Almeida et al., 2017). From the carotid bifurcation, MCA runs in the lateral direction to reach the sylvian fissure (Shalom et al., 2021). It runs posterior to the lesser wing of the sphenoid, turns in the sylvian fissure between the temporal and frontal lobes to reach the insular surface

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(Almeida et al., 2017; Gibo et al., 1981), and divides into two secondary trunks (superior and inferior). MCA tributaries pass through the medial surface of the opercula of the frontal, parietal, and temporal lobes, then run over the brain surface as cortical branches, supplying the lateral and inferior surfaces of the cerebral hemispheres (Ture et al., 2000). As MCA supplies a large part of the cerebral hemispheres, it is the most exposed vessel during surgical intervention and its acute obstruction can lead to the development of brain infarct in most of the cases (Shalom et al., 2021). Awareness of its variations is essential in avoiding unnecessary endovascular procedures and planning the safest interventional practices (Lutz et al., 2018). Though anomalous MCA present as incidental findings, in case of obstruction of main MCA trunk, these vessels may provide a secondary blood supply (Teal et al., 1973).

The bifurcation is the most common branching pattern of MCA with minimum and maximum incidence in cadaveric studies reported to be 48% and 96.5% (Kadam et al., 2018; Reci, 2019), respectively. In cadavers from India, incidence varies from 64.7%-96.5% (Kadam et al., 2018; Gunnal et al., 2019). The bifurcation is seen in 73% to 92.7% in imaging studies (Sadatamo et al., 2013; Vuillier et al., 2008). Occasionally, the main MCA trunk remains as a single vessel. The incidence of such single trunk is highly variable from 1.7 to 20% (Umansky et al., 1988). The single trunk is seen in 3.8% to 20.6% in cadavers and 17% in imaging studies (Umansky et al., 1988; Gunnal et al., 2019; Vuillier et al., 2008). MCA branching 0.5 cm or less from origin is known as early bifurcation (Teal et al., 1973). It is a less common variation and thus reported in few studies. Its incidence varies from 3% to 24% in cadavers (Eve et al., 2021; Reci, 2019). Presence of three or four final MCA trunks is referred as trifurcation or quadrifurcation (Reci, 2019) Incidence of trifurcation is 1.7% to 26.6% in cadaveric studies and 7.3% to 13.8% in angiographic studies (Kadam et al., 2018; Jeyakumar and Veerapandan, 2018; Sadatamo et al., 2013; Brzegowy et al., 2018). Incidence of quadrifurcation is 0.7% to 3.8% (Ogeng'O et al., 2011; Umansky et al., 1988; Gunnal et al., 2019). Rarely, a branch is given off immediately after origin of the two MCA trunks that gives an appearance of pseudotrifurcation (Ogeng'O et al., 2011). Apart from the main trunk, an accessory or duplicated vessel can be present and supply MCA territory. An accessory MCA arises as a branch from anterior cerebral artery (ACA), whereas duplicated MCA comes from the distal ICA (Crompton, 1962). The division of a single vessel into two channels which later fuse together results in fenestration (Uchino et al., 2012).

The prevalence of intracranial MCA aneurysms is approximately 20-43% (Wang et al., 2016). The recognition of MCA branching pattern is essential for handling the cases of aneurysm or stenosis of MCA (Umansky et al., 1988). The ischemic strokes and focal neurological deficits also follow disturbance in arterial circulation due to variations (Yasargil, 1984). MCA is the commonly occurring site for thrombus formation, which can be treated by mechanical thrombectomy. Thus, with the introduction of interventional stroke management, awareness of MCA anatomy has become more critical (Wang et al., 2016). A comprehensive data on variations in the branching pattern of MCA is thus needed for radiologists to interpret diagnostic images and for surgeons to execute complex brain surgeries (Teal et al., 1973).

There are multiple case reports and cadaveric investigations on the variations of MCA but with a narrow sample size. In addition, there is a difference in the prevalence of branching patterns of MCA among diverse populations due to the unpredictability of cerebral vasculature (Jeyakumar and Veerapandan, 2018). Three methods, i.e., computed tomography angiography (CTA), digital subtraction angiography and magnetic resonance angiography are suitable for diagnosis of cerebral vascular malformations (Seidlecki et al., 2021). However, CTA is the standard investigation method during the workup process. As the literature on MCA variations in CTA from Indian population is limited, this study was planned in subjects of a tertiary care hospital in south India.

MATERIALS AND METHODS

This descriptive Hospital-Record-based study was done in the departments of Radiology and

Anatomy in our institute from July 2017 to July 2020. The study was approved by Institute Human Ethics Committee (Ref. No. JIP/IEC/2019/421 dated 12/12/2019.

The CT cerebral angiography and multiphasic contrast enhanced records, from Picture Archiving Communication System (PACS) of the Department of Radiology, were retrieved. The scans in which branching pattern of MCA was not completely visible were excluded from the study. Also excluded were conditions like occlusion, dissection, aneurysm, and vasculitis that effect the normal vascular architecture. The sample size was calculated using formula for estimation of single population. The anatomic variation in the branching pattern of MCA was anticipated to be around 25% in CT Angiography (Jeyakumar and Veerapandan, 2018). The software for Power and Sample was applied at 5% level of significance and absolute precision of 5% for calculation, and the estimated total sample size was 289.

Plain CT brain was followed by CT angiogram. CT Angiogram was done using 128-slice multidetector CT system, Siemens Somatom 64 (3 mm slices were acquired with a 128 X 0.6 matrix and reconstructed to 1 mm slice thickness. A rotation time of 0.5 seconds and a pitch 1.2, delivered an effective mAs of 300 at a voltage of 120 kV. The average acquisition time was around 10 to 15 sec). Non-ionic contrast (400 mg Iodine /ml) at injection rate of 4-6 ml/sec with saline flush of 40 ml was given. The angiographic CT data sets were loaded in Siemens Syngo via server workstation and 3D angiographic images were obtained using Maximum Intensity projection (selected and displayed voxels with high attenuation value) and volume rendered technique (VRT) reconstruction.

Bone removal was done by slab editing to evaluate cerebral vasculature. VRT allowed good visualisation of cerebral vasculature and their 3D relationship. All the CTA images were analyzed under the arterial phase and branching pattern of MCA on both the sides were seen and documented. The variables like age were expressed as mean with standard variation, and gender as frequency and percentage. The variations in branching pattern were summarized as frequency and percentage.

RESULTS

A total of 289 CT cerebral angiograms (right- 289, left- 289), from 180 (62%) males and 109 (38%) females, were studied for variations of MCA. The average age of subjects was 49.3±16.2 years (range- 11 to 85 years). The distribution of records in various age groups is given in Table 1.

The branching pattern of the MCA was determined by the division of the main trunk into smaller or secondary trunks. The four patterns namely single trunk (pattern 1), early bifurcation (pattern 2), bifurcation (pattern 3) and trifurcation (pattern 4) were observed. The bifurcation (fig 1.3) was the most observed pattern (Table 2), in which MCA main trunk divided into two secondary trunks, superior and inferior. MCA bifurcated distal to the genu in 97.5% (551/565), proximal to it in 1.4% (8/565) and at genu in 1.1% (6/565). If the main trunk of MCA did not divide from its origin to the posterior end of lateral cerebral fissure, it was referred to as single trunk or pattern 1 (Fig. 1.1). The diameter and length of single trunk was 2.89 mm and 26.56 mm, respectively. MCA divided at 5 mm or less from its origin in pattern 2 or early bifurcation (Fig. 1.2). The mean length of MCA was 4.4±0.65 mm in this pattern. The length

Table 1. Age group distribution of CT Scan records.

Group	Age (Years)	Male N=180 (%)	Female N=109 (%)	Total No. of scan records N=289 (%)
I	0-20	7 (3.9)	10 (9.2)	17 (5.9)
II	21-40	44 (24.4)	23 (21.1)	67 (23.2)
III	41-60	79 (43.9)	55 (50.4)	134 (46.4)
IV	61-100	50 (27.8)	21 (19.3)	71 (24.5)

Table 2. Termination of middle cerebral artery.

Branching pattern/ variation	Total (%) N=578	Right (%) N=289	Left (%) N=289
Pattern 1/ Single trunk	1 (0.17)	0	1 (0.34)
Pattern 2/ Early bifurcation	3 (0.51)	2 (0.69)	1 (0.34)
Pattern 3/ Bifurcation	565 (97.77)	283 (97.92)	282 (97.57)
Pattern 4/ Trifurcation	6 (1.04)	2 (0.69)	4 (1.38)
Duplicated	2 (0.34%)	2 (0.69%)	-
Fenestration	1 (0.17%)	-	1 (0.34%)

Table 3. Variations in different age groups.

Branching pattern/ variation	Group I N=34 (%)	Group II N=134 (%)	Group III N=268 (%)	Group IV N=142 (%)
Pattern I	-	-	-	1 (0.7)
Pattern 2	1 (2.9)	1 (0.8)	1 (0.4)	-
Pattern 3	32 (94.1)	132 (98.5)	263 (98.1)	138 (97.2)
Pattern 4	-	1 (0.8)	3 (1.1)	2 (1.4)
Duplicated	1 (2.9)	-	1 (0.4)	-
Fenestration	-	-	-	1 (0.7)

on the right and left sides was 4.9±0.1 mm and 3.5 mm, respectively. In pattern 4 (Fig 1.4), the MCA main trunk divided into three secondary trunks (superior, middle, and inferior). The pattern 3 was bilateral in 95.5% (276/289) cases. It was bilateral in 97.8% (176/180) males and unilateral in 2.2% (4/180). In females, it was bilateral in 91.7% (100/109) and unilateral in 8.3% (9/109). All cases of patterns 1, 2 and 4 were unilateral.

A duplicated MCA (Fig 2.1) appeared at the bifurcation of ICA parallel to the main trunk. The mean length of duplicated MCA was 13.7±1.3 mm while the length of main MCA trunk was 14.42 mm. An oval-shaped fenestration (Fig 2.2) was on the distal segment of left MCA at 12.9 mm from its origin. No case of quadrifurcation or multiple trunks (>4) or accessory MCA was observed. The trifurcation was present in patients over 40 years of age, whereas single trunk and fenestration were seen in patients over 60 years (Table 3). MCA variations in males and females are depicted in Table 4.

DISCUSSION

The present study identified four branching patterns of MCA in 289 CT angiography records from tertiary care hospital of south India. Pattern 3 or bifurcation (97.8%) was the most common, followed by trifurcation (1.04%), early bifurcation (0.51%) and single trunk (0.17%). The duplicated MCA and fenestration were seen in 0.34% and 0.17%, respectively.

The incidence of bifurcation in the present study is comparable to that in the study by Kadam et al. (2018). The incidence of bifurcation was higher in males (97.8%) as compared to females (91.7%) in our study. In a study conducted by Ogeng'O et al. (2011), bifurcation was seen in 82.3% cases and it was similar to the study conducted in Nigeria, America and India (Tanriover et al., 2003; Idowu et al., 2002; Pai et al., 2005). The differences in incidence in different populations is due to geographical variation and methodological differences (Ogeng'O et al., 2011). The obstruction of the superior trunk in bifurcation increases risk of contralateral hemiparesis as compared to that in trifurcation and quadrifurcation (Kahilogullari et al., 2012). Emboli are frequently trapped at a bifurcation point, preventing them from migrating further (Shapiro et al., 2020).

When present as single trunk, the main trunk of MCA extends without any division from its beginning to the posterior end of lateral cerebral fissure

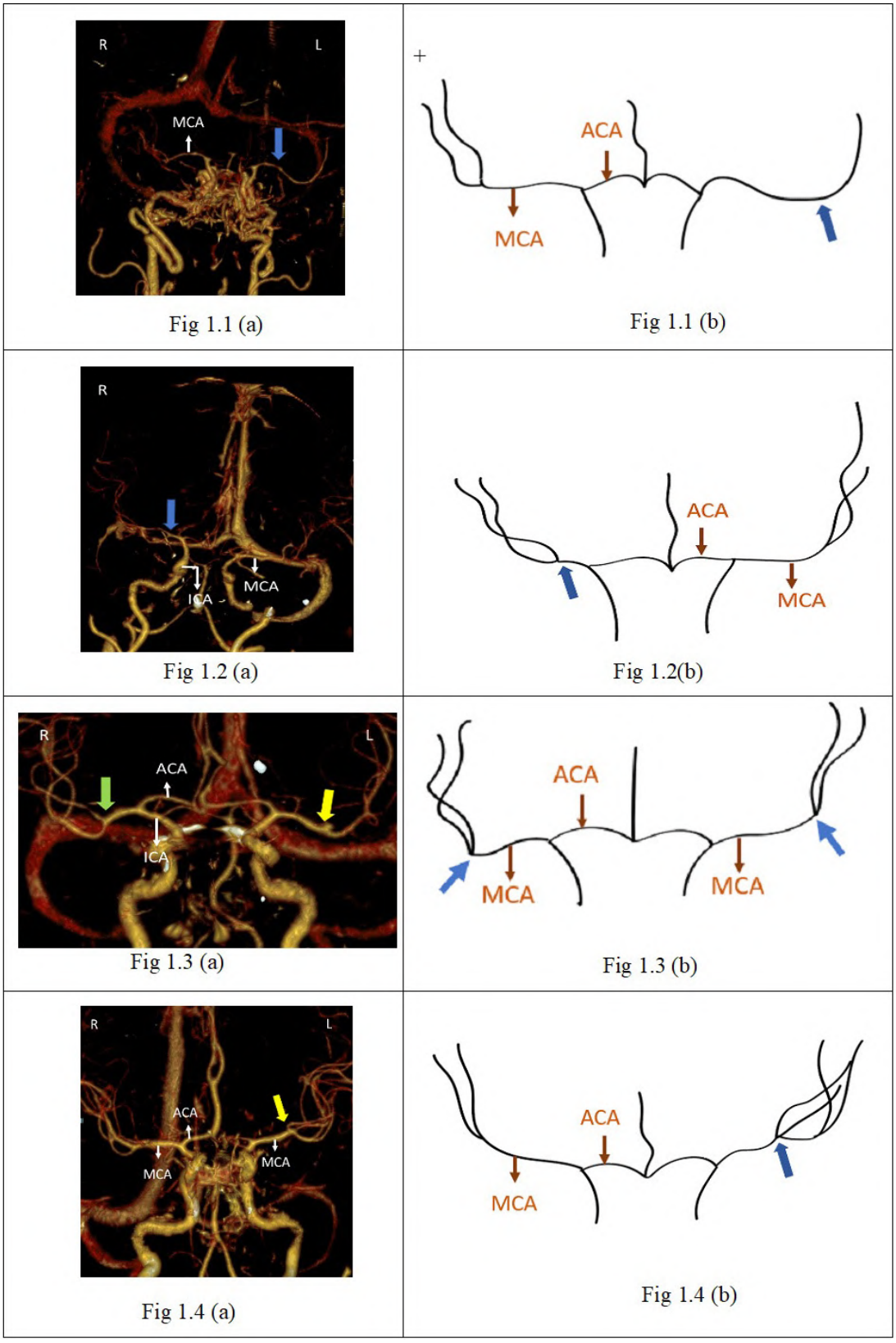

Fig 1.1 (a)

Fig 1.1 (b)

Fig 1.2 (a)

Fig 1.2(b)

Fig 1.3 (a)

Fig 1.3 (b)

Fig 1.4 (a)

Fig 1.4 (b)

Fig. 1.- VRT images (3D) and schematic diagrams showing variations in branching pattern of middle cerebral artery. **1.1 (a):** VRT image (3D) showing unilateral single trunk of middle cerebral artery on the left side. Blue arrow- single trunk middle cerebral artery. **1.1 (b):** Schematic diagram showing unilateral single trunk of middle cerebral artery on the left side. Blue arrow- single trunk middle cerebral artery. **1.2 (a):** VRT image (3D) showing unilateral early bifurcation of middle cerebral artery on the right side. Blue arrow- early bifurcation of middle cerebral artery. **1.2 (b):** Schematic diagram showing unilateral early bifurcation of middle cerebral artery on the right side. Blue arrow- early bifurcation of middle cerebral artery. **1.3 (a):** VRT image (3D) showing bifurcation on both the sides. Green arrow- right middle cerebral artery, Yellow arrow- left middle cerebral artery. **1.3 (b):** Schematic diagram showing bifurcation on both the sides. Blue arrow-Bifurcation of middle cerebral artery. **1.4 (a):** VRT image (3D) showing unilateral trifurcation on the left side, arising from the main trunk of MCA. Yellow arrow- trifurcation. **1.4 (b):** Schematic diagram showing unilateral trifurcation on the left side, arising from the main trunk of MCA. Blue arrow-trifurcation. MCA- middle cerebral artery; ICA- internal carotid artery; ACA- anterior cerebral artery.

(Gunnal et al., 2019). The obstruction of the MCA in this pattern will have a larger area of ischemia as compared to that in the other patterns (Serrador et al., 2000). The incidence of single trunk in a study by Gunnal et al. (2019) was higher than the average in other studies (Gunnal et al., 2019). Even though literature is reserved on the consequences of this variation, it is likely that its significance is closer to trifurcation as few cases resemble trifurcation very closely (Ogeng'O et al., 2011).

Incidence of early bifurcation in present study is slightly less as compared to cadaveric studies (Ogeng'O et al., 2011; Eve et al., 2021). Early bifurcation was found to be significantly higher in a study conducted by Reci (2019) (Table 5). Teal et al. (1973) identified two cases of early bifurcation. In unilateral case on the left side, the division occurred at a distance of 4 mm. The branching was seen at a distance of 3 mm on right side and 4 mm on the left in bilateral presentation (Teal et al., 1973). Dimmick and Faulder (2009) described early bifurcation as when branching occurs at a distance of 1 cm). Incidence in cadaveric study is found to be high compared with angiographic study, as vessels are not clearly identified because of overlapping in case of angiography (Teal et al., 1973). Early bifurcation is mostly related with perforating branches, which arise from post-bifurcation segment of MCA. As a result, extreme caution needs to be exercised during surgical treatment of MCA aneurysms in patients with early bifurcation in order to avoid harm to perforating branches

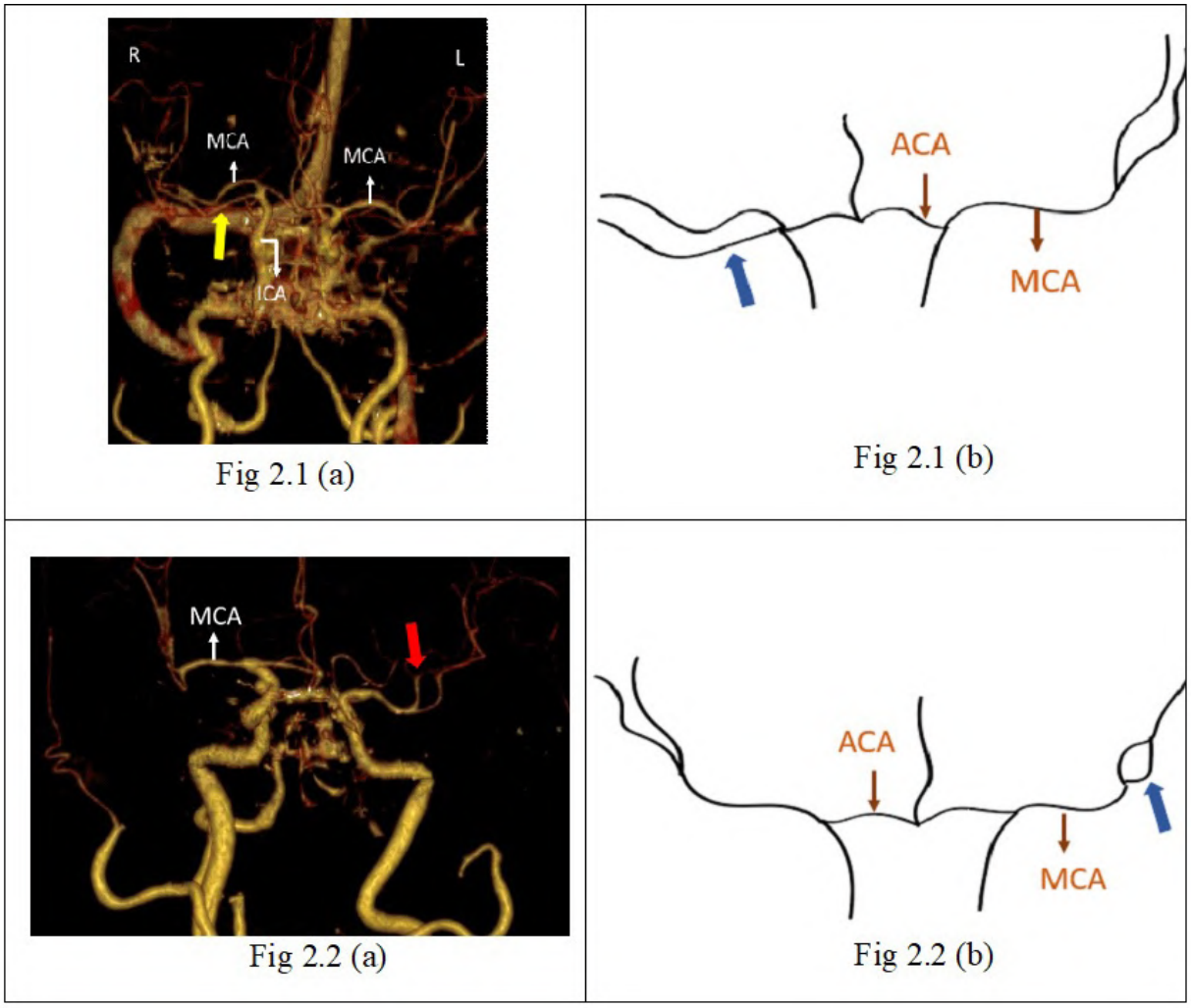

Fig. 2.- VRT images (3D) and schematic diagrams showing anomalies in branching pattern of middle cerebral artery, **2.1 (a):** VRT image (3D) showing unilateral duplicated middle cerebral artery on the right side. Yellow arrow- duplicated middle cerebral artery. **2.1 (b):** Schematic diagram showing unilateral duplicated middle cerebral artery on the right side. Blue arrow-duplicated middle cerebral artery. **2.2 (a):** VRT image (3D) showing unilateral left side fenestration on the distal part of middle cerebral artery. Red arrow-Fenestration. **2.2 (b):** Schematic diagram showing unilateral left side fenestration on the distal part of middle cerebral artery. Blue arrow-Fenestration. MCA- middle cerebral artery; ICA- internal carotid artery; ACA- anterior cerebral artery.

arising from the post-bifurcation section (Eve et al., 2021). As early bifurcation is not related with an increased risk in the formation of aneurysm; it is of relatively less clinical significance (Dimmick and Faulder, 2009).

In our study, females (2.8%) have slightly higher incidence of trifurcation than males (1.7%), while in a study conducted by Idowu et al. (2002) incidence was slightly higher in males than females. In the present study, incidence on the left

Table 4. Variations of middle cerebral artery in males and females.

Branching pattern/ variation	M N=360	F N=218	Group I		Group II		Group III		Group IV	
			M (N=14) (%)	F (N=20) (%)	M (N=88) (%)	F (N=46) (%)	M (N=158) (%)	F (N=110) (%)	M (N=100) (%)	F (N=42) (%)
Pattern I	0	1	-	-	-	-	-	-	-	1(2.38)
Pattern 2	1	2	1(7.14)	-	-	1(2.17)	-	1(0.90)	-	-
Pattern 3	176	100	13(92.85)	19(95)	87(98.86)	45(97.82)	158(100)	105(95.45)	98(98)	40(95.23)
Pattern 4	3	3	-	-	1(1.13)	-	-	3(2.72)	2(2)	-
Duplicated	-	2	-	1(15)	-	-	-	1(0.90)	-	-
Fenestration	-	1	-	-	-	-	-	-	-	1(2.38)

Table 5. The branching pattern of middle cerebral artery in different studies.

Authors, Year, Population	Type of study	Number of cases	Branching pattern				
			Pattern 1	Pattern 2	Pattern 3	Pattern 4	Quadrifurcation
Umansky et al., 1988; USA	Cadaveric	104	3.8%	-	66.3%	26%	3.8%
Meneses et al., 1997; Brazil	Cadaveric	14	-	-	85.6%	7.2%	-
Tanriover et al. 2003; Florida	Cadaveric	50	-	-	88%	12%	-
Vuillier et al., 2008; France	MRA	100	17%	-	73%	9%	-
Ogeng'0 et al. 2011; Kenya	Cadaveric	288	6.2%	5.2%	82.3%%	10.8%	0.7%
Sadatamo et al., 2013; Japan	MRA	124	-	-	92.7%	7.3%	-
Brzegowy et al., 2017; Poland	CTA	500	-	-	86.2%	13.8%	-
Jeyakumar and Veerapandan, 2018; India	Cadaveric	30	-	-	73.3%	26.6%	-
Kadam et al., 2018; India	Cadaveric	58	-	-	96.5%	1.7%	Multiple trunks-1.7%
Reci, 2019; Macedonia	Cadaveric	50	-	24%	48%	26%	-
Gunnal et al., 2019; India	Cadaveric	340	20.6%	-	64.7%	12.4%	2.4%
Pai et al., 2021; India	Cadaveric	10	-	-	80%	20%	-
Eve et al., 2021; Myanmar	Cadaveric	100	12%	3%	72%	16%	-
Present study, 2021; India	CTA	578	0.2%	0.5%	98%	1%	-

was higher than on the right side. In contrast, in a study conducted by Gunnal et al. (2019) incidence was higher on the right side as compared to the left. According to Umansky et al. (1988) incidence of trifurcation or quadrifurcation is seen in 30-40% cases, and the ischemia caused by the obstruction of one trunk will be smaller if there is a higher number of secondary trunks. Thus, obstruction in trifurcation results in less severe neurological impairment compared to bifurcation, which results in contralateral hemiplegia.

The variation in MCA branching has its basis in the development of intracranial vessels. MCA development is associated with that of the lobes of the cerebrum (Brzegowy et al., 2018). In fetal life, ICA branches into two divisions, anterior and posterior (Dudek, 2014). Initially, anterior division gives rise to primitive arteries and these arteries supply the optic and olfactory region (Dudek, 2014). With further development, MCA originates as small buds at 35 days of intrauterine life (11-12 mm stage) from the anterior division. At this stage, the major part of the cerebral hemispheres is supplied by it, but it is still plexiform and is not a true artery. It becomes prominent at 16-18 mm stage, and at this stage a single artery is formed by the fusion of plexiform vessels. Further, division of branches from MCA supply the cerebral hemisphere (Menshawi et al., 2015). In the developmental stage of MCA if there is early disruption before bifurcation, it leads to plexiform arterial network of the M1 segment (Yasargil, 1984). Failure of segmental fusion can result in formation of single trunk, early bifurcation, trifurcation and quadrifurcation patterns.

The duplication is defined as two arteries having different origin points and no caudal arterial junction (Lesley and Dalsania, 2004). Incomplete continuation of arterial twigs results in variation like duplicated MCA (Gunnal et al., 2019). According to Komiyama et al. (1998), duplicated MCA results because of early branching of MCA and is defined as direct bifurcation, as this arises directly from ICA. In present study, incidence of duplicated MCA was 0.7%, similar to the findings by Gunnal et al. (2019), Uchino et al. (2000) and Lee et al. (2005). The main MCA trunk was longer as compared to the duplicated MCA in the present study, which is similar to the observation of Uchino et al. (2000). Incidence was higher in females in our study. However, Uchino et al. (2000) reported higher incidence in males. Cases having both duplicated and accessory MCA are very rare and have been reported in few studies (Dong et al., 1991; Kitami et al., 1985). Distinguishing accessory MCA from duplicated MCA is challenging. Both supply the territory of MCA and have different origins, accessory is a small branch from ACA and duplicated artery is from the distal ICA (Crompton, 1962). The pattern of branching on the opposite side and level of carotid bifurcation helps in identifying the variant (Uchino et al., 2000). The

Table 6. Variations of middle cerebral artery in different studies.

Authors	Year	Population	Method	Number of cases	Variations		
					D	F	A
Uchino et al.	1999	Japan	MRA	850	2.1%	0.5%	1.17%
Gailloud et al.	2002	Switzerland	CTA	2340	-	0.4%	-
Idowu et al.	2002	Nigeria	Cadaveric	100	-	-	1%
Lee et al.	2005	Korea	MRA	34	0.8%	0.1%	0.1%
Dimmick and Faulder	2009	Australia	CTA	300	0.2-2.9%	0.17%	0.2%
Chang et al.	2011	Korea	CTA	1182	0.6%	-	-
Uchino et al.	2012	Japan	MRA	6982	0.1%	0.2%	-
Gunnal et al.	2019	Indian	Cadaveric	340	0.9%	-	2.1%
Reci	2019	North Macedonia	Cadaveric	50	2%	-	2%
Present Study	2021	India	CTA	578	0.3%	0.2%	

D-Duplicated MCA, F-Fenestrated MCA, A-Accessory MCA, CTA-Computed Tomography Angiography, MRA-Magnetic Resonance Angiography.

duplicated MCA provides collateral supply to frontal lobe and basal ganglia (Uchino et al., 2000), and its blockage presents with aphasia or hemiparesis. But this block can be missed in MR Angiography or CT Angiography because of presence of definitive MCA (Pressman et al., 2021). According to some authors, duplicated MCA are of two types: type I arises from ICA at the level of termination and type II originates from ICA or anterior choroidal artery (Gibo et al., 1981; Umansky et al., 1988; Kai et al., 2006). Both the duplicated MCA were of type I in the present study. Duplicated MCA along with increase in cerebral aneurysms are seen in many descriptions but mechanism is not clearly understood (Komiyama et al., 1998). Uchino et al. (2004) noted association of duplicated MCA with aneurysm in 38 cases and aneurysm was located at the origin of duplicated MCA in 15 cases. Since we have excluded the cases of aneurysm in our study, the correlations of aneurysm and this variation could not be determined.

Fenestration is the split of an artery lumen into several channels with muscularis and endothelial layers, with adventitia being shared (Parmar et al., 2005). MCA fenestration suggests the incomplete continuation of more than one arterial twigs, which merges into definitive MCA. In our study, fenestration was located in a distal segment of MCA at a distance of 12.93 mm from the origin of main trunk. In contrast, Uchino et al. (2006) reported it in a proximal segment at a distance of 4 mm from MCA trunk origin and Crompton (1962) reported it at a distance of 8 mm from main MCA trunk. The incidence of fenestration is found to be higher in cadaveric study as compared to angiographic study, because direct observation of anatomic specimens provides better visualization, while indirect observation in CTA restricts the surgical field (Gailloud et al., 2002). Recently, high incidence of MCA fenestration (5.2%) has been seen using 3D rotational angiography (Van et al., 2009).

CONCLUSION

The present study documented the variation in the branching pattern of MCA. Incidence of MCA branching pattern variations like single trunk, early bifurcation, and trifurcation in Indians is less as compared to CTA studies from other populations. This CTA study will help create a significantly more extensive database and perform more precise statistical analysis than anatomical cadaver studies. Future studies involving more patients can extrapolate the information obtained from this study to the general population. The knowledge of MCA variations will be useful for clinicians and surgeons in handling cases of intracranial aneurysms and infarcts. Also, data from this study would help surgeons minimize errors and provide the best possible outcome to the patients.

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Morphometric analysis of the optic canal and the superior orbital fissure in a Brazilian sample – study in CT scans

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SUMMARY

The posterior wall of the orbit is composed by the sphenoid bone and exhibits the optic canal (OC) and the superior orbital fissure (SOF). The comprehensive knowledge of anatomical and morphometric observations of OC and SOF is vital for an accurate diagnosis and management of local pathology. The aim of this study was to conduct a morphometric analysis of the OC and the SOF in CT scans in a Brazilian population. A total of 40 computed tomography (CT) scans of dry human skulls were used (20 males and 20 females). The images were submitted to a segmentation in which the bony structures of interest in the orbit were selected. A three-dimensional reconstruction of the region and the measurements of the perimeter (mm) of the SOF and the volume (mm^3) of the OC were performed. The statistical analysis was performed to verify if there was a difference in sex on each side for each anatomical structure. Regarding the OC, for the left side, there was a statistical difference between the sexes. For the SOF, neither the right side nor the left side showed statistical difference between the sexes. The present study showed new data about anatomical structures of the human orbit, bringing relevant knowledge for surgical and diagnostic procedures in the region. Especially for those anatomical structures evaluated that allow the passage of blood vessels and nerves, specific knowledge of their dimensions in different populations is valuable to avoid injuries during procedures in the orbital region.

Keywords: Optic canal – Superior orbital fissure – Morphology – Computed tomography – Morphometry

INTRODUCTION

The orbit is formed by several bones, such as the frontal, ethmoid, sphenoid, zygomatic and lacrimal. The posterior wall of the orbit is composed by the sphenoid bone sphenoid bone and exhibits the optic canal (OC) and the superior orbital fissure (SOF) (Koenen and Waseem, 2022).

The OC is described as presenting an ovoid shape that is, in the anteroposterior direction, shorter medially than laterally (Rhoton, 2002; René, 2006; Abhinav et al., 2015). Its entrance is located at the medial and posterior end of the optic strut, just inferior to the level of the anterior root of the lesser wing of the sphenoid bone, and its ending is defined as the most anterior level on

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the medial side of the optic strut (Abhinav et al., 2015). The OC links the anterior cranial fossa to the orbit and houses the optic nerve and the ophthalmic artery (Slavin et al., 1994).

Hart et al. (2009) evaluated the OC dimensions, and the degree of OC exposure to the sphenoid sinus were measured on sinus computed tomography images of 96 patients. A total of 191 optic canals were analyzed (111 female subjects and 80 male subjects). The average medial canal wall length was 1.48 cm (range, 0.7 to 2.3 cm). The length in male subjects was 1.61 cm (range, 1.1 to 2.3 cm), as compared to 1.39 cm (range, 0.7 to 2.0 cm) in female subjects ($p < 0.001$). They concluded that a wide variation in the medial canal wall length and exposure of the OC to the sphenoid sinus exist on computed tomography images.

The SOF is a very important region through which important nerves and vessels of the orbit pass. The SOF is found bounded by the body of the sphenoid bone and between the lesser wing and the greater wing of this bone (Govsa et al., 1999; René, 2006). It is a very significant structure, once it connects the middle cranial fossa and the orbit, houses various important vessels of the orbit and the III, IV, V, and VI pairs of cranial nerves (Govsa et al., 1999; René, 2006; Patel et al., 2021; Koenen and Waseem, 2022).

Patel et al. (2021) conducted a study on 30 dry skulls and computed tomography (CT) scans of 30 adult patients. They evaluated morphometric parameters including SOF length and width, distance from foramen rotundum to SOF and distance from the apex of petrous temporal bone to SOF. Most of the parameters did not show any significant differences between the left and right side in both dry skull and CT scan, except the distance of SOF to the foramen rotundum in dry skull, where the right-side distance was significantly higher.

It is important to note that the comprehensive knowledge of anatomical and morphometric observations of OC and SOF is vital for an accurate diagnosis and management of local pathologies. It also helps ophthalmologists and neurosurgeons not only during surgical procedures but also for newer technique advancement. For radiologists and neurosurgeons, the knowledge of morphometry and relation of OC and SOF is also very important (Govsa et al., 1999; Patel et al., 2021).

The aim of this study was to conduct a morphometric analysis of the OC and the SOF in CT scans in a Brazilian population.

MATERIALS AND METHODS

This research was approved by the Research Ethics Committee of Piracicaba Dental School – University of Campinas (Protocol number: 47768921.8.0000.5418).

Sample

A total of 40 computed tomography (CT) scans of dry human skulls were used (20 males and 20 females), aged between 18 and 80 years.

The CT scans were obtained using an Aisteion Multislice 4 CT System device (Toshiba Medical Systems Corporation – Japan), for skull protocol: 100 MA, 120KV, with 1mm slices. The CT scans of these dried human skulls belong to the "Osteológico e tomográfico Prof. Dr. Eduardo Daruge" Biobank from Piracicaba Dental School – University of Campinas (UNICAMP).

CT scans of intact skulls were used, without macroscopic deformities, fractures or any other pathological or surgical alterations.

Processing of tomographic images and obtaining measurements

The Mimics 18.0 (Materialise, NV, Belgium) software was used to perform the segmentation of the images of each CT scan. In the segmentation, the bony structures of interest in the orbit were selected. After segmentation, a three-dimensional reconstruction of the region was performed.

In the three-dimensional reconstruction, a measurement was performed to obtain the perimeter (mm) of the SOF (Fig. 1). In the axial section of the CT scan, the volume (mm^3) of the OC was measured (Fig. 2). Both the three-dimensional reconstruction and the acquisition of measurements were performed using the Mimics 18.0 (Materialise, NV, Belgium) software.

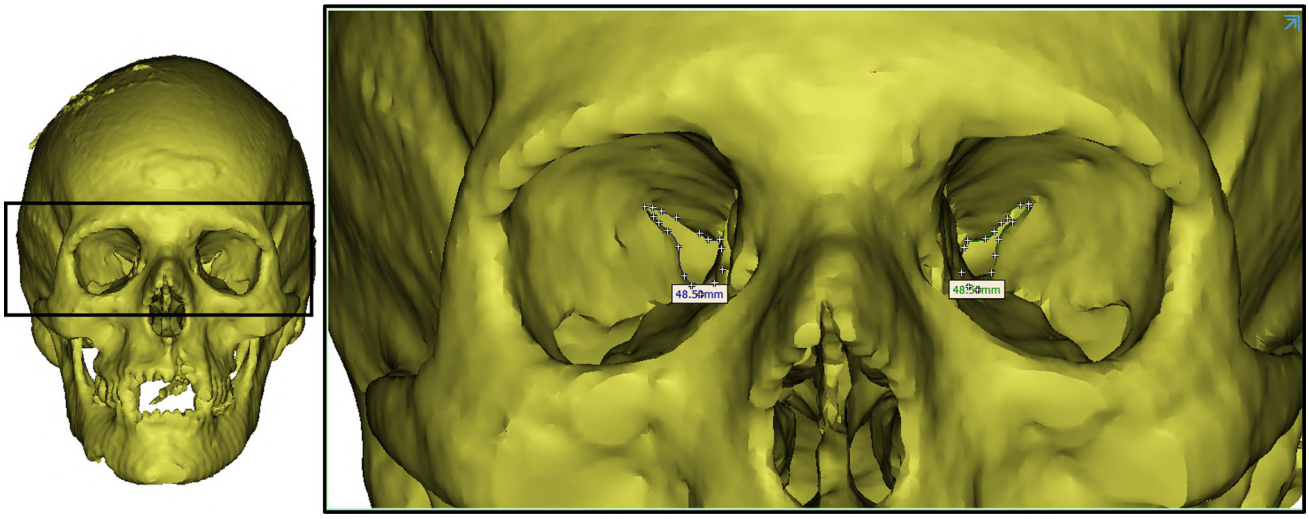

Fig. 1.- Measurement of the SOF perimeter (mm) in the three-dimensional reconstruction (Mimics 18.0 software - Materialise, NV, Belgium).

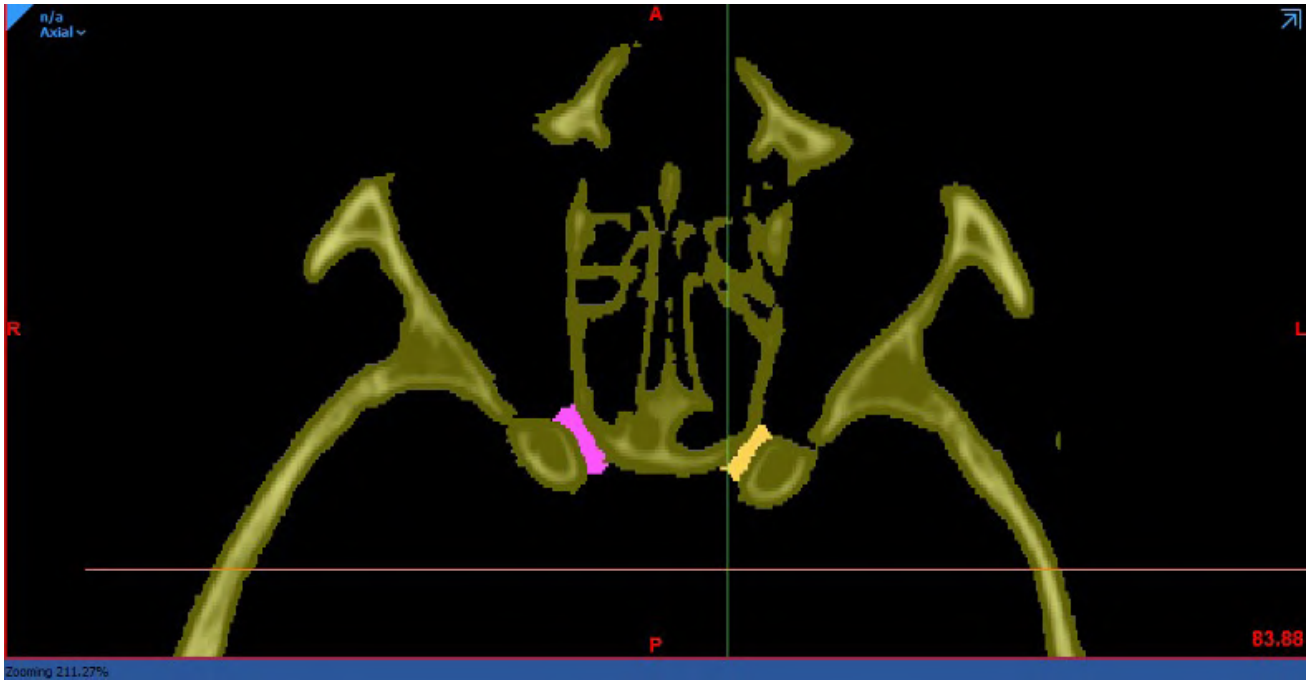

Fig. 2.- Measurement of the OC volume (mm3) in the axial section of the CT scan (Mimics 18.0 software - Materialise, NV, Belgium).

Statistical analysis

After collecting all the data, they were tabulated in the Microsoft Office Excel package. The non-parametric Mann-Whitney U test (two-tailed) was performed to verify if there was a difference in sex on each side for each anatomical structure evaluated (OC and SOF).

The descriptive statistical analysis was performed for both anatomical structures evaluated (OC and SOF). For all analyses, a significance level of $p<0.05$ was considered. All data were analyzed using GraphPAD Prism v.8 software (San Diego, CA, USA). The level of significance of $p <0.05$ was considered.

RESULTS

OC

The descriptive statistical analysis was performed (Table 1). The volume (mm^3) of the OC was obtained. For right side, the Mann-Whitney U test (two-tailed), showed no differences (P=

Table 1. Descriptive analysis of the OC volume (mm^3) in both sexes and both sides.

	Mean (Right side)	Standart deviation (Right side)	Standard error of mean (Right side)	Mean (Left side)	Standard deviation (Left side)	Standart error of mean (Left side)
FEMALE	88.07	28.88	6.458	84.73	30.51	6.823
MALE	107.9	33.99	7.601	105.1	27.43	6.133

0.1096) for the comparison between the sexes. For left side, the Mann-Whitney U test (two- tailed) showed a statistical difference between the sexes (P= 0.0263) (Fig. 3).

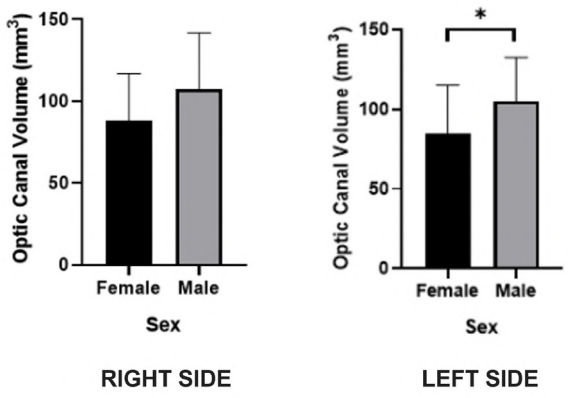

Fig. 3.- OC volume (mm^3) of both sexes and both sides. *Means statistically significant difference between groups. (P= 0.0263).

relationships of the orbit by morphological studies, such as the dimensions of the OC and SOF, can facilitate the diagnosis and treatment to different orbital diseases and can allow surgeons to develop a safe approach to a variety of techniques in this location, as well as to prevent some disorders (Slavin et al., 1994; Sinanoglu et al., 2016).

The risk of vascular and nerve structures injuries during a procedure is high, and detailed knowledge of this area is essential, mainly according to sex, side and populations. Due to its importance, studies have investigated the OC and the SOF and its different landmarks and variations (Govsa et al., 1999; Sinanoglu et al., 2016; Patel et al., 2021). The anatomic data about the OC and SOF has been studied by quantitative evaluations of human cadavers and morphometric parameters from skull CT scans (Habal et al., 1977; Berlis et al., 1992;

SOF

The descriptive statistical analysis was performed (Table 2). The perimeter (mm) of the SOF was obtained. For right side, the Mann-Whitney U test (two-tailed), showed no differences (P= 0.3834) for the comparison between the sexes. For left side, the Mann-Whitney U test (two- tailed), showed no differences (P= 0.1572) for the comparison between the sexes (Fig. 4).

DISCUSSION

The orbit is a target area of different medical and surgical procedures. Determining the anatomical

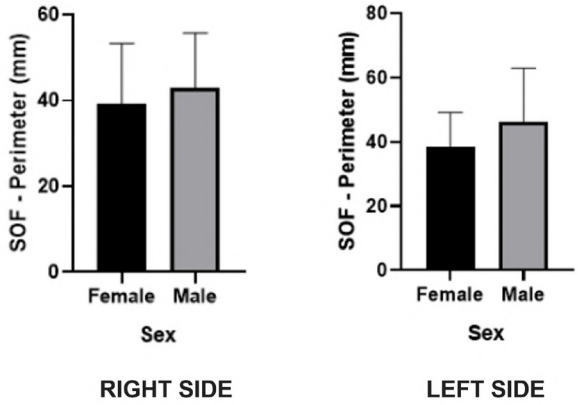

Fig. 4.- SOF perimeter (mm) of both sexes and both sides. (P= 0.1572).

Table 2. Descriptive analysis of the SOF perimeter (mm) in both sexes and both sides.

	Mean (Right side)	Standart deviation (Right side)	Standard error of mean (Right side)	Mean (Left side)	Standard deviation (Left side)	Standart error of mean (Left side)
FEMALE	39.20	14.07	3.147	38.32	10.87	2.432
MALE	42.92	12.79	2.860	46.45	16.46	3.681

Slavin et al., 1994; Govsa et al., 1999; Kazkayasi et al., 2003; Patel et al., 2021).

In the present study, when the volume (mm^3) of the OC was compared between the sexes (male and female), the results showed a significant statistical difference for the left side, and it was possible to note that the volume of the OC was higher in the male sample than in the female sample.

Some previous studies also reported significant differences in OC anatomy between the sexes (Hart et al., 2009; Liu et al., 2013; Sinanoglu et al., 2016). Hart et al. (2009) showed that the OC exposure to the sphenoid sinus exhibits anatomical differences between sexes. Liu et al. (2013) reported a sex influence in the distance between the cranium end of the OC and nasion. Sinanoglu et al. (2016) reported that sex exert influence on the orbit surrounding structures, such as the distance between the orbit end of the OC and nasion, with a male dominance. Although there are reports of significant differences between the sexes (Hart et al., 2009; Liu et al., 2013; Sinanoglu et al., 2016), there are no reports of differences between sides in the same sex (Sinanoglu et al., 2016). It's a consensus that the OC of male sex sample had a predominance of the dimensions.

Regarding SOF, in the present study there were no significant differences in its perimeter (mm) for the comparison between the sexes, neither to the right side nor to the left side. Patel et al. (2021) and Govsa et al. (1999) performed a series of measures in dry skulls, adult cadaveric heads and CT scans to characterize the morphology of the SOF. The authors reported that no differences were observed between the right and the left sides for the measurements (Govsa et al., 1999; Patel et al., 2021), except for the distance of SOF to foramen rotundum in dry skull in the study conducted by Patel et al. (2021). It is interesting to note that no studies were found comparing SOF dimensions between the sexes, only between the sides. Considering that the CT scans are important to visualize anatomical structures with accuracy (Deniz et al., 2018), the importance of the tridimensional bony assessments in clinical practice, and the specific quantitative variations of the populations, the present study showed new data about anatomical structures of the human orbit, bringing relevant knowledge for surgical and diagnostic procedures in the region. Especially for those anatomical structures evaluated that allow the passage of blood vessels and nerves, specific knowledge of their dimensions in different populations is valuable to avoid injuries during procedures in the orbital region. The morphometric analysis of present study in a Brazilian population may help professionals in the evaluation of patients of both sexes.

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Evaluating the features of interdigital neuroma using 3-Tesla magnetic resonance imaging

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SUMMARY

Interdigital neuroma is an entrapment neuropathy of the interdigital nerve. Previously, studies on interdigital neuroma were done with 1 Tesla Magnetic Resonance Imaging and more often 1.5 Tesla Magnetic Resonance Imaging. We used 3 Tesla Magnetic Resonance Imaging in our study and we did not encounter as much as we know about the study with 3 Tesla Magnetic Resonance Imaging in the literature. Between 2013 and 2019, the 3 Tesla Magnetic Resonance Imaging results of 39 consecutive surgically-confirmed interdigital neuromas and patients' files were retrospectively evaluated. The soft tissue surrounding the prominent interdigital nerve "target sign" were assessed. Spearman's rho, Pearson's correlation tests, and Mann-Whitney U-tests were used. Of the 39 cases (mean transverse dimension = 4.64 mm), 35 (89.7%) were hypointense on T1-weighted sequencing, 34 were intermediate (87.1%) on short tau inversion recovery sequencing, and 29 (74.3%) had slightly-moderately enhanced neuromas on post-contrast spectral presaturation with inversion recovery sequences. A statistically significant negative relationship was found between contrast enhancement and disease duration (p = 0.020). On short tau inversion recovery or spectral presaturation with inversion recovery series, the intralesional nerve view "target sign" was observed in 23 (58.98 %) of 39 neuromas. This is the first study in the literature with 3 Tesla Magnetic Resonance Imaging that shows the visual characteristics of interdigital neuroma and its possible contribution to the diagnosis of the disease.

Key words: Morton neuroma – Interdigital neuroma – 3-Tesla MRI – Metatarsalgia – Foot pain

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ABBREVIATIONS

MRI, Magnetic Resonance Imaging

SPIR, Spectral Presaturation with Inversion Recovery

STIR, Short Tau Inversion Recovery

T1W, T1-weighted

TSE, Turbo Spin Echo

US, Ultrasonography

INTRODUCTION

Interdigital neuroma, widely known as Morton's neuroma, is an entrapment neuropathy of the interdigital nerve, and is more frequently diagnosed in middle-aged women (Wu, 1996). Specific physical examination findings (such as Mulder's sign, Tinel's sign, etc.) used in interdigital neuroma diagnosis was defined in the literature and some authors state that the diagnosis can be made using both clinical and physical examination findings (Zanetti et al., 1997a, b; Shapiro et al., 1995; Levine et al., 1998). MRI (magnetic resonance imaging) and US (ultrasonography) are used for the possibility of comorbid conditions or for legal reasons, or to confirm the initial diagnosis (Zanetti et al., 1997a; Biasca et al., 1999). In cases of interdigital neuroma, an increased transverse relaxation time (T2) signal, greater calibration, and increased contrast uptake may be seen on MRI due to the affected interdigital nerve. Some authors have also reported a relationship between neuroma and the interdigital nerve (Simmons, 2008; Waizy et al., 2010). The term "target sign" is used for central hypointense and peripheral hyperintense-looking round tumors derived from neural tissue (Bhargava et al., 1997). Although this sign is highly suggestive of peripheral nerve sheath tumors like as neurofibroma, in this study we observed the slightly edematous interdigital nerve and surrounding soft-tissue view "target sign" in some of our interdigital neuroma cases (Fig. 1). Observing the affected nerve using 3T (Tesla), MRI can be interpreted as a positive indicator in the diagnosis of interdigital neuroma. Previously, studies on interdigital neuroma were done with 1T MRI and more often 1.5T MRI (Zanetti et al., 1997a; Lee et al., 2007; Williams et al., 1997; Erickson et al., 1991; Bencardino et al., 2000). We used 3T MRI in our study and we did not encounter as much as we know about the study with 3T MRI in the literature.

The aim of this study was to evaluate the visual characteristics of interdigital neuroma with 3T MRI and its contribution to diagnosis.

MATERIALS AND METHODS

Study population

Approval for this study was obtained from the local ethics committee (number and date: 108400987-173/2015). Between 2013 and 2019, the 3T MRI results of 39 consecutive surgically-confirmed interdigital neuromas in 30 patients

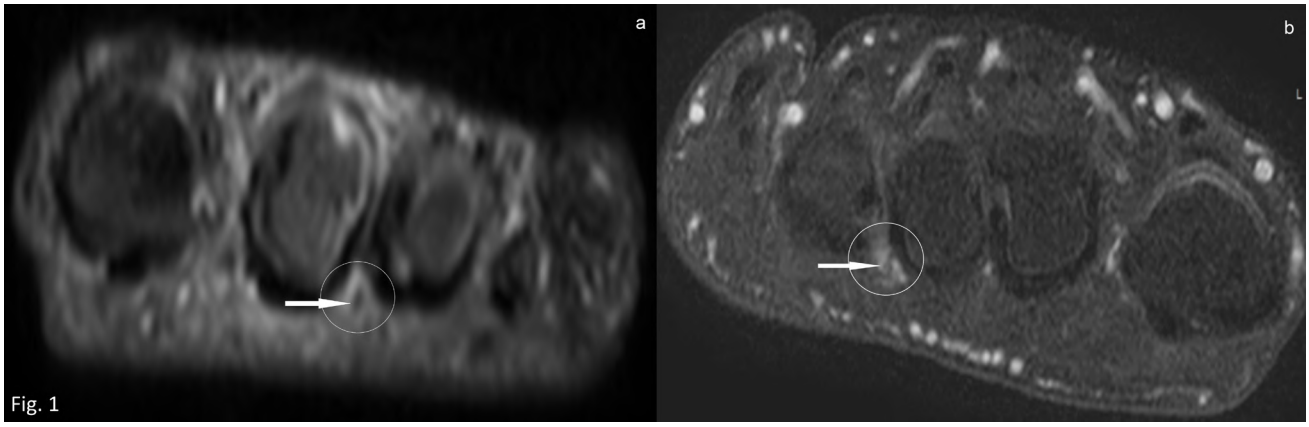

Fig. 1

Fig. 1.- Magnetic resonance imaging view of the "target sign'' and its histopathological reflection. (**a)** The "target sign'' in 44-year-old man with interdigital neuroma. The prominent and mildly-hyperintense interdigital nerve (arrow) can be seen in the 2nd web space on the coronal short tau inversion recovery (STIR) image. (**b)** A 51-year-old woman with interdigital neuroma. On the coronal post-contrast spectral presaturation with inversion recovery (SPIR) image, a moderately-contrasted soft-tissue formation (circled) surrounding the slightly visible interdigital nerve (arrow) can be seen within the 3rd web space: "target sign''.

were retrospectively evaluated. Of the 30 included patients, 18 (60%) were female and 12 (40%) were male. Nine cases had lesions in two web spaces (the 2nd and 3rd web spaces), and a total of 39 interdigital neuromas were included in the study. The mean age of the neuroma patients was 40.77 years (range, 21-71 years). Patients who were treated conservatively for forefoot pain but did not respond to these treatments were included in the study. In the evaluation based on both physical and MRI examinations, patients diagnosed with interdigital neuroma underwent surgery, and the diagnosis was confirmed histopathologically. The interdigital neuromas were reviewed independently by two radiologists experienced in the musculoskeletal system. We excluded cases with a medical history of previous surgery on the same foot, trauma occurring at least 6 months prior, any congenital deformity of the foot, diabetes, and any vascular disease of the foot.

Consequently, The 3T MRI features of 39 interdigital neuromas that were diagnosed histopathologically were retrospectively evaluated.

Magnetic Resonance Imaging

MRI studies were conducted with a 3T scanner (MR Systems Achieva Release 3.2.3.1, Philips Medical Systems, Holland) using a sense foot/ankle coil with eight channels. The routine protocol we used for interdigital neuroma is described in supplementary material. Ovoid or round mass lesions between the metatarsal heads with substantial demarcation were investigated for interdigital neuroma, as described in the literature (Gougoulias et al., 2019; Bhatia and Thomson, 2020). If a lesion was present, the location, dimension, signal characteristics on T1W, STIR (Short Tau Inversion Recovery), and contrast series, and the duration time of the disease as well as the relationship among these factors were evaluated. The lesion conspicuity was evaluated qualitatively for T1W, STIR and post contrast sequences, as it was done in the literature (Terk et al., 1993; Lee et al., 2007; Williams et al., 1997; Erickson et al., 1991). An accumulation of fluid greater than 3 mm in the transverse plane in the intermetatarsal bursa has been described as bursitis (Zanetti et al., 1997b). In addition to these factors, coexisting pathologies, such as intermetatarsal bursal fluid accumulation (bursitis), were also assessed. The target sign, which is defined as the soft tissue appearance described as the hypointense centrally and hyperintense peripherally, was examined. The relationship between the features of the lesion and target sign were assessed. All the neuromas were reviewed by both radiologists to determine the diagnostic value of the 3T MRI sequences. In disputed cases, a consensus was reached after a mutual review of the data.

Statistical Analysis

Descriptive statistical methods were used during the data review. Spearman's rho and Pearson's correlation tests were used to define the correlation between the factors. To define the significant differences, the chi-square and Mann-Whitney U tests were used. The results were reviewed with regard to the 95% confidence interval and 5% significance level. SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY, USA) and Microsoft Excel 2007 (Microsoft, Redmond, WA, USA) were used for the statistical analysis.

RESULTS

Of the 30 included patients, the mean duration of the disease was 31.95 months (range, 1-120 months). Most of the lesions were in the 3rd intermetatarsal space. The mean neuroma size was 4.64 mm (range, 2.70-9 mm). If we removed a single large 9 mm lesion, the average neuroma size was 4.53 mm. Only one of 39 neuromas could not be detected on MRI. The diagnostic accuracy was found to be 97.4%. No correlation was detected between disease duration and the age of the patient ($r= 0.086$, $p=0.610$), and there was no statistically significant correlation between the neuroma size measured with MRI and the disease duration ($r = 0.024$, $p = 0.890$). Eight of the 39 lesions (20.5%) had intermetatarsal bursitis, and their mean size was 3.68 mm (Table 1). 46% (21 cases) of interdigital neuromas had accompanying intermetatarsal bursal effusion. It was observed that neuromas exceeded the intermetatarsal line by an average of 3.20 mm (range, 1.2-5.5 mm).

Table 1. The features of interdigital neuroma.

		Total	1st Web N (%)	2nd Web N (%)	3rd Web N (%)	Duration Time (months)	
Interdigital Neuroma		39 (in 30 pts)	1 (2.57%)	10 (25.64%)	28 (71.79%)		
Sex	Female	25 (64.1%)	1 (4%)	6 (24%)	18 (72%)		
	Male	14 (35.9%)	0 (0%)	4 (28.6%)	10 (71.4%)		
I.N. size (mm)		4.64 (2.7-9)	9	4.58 (3.2-7.3)	4.51 (2.7-7)		0.23**
Bursitis (mm)		2.77 (1.3-5.3)	3.6	3.07 (2.1-3.7)	2.66 (1.3-5.3)		0.32**
''Target Sign''	-	16 (41.02%)	1(6.25%)	5 (31.25%)	10 (62.5%)	40.94 (1-120)	0.35*
	+	23 (58.98%)	0 (0%)	5 (21.73%)	18 (78.26%)	25.69 (1-96)	
T1W im		4 (10.26)	0 (0%)	0 (0%)	4 (100%)	29.5 (1-96)	0.42*
T1W hypo		35 (89.74%)	1 (2.9%)	10 (28.6%)	24 (68.6%)	32.23 (1-120)	

*: Statistical difference between the 1st, 2nd and 3rd web spaces (*Chi Square Test*).
**: Statistical difference between 2nd and 3rd Web spaces (*Mann Whitney U Test*).
I.N.: Interdigital neuroma, im: intermediate, hypo: hypointense.

The target sign view was observed in 23 (59%) of the 39 lesions; it could not be detected in 16 lesions (41%). Only 5 out of the 23 target sign views were seen in the 2nd intermetatarsal web space; the rest were in the 3rd intermetatarsal web space. A statistically significant relationship between the target sign and disease duration or the lesion size was not detected (disease duration with target sign: r = −0.195, p = 0.230; size in MRI with target sign: r = 0.053, p = 0.747, respectively). The mean duration time of 16 cases without a target sign is 40.94 months (range,1-120 months); the mean duration time of the 23 cases with a target sign is 25.69 months (range, 1-96 months).

Among the total cases, 35 (89.7%) were hypointense and 4 (10.3%) had an intermediate signal on the T1W sequences. On the STIR sequences,

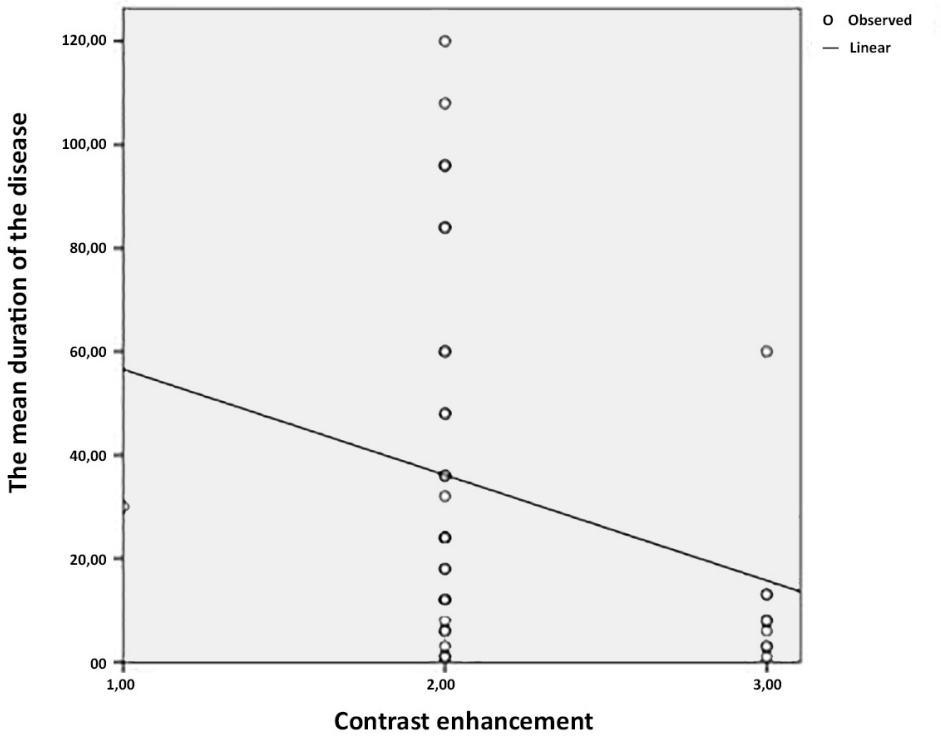

Fig. 2.- The relationship between the mean duration of the disease and contrast enhancement.

34 (87.1%) cases were intermediate, 1 (2.6%) was hypointense, and 4 (10.3%) were hyperintense. There were 29 (74.3%) cases which were slightly-moderately enhanced and 9 (23.1%) cases with a significantly enhanced neuroma on the post-contrast series. Contrast enhancement was not detected in one case. The disease duration for the lesions that were slightly-moderately enhanced was 37.97 months (standard deviation 36.59; range, 1-120 months); for significantly enhanced lesions, it was 12.78 months (standard deviation 18.21; range, 1-60 months). The disease duration difference for contrast enhancement was statistically significant. A statistically significant negative relationship was found between contrast enhancement and disease duration ($r = -0.37$; $p = 0.020$). Disease duration is shorter as the contrast enhancement increases (Fig. 2).

For the T1W sequences, the disease duration for the lesions visible at the intermediate signal level was 29.5 months (range, 1-96 months); however, this duration increased to 32.23 months (range, 1-120 months) when the signal was hypointense.

When the diagnostic benefits (lesion identification level) of the T1, STIR, and post-contrast SPIR (Spectral Presaturation with Inversion Recovery) sequences were assessed, 26 (66.7%) out of a total of 39 lesions were best viewed on the T1 sequences, 6 (15.4%) were best viewed on the STIR sequences, and 7 (17.9%) were best viewed on the post-contrast SPIR sequences.

DISCUSSION

Interdigital neuroma is one of the most common causes of forefoot pain (Zanetti et al., 1997a, b). In the evaluation based on both physical and MRI examinations, 30 patients underwent surgery and the condition was confirmed histopathologically (39 interdigital neuromas in 30 patients). It was observed that 1 of these 39 cases could not be detected on MRI because of the presence a small, double lesion. With this result, the diagnostic accuracy was found to be 97.4%.

In our study, interdigital neuroma was mainly diagnosed within the 3rd web space, and our results were consistent with those reported in previous studies in the literature (Gougoulias et al., 2019; Choi et al., 2021). In the literature average size of neuroma was reported 7.5 ± 0.7 mm (Samaila et al., 2021). Ruiz et al. (2019) reported that the transverse axis of lesion was 5.5 mm. We found that the mean dimension was 4.64 mm (range, 2.7-9 mm). If we removed a single large 9 mm lesion, the average neuroma size was 4.53 mm. It is possible to detect small lesions with 3T MRI due to the increased resolution. Bencardino et al. (2000) reported that the mean transverse diameter of symptomatic neuromas was 5.3 mm (standard deviation, 2.14), whereas that the mean transverse diameter of asymptomatic neuromas was 4.1 mm (standard deviation, 1.75). Sharp et al. (2003) stated that interdigital neuromas smaller than 6 mm can also show clinical symptoms. In our study, we found the mean size of the symptomatic lesion was even smaller (4.64 mm).

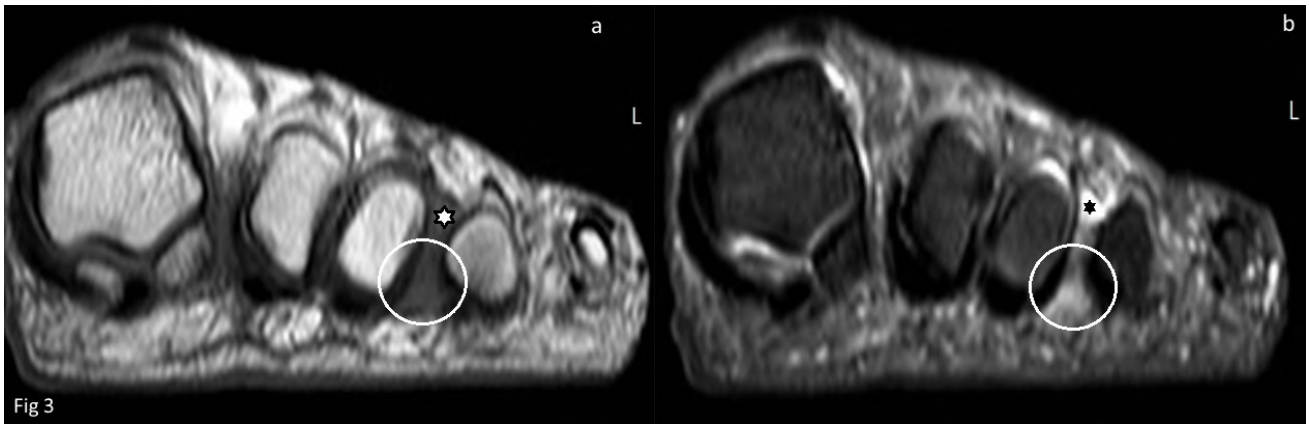

Fig. 3.- An interdigital neuroma with intermetatarsal bursal effusion. A 48-year-old man with interdigital neuroma. On images **(a)** coronal Turbo spin echo (TSE) T1, and **(b)** coronal STIR, interdigital neuroma (circled) is visible in the 3rd web space as T1 hypointense and STIR intermediate. An intermetatarsal bursal effusion is also prominent (asterisk*) in the adjacent superior area.

In our study, 46% (21 cases) of our interdigital neuroma cases had accompanying intermetatarsal bursal effusion (Fig. 3). However, bursal effusion wider than 3 mm was only present in 8 cases (20.5%) and the mean size of the coronal plane was 3.68 mm.

If a lesion is sufficiently large, a significant plantar extension pass across the intermetatarsal line is seen, which allows for an easier diagnosis. In our study, it was observed that neuromas exceeded the intermetatarsal line by an average of 3.20 mm (range, 1.2-5.5 mm). However, if the lesion does not exceed the intermetatarsal line, diagnosis can be difficult. In small-dimensioned neuromas, the obliteration of the hyperintense signal arising from the fatty tissue located in the conic-shaped space (along with the nerve) by the lesion can serve as a warning sign (Fig. 4).

Interdigital neuroma reportedly displays different signal characteristics in different magnetic field strengths, and the diagnostic benefit of the sequences that are used also varies. George et al. (2005) reported that STIR is the most sensitive sequence in their 1-Tesla (1T) study. However, studies conducted by Zanetti et al. (1T), Lee et al. (1.5T), Bencardino et al. (1.5T), Williams et al. (1.5T), and Erickson et al. (1.5T) all reported the T1W sequence to be the most sensitive (Zanetti et al., 1997a, b; Lee et al., 2007; Williams et al., 1997; Erickson et al., 1991; Bencardino et al., 2000). Furthermore, Terk et al. (1993), George et al. (2005), and Unger et al. (1992) also reported the beneficial use of contrasted series. However, Zanetti et al. (1997a), Lee et al. (2007), and Williams et al. (1997) did not report the superiority of post-contrast T1 images over other sequences used for diagnosis.

In our study, in comparison to the adjacent fat planes, 35 (89.7%) of the neuroma cases provided a hypointense signal on the T1W sequences, in 34 cases the signals were intermediate (87.1%) on the STIR sequences, and in 38 (97.4%) cases the signals were slightly-moderately enhanced on the post-contrast series. Based on these findings, we can say that, in general, interdigital neuromas are viewed as a hypointense signal on T1W, an intermediate signal on the STIR sequences, and a slightly-moderately enhanced signal on the post-contrast series with 3T MRI. Out of a total of 39 lesions, 26 (66.7%) were best viewed on the T1 sequences, 6 (15.4%) were best viewed on STIR sequences, and 7 (17.9%) were best viewed on the post-contrast SPIR sequences. As detailed, the T1W sequences were the most diagnostically beneficial sequences. However, a detailed review of the STIR and post-contrast SPIR sequences may assist in clinical decision making for the diagnosis of small lesions, especially if other or accompanying lesions are causing metatarsalgia.

In the literature, general expressions about the signal properties of interdigital neuroma in T1W and T2W sequences have been used. T2W sequences were taken as non-fat-saturated in some of the studies and as fat saturated T2W or as STIR

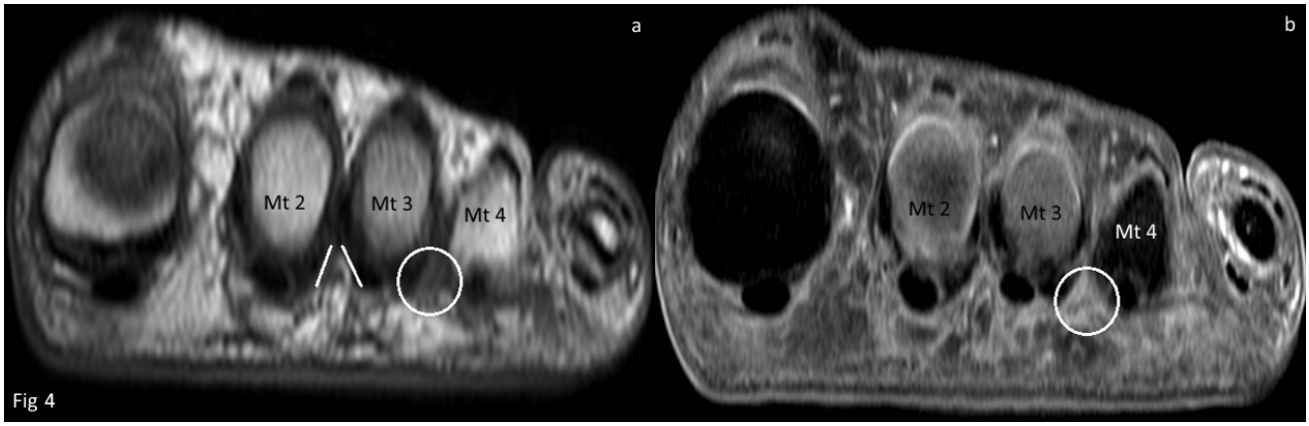

Fig. 4.- The fatty tissues are obliterated by the interdigital neuroma. A 37-year-old woman with metatarsalgia. On images **(a)** coronal TSE T1, and **(b)** coronal post-contrast SPIR, straight lines indicate the conical area within the 2nd web space formed by deep transverse metatarsal ligaments, and the dorsal and plantar interosseous tendons. This hyperintense area due to fatty tissue can be easily identified. In the 3rd web space, fatty tissues are obliterated by the interdigital neuroma (circled).

in other studies. In their 1T MRI study, Zanetti et al. (1997a) defined the interdigital neuroma signal as low in all the T1W and T2W series and generally high (9/14) in the STIR sequence. Sharp et al. found that the interdigital neuroma signal was low or intermediate (isointense with muscle) in the T1W series; in their study with 1.5T MRI, they reported that the T2W findings were highly variable and the T2W signal increased in 18/24 lesions (Sharp et al., 2003).

In musculoskeletal examinations in 3T MRI systems, the T1 value ranges between 10-30%, which is higher than it is in 1.5T MRI systems (Mosher, 2006). Again, as the magnetic field strength of the device increases, the T2 values of the tissues remain constant or decrease slightly (Bottomley et al., 1984). If we ignore the effects of time on lesions, in our study, the lesions were mostly hypointense on the T1W series (35/39) and intermediate on the STIR sequence (34/39), probably due to these effects.

Betts et al. (2003) reported that, due to the inflammatory response and fluid accumulation in the early period, there is echo enhancement in the distal portion of the lesion on US; however, as the disease duration increases, the lesion becomes more solid and difficult to see distinctly from the surrounding structures. Using the same mechanism, in our study, although the relationship between disease duration and T1 signal was not statistically significant, the mean duration of the lesions seen in the intermediate signal in the T1W series was 29.5 months; this time increased to 32.2 months when the signal returned to hypointense. (It should be noted that the duration of the disease is obtained from the patient's medical history, thus the information might not be reliable). This is in accordance with the fact that fibrosis increases with the progression of the disease and, thus, hypointensity becomes more prominent (Fig. 5). Contrast enhancement, which is more common in the early stages of the disease, decreases due to fibrosis as the disease progresses.

The normal plantar digital nerve calibration is approximately 1-2 mm at the level of the metatarsal head (Nissen, 1948). In MRI images, the hyperintense signal on the STIR sequence is secondary to edema, and increased calibration of the nerve can be observed. Calibration increases with long-term nerve fiber degeneration, and excessive intraneural and juxtaneural reparative fibrosis (Wu, 1996). However, our cases showed no significant calibration increase in the nerve. It has been reported that the best diagnosis method is the visibility of the digital nerve within the lesion (Simmons, 2008). Waizy et al. (2010) argued that to diagnose interdigital neuroma, the lesion should be viewed within the neurovascular bundle. The term, target sign, is used for central hypointense and peripheral hyperintense-looking round tumors (peripheral nerve sheath tumors, such as neurofibroma) derived from neural tissue (Bhargava et al., 1997). We found that, on the post-contrast series and even on the STIR images in some of the cases, the

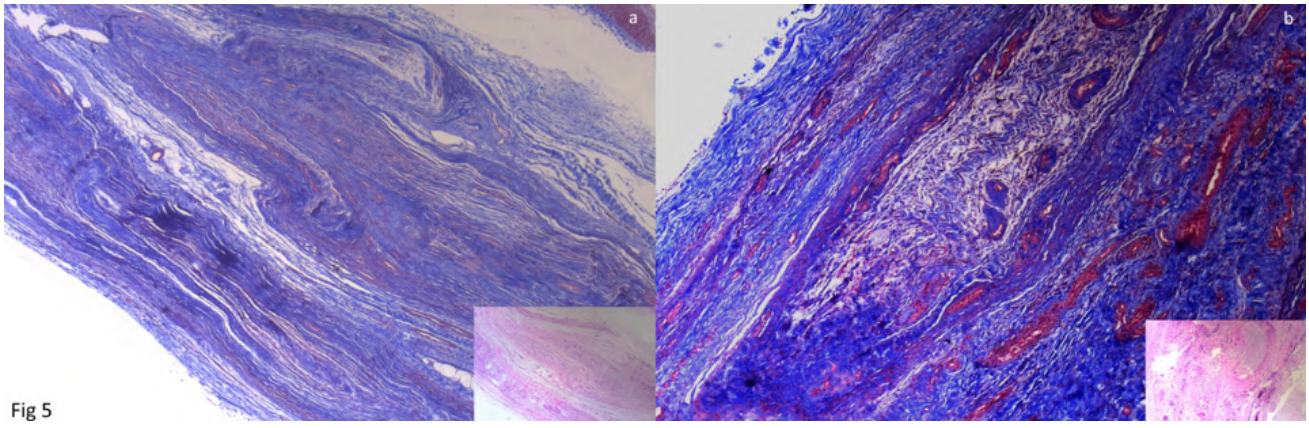

Fig. 5.- Pathological specimens of two different interdigital neuroma patients. First case (54-year-old woman). **(a)** has an earlier lesion than the second one (28-year-old woman). **(b)** Fibrosis and the connective tissue surrounding the nerve are more prominent in b than a. Marked fibrosis is stained darker blue with Masson Trichrome staining in b than a. (a, b = x40 MT; a-inset, b-inset = x40 HE).

hypointense nerve in the surrounding enhanced and hyperintense (to varying degrees) soft tissue makes the appearance of the target sign (Fig. 1). This finding was observed in 23 (59%) of the 39 neuromas.

Some studies claimed that a contrasted series is diagnostically useful (Terk et al., 1993; George et al., 2005; Unger et al., 1992). Lee et al. (2007) also stated that contrast-enhanced series and T2W images are not essential for diagnosis, but are useful in differential diagnosis. Santiago et al. (2018) reported that, if clinically supported, a contrast enhanced series is not required for a reliable diagnosis of interdigital neuroma. We think that the target sign can increase the reliability of the diagnosis of interdigital neuroma by showing the nerve inside the lesion. At this point, and in addition to the information presented above, we believe that the post-contrast series can be useful.

Conservative and surgical treatment options are available in the treatment of interdigital neuroma. Conservative treatments such as shoe modification, use of insoles, and administration of anti-inflammatory drugs, can be tried in the early stages of the disease. Percutaneous therapies can be used, such as injections of local anesthetics, with or without steroids, or of alcohol (Samaila et al., 2020; Sato et al., 2022). Some studies reported that the size of the lesion will affect the treatment option (Biasca et al., 1999; Makki et al., 2012; Park et al., 2018). Surgical treatment is indicated in cases that do not respond to any other treatments. Neurectomy can be performed with a dorsal or plantar approach. Surgical treatment success rates range from 88-94% (Valisena et al., 2018). However, surgical treatment may not always yield a positive result. This failure may be due to the incorrect indication for surgery or to excising the asymptomatic interdigital nerve (Weinfeld and Myerson, 1996). This reinforces the importance of making a correct diagnosis. When the lesion is small, 3T MRI can be used diagnose it early due to increased resolution.

This study has some limitations. The retrospective nature of the study design is the primary limitation. The sensitivity of our study was based on histopathologically confirmed cases, but due to ethical values and legal reasons, the sensitivity could not be calculated because the true-negative ratio was unknown. While we consider that the target sign can be seen with 1.5T MRI, it might be better evaluated with 3T MRI due to increased resolution. However, we could not encounter any article in the literature that assessed the appearance of the target sign with 1.5T MRI in interdigital neuroma.

CONCLUSION

In conclusion, to the best of our knowledge, this is the first study in the literature on 3T MRI that shows the visual characteristics of interdigital neuroma and its possible contribution to the diagnosis of the disease. Our results show that the most useful sequence in diagnosis appears to be the T1W sequence in 3T MRI, and that the identification of the nerve within the soft tissue, the appearance of the target sign, can guide the diagnosis. The high-resolution images obtained via 3T MRI mean that it becomes much easier to detect small lesions, which are potential causes of metatarsalgia. Diagnosing the lesions when the lesion sizes are smaller in the early period of interdigital neuroma may increase the chances of treating patients without surgery. Thus, early diagnosis can help manage the treatment of interdigital neuroma.

Patient Confidentiality and Consent to Publication: This study have been performed according to the Declaration of Helsinki.

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SUPPLEMENTARY MATERIAL

The following routine protocol for interdigital neuroma was used:

- Coronal longitudinal relaxation time-weighted (T1W) spin-echo MRI (400/12 [repetition time (ms)/echo time (ms)], 2-mm section thickness, 0.5-mm intersection space, acquisition of two signals, 12 x 6-cm field-of-view, and 572 x 262 matrix).
- Coronal STIR MRI (5373/30 [repetition time (ms)/echo time (ms)], 2-mm section thickness, 0.5-mm intersection space, acquisition of two signals, 12 x 6-cm field-of-view, and 208 x 115 matrix).
- Axial T1W spin-echo MRI (650/15 [repetition time (ms)/echo time (ms)], 2-mm section thickness, 0.3-mm intersection space, acquisition of two signals, 15 x 10-cm field-of-view, and 716 x 318 matrix).
- Coronal post- contrast SPIR (450/12 [repetition time (ms)/echo time (ms)], 2-mm section thickness, 0.5-mm intersection space, acquisition of two signals, 12 x 6-cm field-of-view, and 572 x 262 matrix).

All sequences were obtained using high resolution and with the subject in the supine position. The following MRI contrast agent was used: 0.2 mL/kg gadoterate meglumine (Dotarem, Guerbet, France).

Association between the sinus of Valsalva height and biometric parameters in patients with Marfan syndrome associated with aortic root aneurysm

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SUMMARY

Patients with Marfan syndrome and aortic root aneurysm require pre-surgical analysis of aortic root geometry for aortic reconstruction. The aim of this study is to perform the morphometric analysis of the sinus of Valsalva height and correlation between the former, age, weight, height, body mass index (BMI), and body surface area (BSA) in patients with Marfan syndrome and aortic root aneurysm. Data from 34 patients (28 men, 6 women) with Marfan syndrome and an ascending aortic diameter exceeding 45 cm were obtained using computed tomography angiography.

Gender-based differences were observed in the height of the left aortic sinus – by 47.23% (36.47±12.48 mm in men against 24.77±4.26 mm in women, p=0.0003). In men, a strong direct correlation has been identified between height and the right aortic sinus height (r=+0.75, p<0.0001), the posterior aortic sinus height (r=+0.71, p<0.0001), and the left aortic sinus height (r=+0.75, p<0.0001). Moderate reverse correlation has been discovered between the sinus of Valsalva height and BMI. No correlations have been identified between weight, BSA and the sinus of Valsalva height (p>0.05). In women, a strong direct correlation (Pearson) has been identified between age and the right aortic sinus height (r=+0.84, p=0.04), between weight and the left aortic sinus (r=+0.73, p=0.04) and between BSA and the left aortic sinus (r=+0.73, p=0.04).

Aortic sinus height in men increases with height and decreases with higher BMI and age. Weight and BSA do not affect the sinus of Valsalva height. In women, the sinus of Valsalva height is impacted by age, weight and BSA.

Key words: Sinus of Valsalva – Aorta – Computed tomography angiography – Marfan syndrome – Aneurysm

INTRODUCTION

Marfan syndrome is an inherited disease connected with fibrillin-1 gene defect (FBN1) (Renner et al., 2019). Patients with Marfan syndrome suf-

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fer from cardiovascular pathologies (Goyal et al., 2017; Grewal and Gittenberger-de Groot, 2018; Xuan et al., 2021). Aortic pathologies are reported in 90% of cases (Martín et al., 2020; Vanem et al., 2018). One of the forms of pathologies is the dilatation of the sinuses of Valsalva, which results in an aortic root aneurysm. In patients with Marfan syndrome and aortic root aneurysm, the mortality rate caused by aortic dissection without surgical intervention is 50% (Goyal et al., 2017). Most patients (90%, according to Goyal) require pre-emptive surgical intervention.

Reconstructive surgery options are valve-sparing aortic root replacement or valved conduit aortic root replacement (Pepper et al., 2020). Indications for surgery are aortic diameter of more than 50 mm or more than 45 mm with concurrent risks and a growth rate of more than 5 mm/year (Goyal et al., 2017; Martín et al., 2020). However, research shows that not only the diameter is a predictor for the dissection and it should not be the sole indicator for intervention (Wenzel et al., 2021). Age (Pape et al., 2007), height, weight (Wenzel et al., 2021), sex (Vanem et al., 2018) may also be predictors of dissection or lethality. In previous studies the connection between aortic diameter, age (Bahlmann et al., 2011) and anthropometric measurements (Nagpal et al., 2020) was mentioned. Most studies on the measurement of the sinus of Valsalva height are conducted in patients with aortic stenosis since this measurement is obligatory when qualifying patients for transcatheter aortic valve implantation (TAVI) (Francone et al., 2020). We have not found data on the sinus of Valsalva height in patients with Marfan syndrome associated with aortic root aneurysm. Nevertheless, pre-surgical planning of cardiovascular intervention for aortic root/ascending aortic reconstruction includes an analysis of aortic root geometry. The sinus of Valsalva height influences the choice of surgical intervention type: valve-sparing aortic root replacement or valved conduit aortic root replacement.

The study presents a morphometric analysis of the sinus of Valsalva height in patients with Marfan syndrome and aortic root aneurysm. We tried to establish a connection between age, weight, height, body mass index (BMI), and body surface area (BSA) and the sinus of Valsalva height in men and women with Marfan syndrome and aortic root aneurysm.

MATERIALS AND METHODS

A retrospective study included analysis of pre-operative contrast-enhanced CT images of the aorta in patients with Marfan syndrome. The data had been taken from the registry of the Cardiac Surgery Department of Lviv Regional Clinical Hospital between 2019 and 2021. Inclusion criteria: patients over 18 years old, with diagnosed Marfan syndrome (based on Ghent nosology or genetic testing) (Renner et al., 2019), and with sinuses of Valsalva diameter of more than 45 cm (posterior sinus). Exclusion criteria: congenital heart defects, reconstructive surgeries of the ascending aorta, prosthetic aortic valve, incomplete anthropometric details of patients, and inappropriate image quality. Analysis of the 128 DICOM exams revealed that 34 patients met the criteria (28 men, 6 women). They were later divided into two groups based on gender.

CT angiography of the aorta was conducted on LightSpeed 64 VCT XT (General Electric, Boston, USA) with ECG synchronisation and Ultravist 470 (Bayer Healthcare, Berlin, Germany). Measurement of the sinus of Valsalva height was performed from the lower point of aortic valve cusps in the area of the left ventricular outflow tract (LVOT) up to the projection of the sinotubular junction (Hennessey et al., 2020). Image analysis has been conducted independently by two radiologists using radiology imaging viewer software RadiAnt DICOM Viewer v.5.0.2 (Poznan, Poland) in double-oblique projection (Francone et al., 2020). The sinus of Valsalva height is presented in cm. Clinical data of patients: sex, age, weight, and height, BMI and BSA (Mosteller formula).

The study was conducted in compliance with the ethical standards of the 1964 Helsinki Declaration and approved by the Bioethics Commission of Lviv National Medical University (Protocol No. 10 of 20 December 2021). Formal informed consent of the patients is not required.

Statistical analysis was conducted in R Commander (version 2.7-2. GNU General Public Li-

cense, Ontario, Canada) and SPSS (version 22.0. IBM Corp. Armonk, NY, USA). Student's t- test was used to analyze average values of biometric measurements (Gaussian data distribution). Calculation of pair connections between age and anthropometric indicators and the sinus of Valsalva height has been conducted using Pearson's linear correlation. The multiple connection between independent variables – biometric measurements (age, weight, height, BMI, BSA) and dependent variables – the sinus of Valsalva height – was examined with the help of multiple regression analysis. In all studies, $p<0.05$ was considered valid.

RESULTS

In men with Marfan syndrome and aortic root aneurysm (average age – 56.61±16.11 years, height 1.78±0.09 m, n=28), the average values of the height of the posterior and right aortic sinuses were practically on the same level (Fig. 1, Fig. 2). The average value of left aortic sinus height was slightly lower and equaled 36.47±12.48 mm. In women (average age 44.33±13.08 years, height 1.67±0.05 m, n=6), the height of posterior and right aortic sinuses is higher in comparison with the left sinus (Table 1). Gender-based differences were observed in the height of left aortic sinus

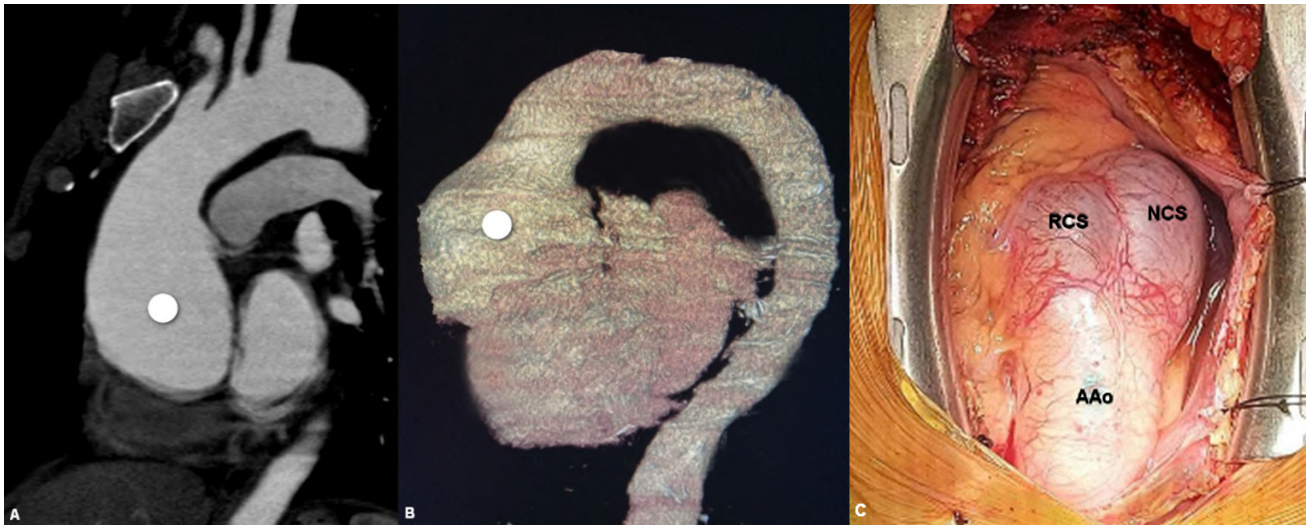


Fig. 1.- Computed tomography and intraoperative images demonstrating aortic root aneurysm in patient with Marfan syndrome. (**A**) A curved multiplanar reformatted view. (**B**) Volumetric rendering (3D reconstruction). (**C**) Intraoperative imaging of the right coronary sinus (RCS), the posterior or non-coronary sinus (NCS), and ascending aorta (AAo).

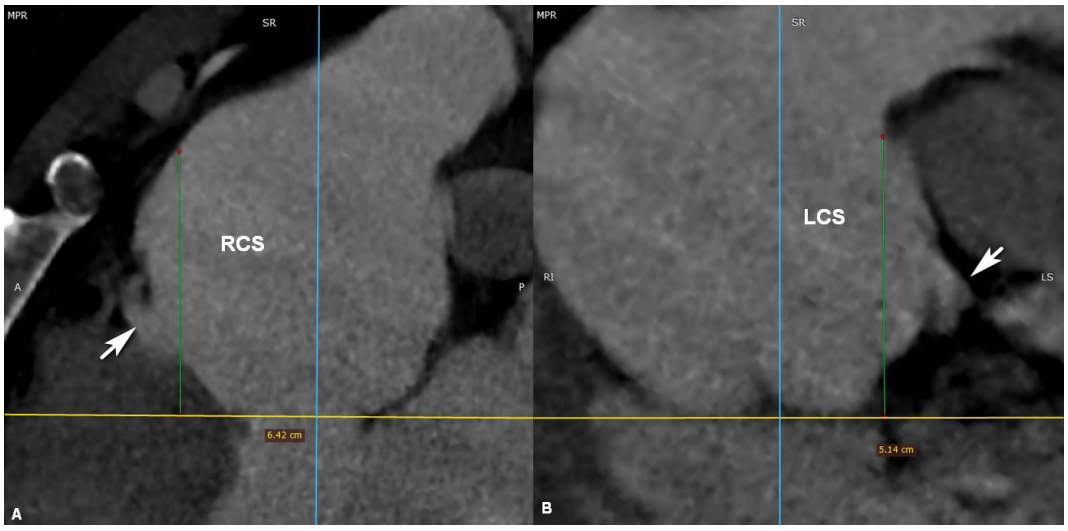


Fig. 2.- Computed tomography images of the measurement of the sinus of Valsalva height in male with Marfan syndrome and aortic root aneurysm. (**A**) The height of the right coronary sinus (RCS) and (**B**) the left coronary sinus with the appropriate coronary arteries (white arrow).

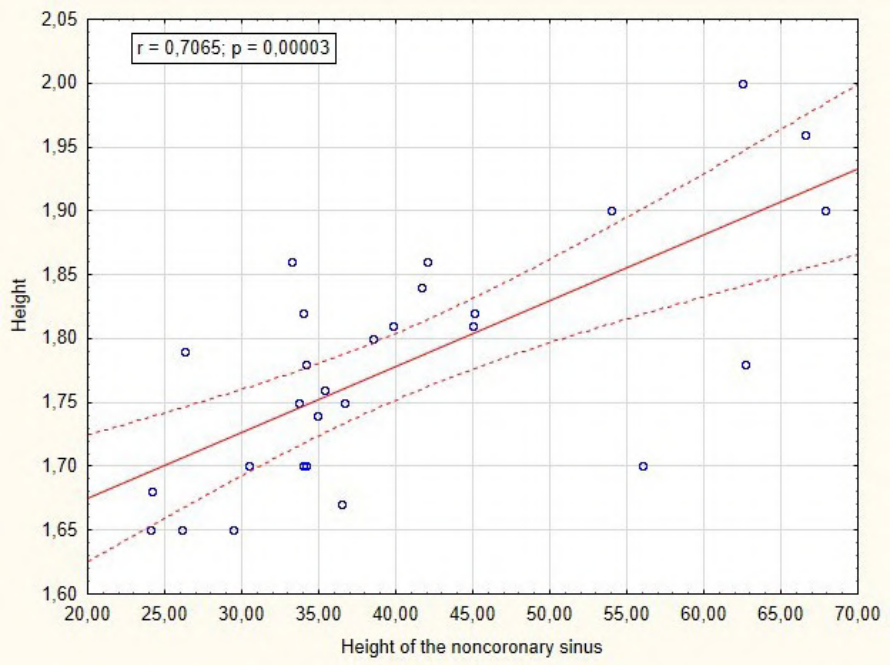
– by 47.23% (36.47±12.48 mm in men against 24.77±4.26 mm in women, p=0.0003). The height of the right and posterior sinuses of Valsalva in men is higher than in women with no statistical significance (p>0.05).

Significant correlation between height and the sinus of Valsalva height has been identified (Pearson). In men, strong direct correlation has been determined between height and the right aortic sinus height (r=+0.75, p<0.0001), the posterior aortic sinus height (r=+0.71, p<0.0001), the left aortic sinus height (r=+0.75, p<0.0001) (Table 2, Graphic 1). Moderate reverse correlation has been identified between the sinus of Valsalva height and BMI (correlation coefficient varied between r=-0.55, p=0.002 for the right aortic sinus height and up to r=-0.39, p=0.042 for the posterior aortic sinus height). No correlations have been discovered between weight, BSA and the sinus of Valsalva height (p>0.05). Moderate reverse correlation was found between age and the right aortic sinus height (r=-0.60, p=0.001), the posterior aortic sinus height (r=-0.50, p=0.006) and the left aortic sinus height (r=-0.48, p=0.009) (Graphic 2). Logically, significant correlations were proved between the height of the right, left and posterior sinuses of Valsalva (p<0.0001).

In women, strong direct correlation (Pearson) has been identified between age and the right aortic sinus height (r=+0.84, p=0.04), between weight and the left aortic sinus height (r=+0.73, p=0.04) and between BSA and the left aortic sinus height (r=+0.73, p=0.04) (Tab. 3, Graphic 3). Direct correlation was found between age and the left aortic sinus height (r=+0.41); between weight and the posterior (r=+0.55) and the right aortic sinus height (r=+0.49). BMI is directly correlated with all sinuses of Valsalva height (for the posterior (r=+0.55), the left (r=+0.52) and the right (r=+0.49)). The same correlation was detected between BSA value and the posterior aortic sinus height(r=+0.54) and the right aortic sinus height (r=+0.51).

Table 1. Comparison of blood vessel indicators in men and women with Marfan syndrome and aortic root aneurysm (M±SD, mm).

Indicators	Men (n=28)	Women (n=6)	p	Difference by gender (%)
Posterior aortic sinus height	40.33±12.76	34.23±9.33	0.19	17.82
Left aortic sinus height	36.47±12.48	24.77±4.26	0.0003	47.23
Right aortic sinus height	39.41±16.40	32.22±9.63	0.16	22.32

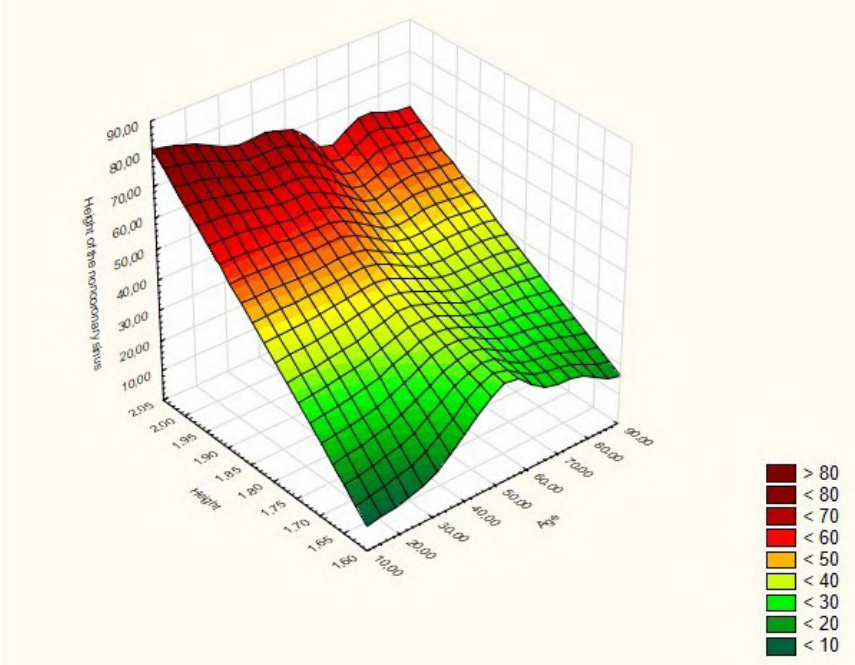


Graphic 1.- Correlation between height and posterior aortic sinus height indicators in men with aortic root aneurysm and Marfan syndrome.

Multiple regression analysis of the sinus of Valsalva height with a choice of optimal set of independent predictors (age, height, weight, BMI, BSA) in men with Marfan syndrome and aortic root aneurysm has confirmed several influences. The posterior aortic sinus height has been proven to be strongly influenced by age (reverse influence) and all anthropometric measurements (direct influence of height and BMI and reverse influence of weight and BSA): R=+0.81 with p<0.0002 (Fisher's exact test) and standard error of evaluation (SEE) 8.33. Adjusted coefficient of multiple determination R2adj=+0.57 points to the influence of these independent predictors on the posterior aortic sinus height in 57.4% cases. The left aortic sinus height has been strongly influenced by a set of 4

Table 2. Correlation (r) between the blood vessel, age and anthropometric indicators in men with Marfan syndrome and aortic root aneurysm. BMI: body mass index, BSA: body surface area.

Indicators		Posterior aortic sinus height	Left aortic sinus height	Right aortic sinus height
Age	r	-0.50	-0.48	-0.60
	p	0.006	0.009	0.001
Height	r	0.71	0.70	0.75
	p	<0.0001	<0.0001	<0.0001
Weight	r	-0.02	-0.06	-0.18
	p	0.93	0.76	0.35
BMI	r	-0.39	-0.42	-0.55
	p	0.042	0.024	0.002
BSA	r	0.18	0.13	0.05
	p	0.35	0.50	0.82
Posterior aortic sinus height	r		0.90	0.90
	p		<0.0001	<0.0001
Left aortic sinus height	r	0.90		0.89
	p	<0.0001		<0.0001
Right aortic sinus height	r	0.90	0.89	
	p	<0.0001	<0.0001	

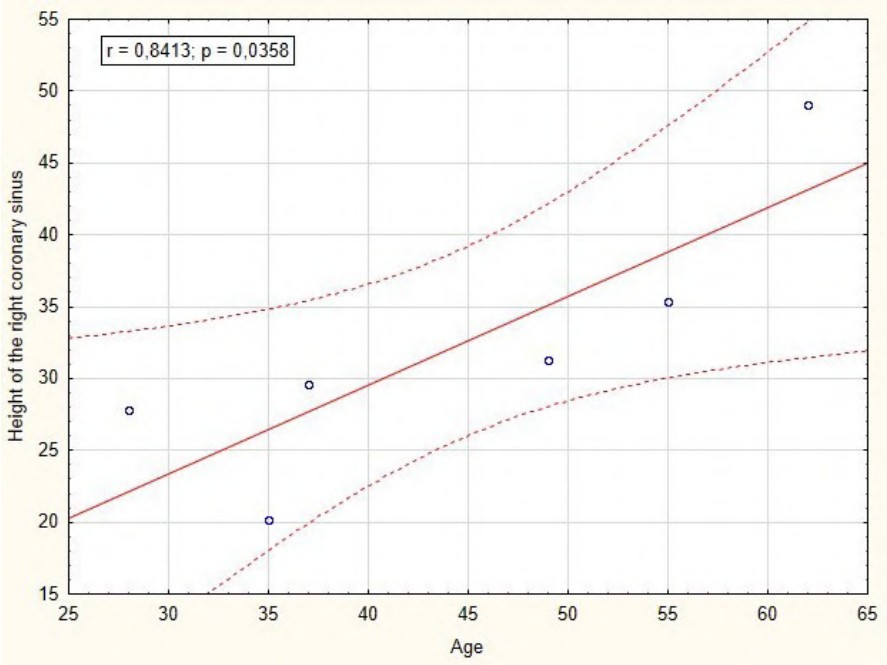


Graphic 2.- Correlation between height, age and posterior aortic sinus height indicators in men with aortic root aneurysm and Marfan syndrome.

independent predictors: direct influence of height and weight, and reverse influence of age and BSA. Multiple correlation coefficient accounted for R=+0.81 with p<0.0002 (Fisher's exact test) and SEE=8.12. Adjusted coefficient of multiple determination R2adj=+0.57 proves influence of independent predictors on the left aortic sinus height in 57.5% cases of this group. The right aortic sinus height depends on height, BSA (strong direct influence), age, weight, BMI (direct reverse influence): R=+0.875, p<0.0001, SEE=8.78. Adjusted coefficient of multiple determination R2adj=+0.71

Table 3. Correlation (r) between the sinus of Valsalva height, age and anthropometric indicators in women with Marfan syndrome and aortic root aneurysm. BMI: body mass index, BSA: body surface area.

Indicators		Posterior aortic sinus height	Left aortic sinus height	Right aortic sinus height
Age	r	0.28	0.41	0.84
	p	0.59	0.42	0.04
Height	r	-0.19	-0.01	-0.17
	p	0.72	0.98	0.74
Weight	r	0.55	0.73	0.49
	p	0.26	0.04	0.32
BMI	r	0.55	0.52	0.49
	p	0.26	0.29	0.33
BSA	r	0.54	0.73	0.51
	p	0.26	0.04	0.30
Posterior aortic sinus height	r		-0.21	0.17
	p		0.69	0.74
Left aortic sinus height	r	-0.21		0.77
	p	0.69		0.07
Right aortic sinus height	r	0.17	0.77	
	p	0.74	0.07	
	p	0.63	0.03	0.08



Graphic 3.- Correlation between age and the right aortic sinus height indicators in women with Marfan syndrome and aortic root aneurysm (Height, Age, Height of the right coronary sinus).

proves influence of independent predictors on the right aortic sinus height in 71.3% cases of this group.

Relevant risk analysis in comparison groups did not prove a significantly higher risk of abnormal values of the studied parameters of aortic sinus height in women with aortic root aneurysm compared with men who have the same pathology: RR was in the range of 0.32 to 1.07 ($p>0.05$).

DISCUSSION

Morphometric analysis of the sinus of Valsalva height in patients with Marfan syndrome and aortic root aneurysm identified higher values of the left aortic sinus in men than in women ($p=0.0003$). The height of the right and posterior sinus of Valsalva in men was also higher, yet without statistical significance ($p>0.05$). A correlation has been identified between age, weight, height, BMI, BSA and the sinus of Valsalva height separately in the group of men and the group of women. In men, a strong direct correlation between height and the right, left and posterior aortic sinuses height has been determined ($p<0.0001$). Moderate reverse correlation has been confirmed between BMI and the height of posterior sinus ($p=0.002$) and left sinus ($p=0.042$).

Reverse moderate correlation has been identified between age and the height of the right ($p=0.001$), posterior ($p=0.006$) and left aortic sinus ($p=0.009$). In women, age had a direct influence on the right aortic sinus height ($p=0.04$), weight and BSA affected the left aortic sinus height ($p=0.04$). Direct moderate correlation (from $r=+0.41$ to $r=+0.55$) has been established between age and the left aortic sinus height; between height, BSA and the posterior and right aortic sinus height; a correlation between BMI and the height of all aortic sinuses has not been proven due to limited sampling ($n=6$). Nevertheless, we consider it necessary to mention those correlations between age and anthropometric details and the sinus of Valsalva height. They might be important, when modelling an identical situation with more extensive sampling.

Multiple regression analysis has proven that the posterior aortic sinus height in men is strongly influenced by height and BMI and is reversely influenced by age, weight and BSA. The left aortic sinus height is strongly influenced by age and weight and is reversely affected by age and BSA. The right aortic sinus height is strongly influenced by height and BSA and is reversely influenced by age, weight and BMI.

These findings go in line with the statement that age has an influence on aortic dimensions (Erbel, 2006; Forte et al., 2020; Nagpal et al., 2020). In particular, the coronary sinus of Valsalva height in men is higher than in women (Stolzmann et al., 2009). It has been established that in patients with Marfan syndrome and aortic root aneurysm, age and height influence sinuses of Valsalva size just as in patients without diagnosed connective tissue disorders (Bahlmann et al., 2011; Nagpal et al., 2020; Plonek et al., 2019). The identified reverse correlation between age and sinus height proves that the value of aortic sinus height decreases with increased age in men with Marfan syndrome and aortic root aneurysm. Gender-based correlation between BSA and aortic size remains debatable (Forte et al., 2020; Nagpal et al., 2020). The question of correlation between biometric measurements and sinuses of Valsalva height in patients with Marfan syndrome and aortic root aneurysm still stands.

The sinus of Valsalva height is essential when planning cardiac surgeries for aortic root/ascending aortic aneurysms. Among all thoracic aortic aneurysms, the aneurysm of this segment is the most commonplace (approximately 60% of cases) (Nagpal et al., 2020). As of today, two options for aortic root aneurysm surgeries are available: valve-sparing aortic root replacement or remodeling (David operation, Yacoub procedure, Urbanski operation, neocuspidalization by Ozaki) and valved conduit aortic root replacement (Bentall-de-Bono surgery, full root technique, Wheat procedure) (Hennessey et al., 2020; Task et al., 2014; Valdis et al., 2019). Almost all procedures (except Wheat procedure, Ozaki procedure) require reimplantation of coronary ostia (Pidvalna et al., 2022). The criteria for selecting the type of surgery are the following: the higher the sinuses of Valsalva height, the higher the chances of a valve-sparing procedure. The lower the sinuses

of Valsalva height, the stronger the recommendations for valve-replacement surgery. For cardiologists, another critical indicator is the height of the posterior sinus, which is located close to the septum and right atrium. Adequate morphometric assessment of the aortic root ensures higher chances of a successful procedure and the functioning of a reconstructed aortic segment.

The analysis was conducted for each vessel parameter (dependent predictors) with a selection of an optimal set of independent predictors (age and anthropometric indicators). As a result of the present study, groups of independent predictors were formed, which had a valid strong influence on the values of the sinus of Valsalva height in persons with Marfan syndrome and aortic root aneurysm, which is proven by relevant validity criteria. Nevertheless, the study has its limitations. Firstly, it includes persons in their middle adulthood, which should be considered when assessing the influence of age on aortic dimensions. Secondly, a small sampling of women (n=6) had an effect on the unconfirmed correlation between age, anthropometric indicators and aortic sinus height. Thirdly, we did not assess the anatomy of the aortic valve (bicuspid or tricuspid), which may affect the aortic root geometry.

To conclude, the significant valid correlation has been identified between anthropometric indicators and the sinus of Valsalva height based on data of CT images of patients with Marfan syndrome and aortic root aneurysms. Aortic sinus height in men increases with increased height and decreases with increased BMI and age. Weight and BSA do not affect the height of sinuses of Valsalva. In women, the height of aortic sinuses is influenced by age, weight and BSA.

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Postulating a pathophysiological association between hallux valgus and plantar venous thrombosis through cadaveric dissections – Geometric measurements pedobarographic and phlebology correlates and literature review

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SUMMARY

This original article postulates a pathophysiological association between two uncommon clinical entities in a cadaveric subject. A female cadaver from a willed body donor was procured for educational and research purposes.

During surgical dissection, the subject was observed to have hallux valgus (HV) and lateral plantar venous thrombosis (PVT) on the left foot. Clinical significance of HV was confirmed by geometric measurements of the great toe and first metatarsal.

Severity of lateral PVT was established by meticulous dissection along full course of the vein and all its grossly accessible tributaries. Dissections in other regions of the same cadaveric subject did not reveal evidence of venous thrombosis elsewhere.

Extensive search of the contemporary literature confirmed HV is most common in elderly females, though not very common in the general population. It also established that isolated PVT is very rare, the medial type being rarer. No study mentioned both HV and PVT in the same subject or tried to establish a pathophysiological association between both entities.

Analyzing the pedobarographic and phlebology literature on HV, PVT, foot veins, gait, posture, and foot pressure points led the authors to postulate that flattening of medial arch and increased medial forefoot pressure from HV during life in elderly females could render Uhl-Gillot's postulated 'foot-pump' incompetent. Since the principal conduit of the foot-pump is the lateral plantar vein (LPV), ineffective foot-pump could lead to lateral PVT. Considering the paucity of literature on coexisting HV and PVT in living and cadaveric subjects, more studies are required to confirm our hypothesis of this pathophysiological association.

Keywords: Hallux valgus – Plantar venous thrombosis – Cadaveric subject – Foot pump – Pathophysiological association

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INTRODUCTION

A postmortem dissection study is presented wherein both hallux valgus (HV) and plantar venous thrombosis (PVT) coexisted on the same side in an elderly female cadaveric subject. HV *per se* is a well-documented entity, with a plethora of references over the last 90 years (Piggott, 1960; Inman, 1974; Wilson, 1980; Mann, 1993; Perera, 2011; Kohls, 2022). One of the earliest descriptions of HV was in 1928, when they described a conservative lateral ligament release surgery for 'bunion', a hoary procedure that carries the surgeon's name till this day (McBride, 1928). Isolated PVT, on the other hand, has been much less frequently reported than HV, with the exact prevalence still being debatable. One study documented 78 cases of PVT from the 1990's to the 2020's (Rastel, 2021). Another study reported less than 20 cases of PVT before 2013 (Karam, 2013). Bernathova (2005) was among the first to demonstrate PVT using sonography and magnetic resonance imaging (MRI). All cases of PVT documented thereafter coincided with advances in radiological techniques (Czihal, 2015; Quinn, 2018; Rastel, 2021). No description of PVT in a cadaveric subject could be found in the literature. Neither did we find the coexistence of HV and PVT in the same individual after extensive search of the literature.

Pathophysiology of calf deep vein thrombosis (DVT) after HV surgery has been well established (Radl, 2003; Saragas, 2014; Kohls, 2022). However, no pathophysiological association between HV and PVT has ever been described or postulated. Therefore, the objective of this study was to postulate a pathophysiological association between HV and PVT in the same individual. To achieve that objective, this study focused on geometric measurements of the cadaveric subject's foot, analysis of HV-associated gait, followed by correlation with pedobarographic and lower limb phlebology literature (Blomgren, 1991; Bryant, 1999; Menz, 2005; Uhl, 2010). Consistent with the study objective, Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines were considered redundant in this study (Page et al., 2021).

MATERIALS AND METHODS

A cadaveric subject wrapped in custom fixative was procured from Research for Life, Phoenix, AZ. after it was approved for release. The cadaver was a donated non- clinical human tissue, intended for medical research and education purpose only, with permission to be exported, with the dissected remains imported back to the lending institution in the United States for cremation under government regulations stipulated under the Pan American Health Organization (PAHO) resolution of October 1996 XVII Conference. A donor form giving permission from the executor of the deceased is on file at the lending institution. This form may not be released to anyone because of the United States HIPAA (Health Insurance Portability and Accountability) Law, which was enacted to give privacy in the medical field to all patient information.

As per legally disclosed information at the receiving institution, at the end of life the cadaveric subject was an 84-year-old Caucasian female, 5 feet tall, weighing 70 pounds. Serology tests on the cadaver for hepatitis B surface antigen, anti-hepatitis C virus antibody and anti-human immunodeficiency virus (HIV) 1 and 2 antibodies were non-reactive or negative. The cause of death of the subject was a stroke.

The cadaveric subject was placed in a prone position such that both feet were plantar flexed, heels were pointing up and soles were facing out. The position of the toes and the condition of the skin of the sole in both feet were noted. A curvilinear, inverted U-shaped incision was made on the left foot from lateral to medial, bridging across the calcaneal tuberosity. The skin of the sole was carefully dissected out from the underlying plantar aponeurosis (PA) and lifted as a flap based on heads of the metatarsal (MT) bones. The preliminary findings superficial to PA and plantar fasciae were noted. Next, the PA was incised at its proximal attachment to the calcaneus and carefully dissected off to expose the structures in first anatomical layer of sole.

The flexor digitorum brevis (FDB) was released from its proximal attachment to the calcaneus and reflected distally, based on its distal digital attach-

ments. Next, the abductor digiti minimi (ADM) was incised at its distal attachment and reflected laterally, thereby completely exposing the structures deep to the first anatomical layer of the sole. Finally, the lateral plantar vein (LPV), artery and nerve, and their branches and tributaries were meticulously dissected out to their maximum extent from their origin medial to the ankle to their grossly visible limits distally and deeply. The condition of these neurovascular structures as well as the orientation of the bones of the forefoot were noted. The dissected tissues were sprayed with proprietary Carolinas Perfect Solution® (www.carolina.com) to preserve the tissues, prevent desiccation and enable high-contrast image acquisition.

Using dual iPhone 13 camera, with 12-megapixel (MP), f/1.6, 26 mm (wide), 1.7 µm, dual pixel phase-detection autofocus (PDAF) features, and sensor-shift optical image stabilization (OIS) 12-MP, f/2.4, 13 mm, 120° (ultrawide) capabilities, all findings were graphically documented in landscape mode in high resolution and contrast.

A high-resolution image of the dissected sole of left foot was scaled to its real size with Microsoft Photos (©2022 Microsoft). Black circles were drawn on the image to denote the location of medial and lateral sesamoid bones under the head of first MT, which were visible and palpable. Next, one red line was drawn on the scaled image along the long axis of the proximal digit of the left great toe and extended proximally till the head of the first MT. A second red line was drawn along the long axis of the first MT on the same image (Fig. 1). Next, this image was superimposed on the image of an Online Protractor (OP) from an online app Ginifab© that was freely available on the Web (copyright © www.ginifab.com). The digital controls on the app were adjusted till the orientation and lines on the OP matched the lines drawn on the image. The angulation between the two red lines was noted on the OP (Fig. 2 / Graphic 1).

Extensive search of the literature published from the 1920's onwards was conducted. The keywords used in search query were, but not limited to: 'plantar vein', 'plantar venous thrombosis', plantar vein thrombosis pathophysiology', 'hallux valgus', 'plantar vein thrombosis AND hallux valgus', 'hallux valgus and gait', 'hallux valgus and foot pressure', 'hallux valgus and posture', 'hallux valgus AND deep vein thrombosis'. The search databases and repositories included Pubmed, Medline, Google Scholar, Public Library of Science (PLOS) and ScienceDirect, among others.

The search queries were structured to extract the contemporary pedobarographic and lower

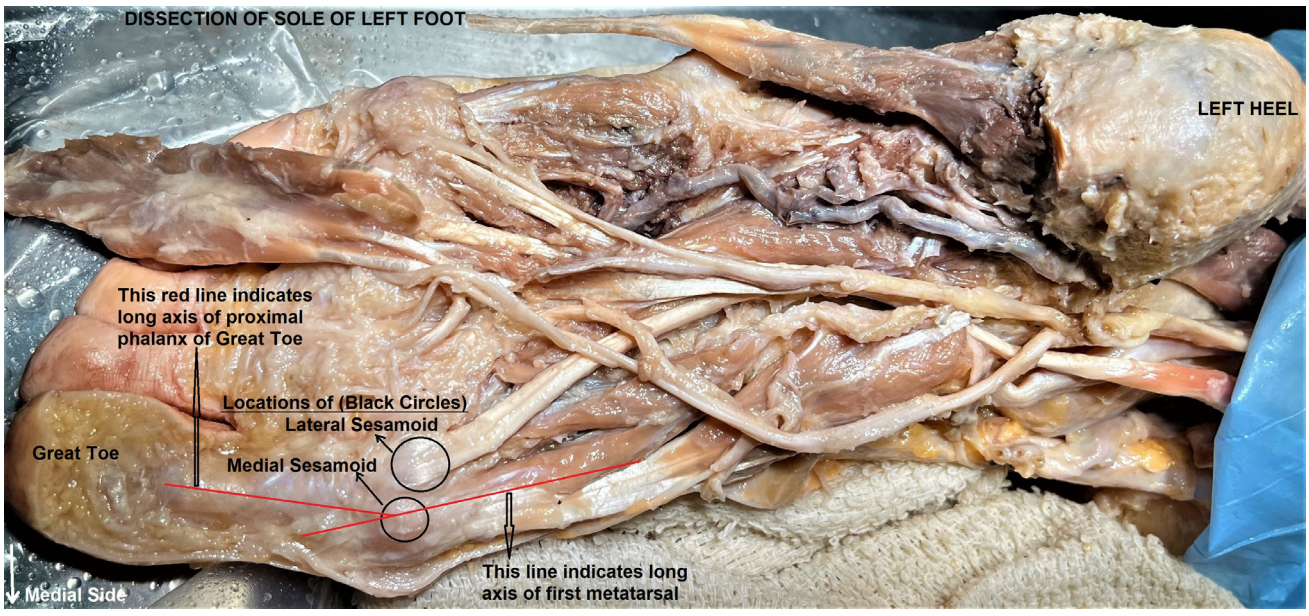


Fig. 1.- Image of dissected sole of left foot to demonstrate how HV angle was delimited on the image and elucidated in the subject's foot. Plantar aponeurosis has been removed. Black circles denote location of sesamoid bones, which are displaced laterally, under head of the medially deviated first MT. Distal red line indicates axis of proximal phalanx of great toe. Proximal red line denotes long axis of first MT. Acute angle between the red lines denotes the HV angle.

limb phlebology literature in relation to HV and PVT. This study was not intended to be a systematic review or meta-analysis of HV and PVT literature. Hence, Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021) were considered redundant in this study.

RESULTS

The first level of dissection of the sole of the left foot revealed numerous punctate and linear bluish-black discolorations, extending from the medial side of the ankle, going under the PA, then progressing along the lateral aspect of the sole till the distal end of the fifth MT. These discolorations were observed piercing through the lateral plantar but not the medial plantar fascia. A few punc-

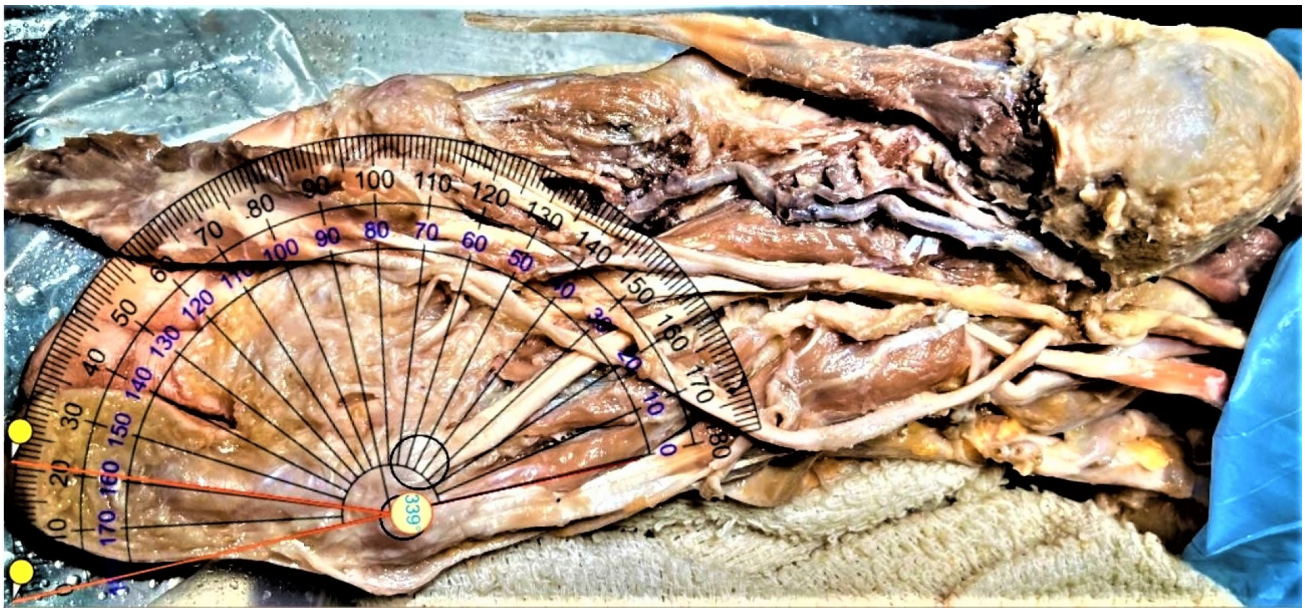
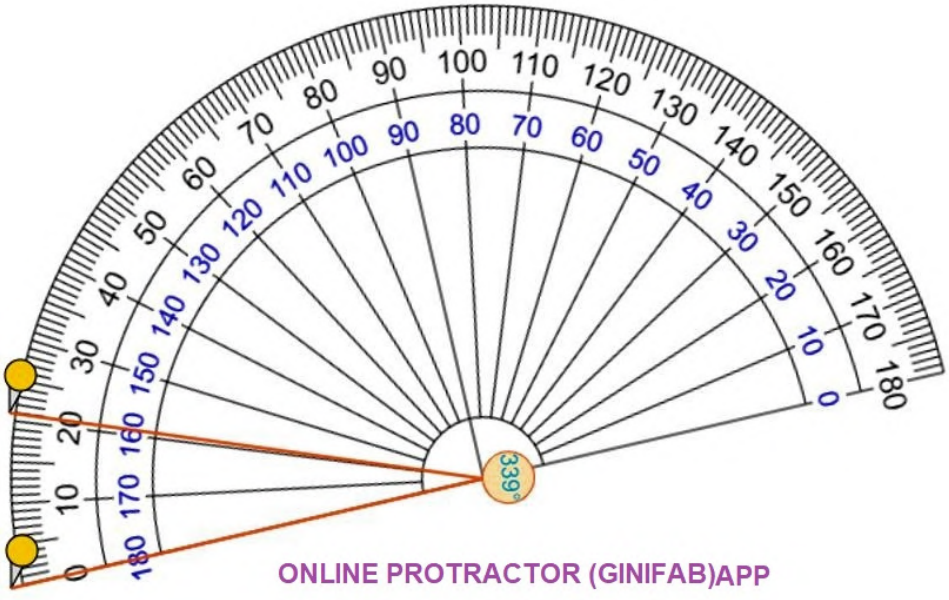


Fig. 2.- Image of dissected sole of foot to demonstrate how HV angle was recorded using the online app OP from Ginifab©. The image of OP is superimposed on image of Fig. 1. Coordinates of OP are adjusted to match the red lines drawn in Fig. 1. The acute angle between long axis of first MT and proximal phalanx of great toe was calculated as 21° (= 360° - 339°). This is suggestive of clinically significant HV (Normal HV angle is <15°).



Graphic 1. Isolated graphic of OP from Ginifab© showing angulation between long axis of first MT and proximal phalanx of great toe. 339° subtracted from 360° gives 21°, which is the angle between long axis of first MT and long axis of proximal phalanx of great toes. This is suggestive of clinically significant HV (Normal HV angle is <15°).

tate spots were also observed piercing through the proximal part of the PA, but most were distributed along its lateral margin (Fig. 3). The sole of the right foot appeared clinically normal.

Deeper dissection under the PA, and especially under the first anatomical layer of the sole, revealed extensively thrombosed LPV along its entire extent, starting proximally superficial and medial to the ankle, and extending distally and laterally. The proximal part of the thrombosed LPV was in the surgical plane between FDB and quadratus plantae (QP) muscles, which are typically characterized as the first and second anatomical layers of the sole respectively (Moore et al., 2021). The thrombotic processes even included the superficial, deep, and muscular tributaries of LPV. Thrombosis of muscular tributaries of LPV from FDB and proximal part of ADM muscles had rendered a bluish-black discoloration to these muscles as well. The left medial plantar vein was very small and otherwise normal. The veins in other areas of the body were normal (Fig. 4).

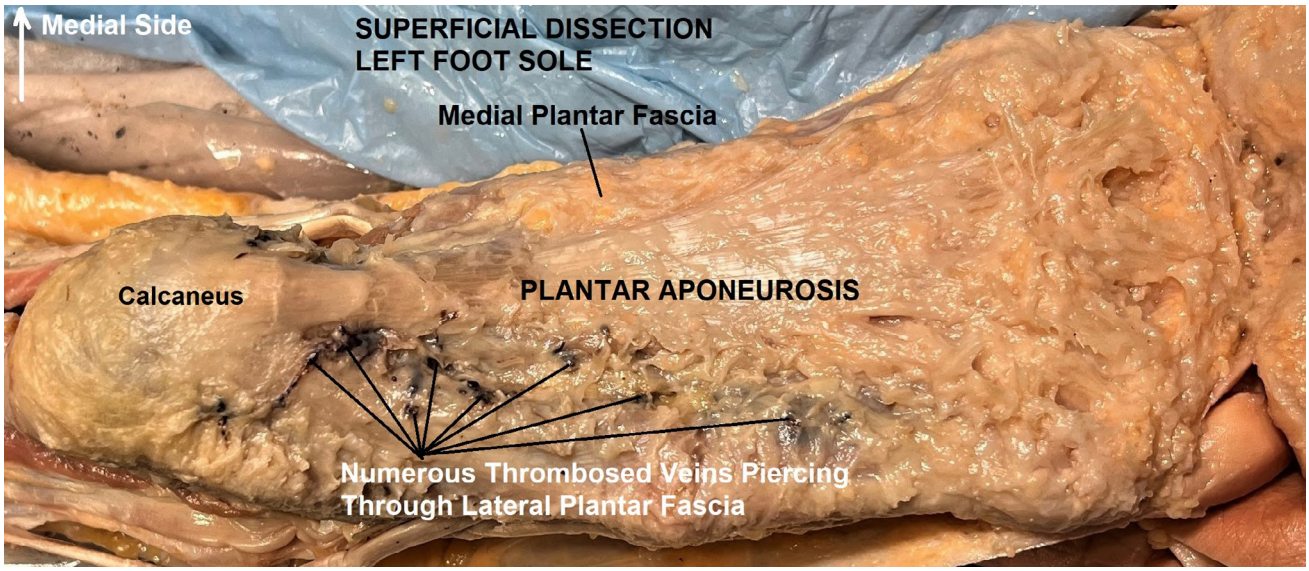


Fig. 3.- Image of dissected sole of left foot immediately after removal of the skin of sole. Thrombosed veins are visible extending from medial side of left ankle and progressing to lateral side of left foot. Most of the thrombosed venules are seen piercing through the lateral plantar fascia but not through medial plantar fascia. Some thrombosed veins are piercing through the proximal part of PA also.

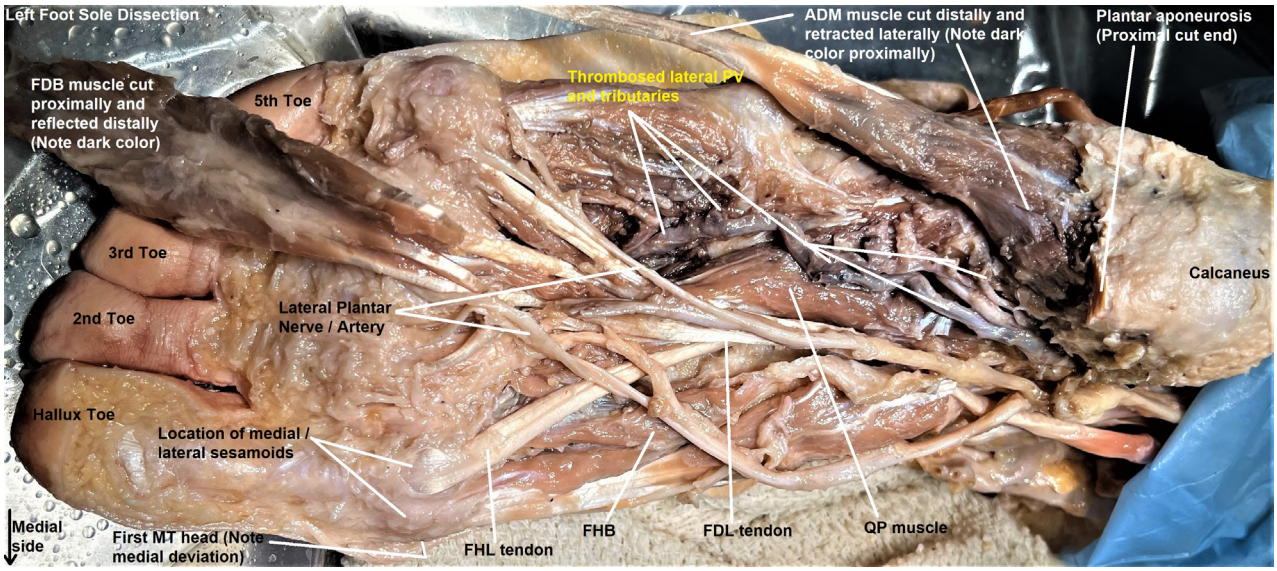


Fig. 4.- Image of dissected sole of left foot, showing structures in first and second anatomical layers of sole. PA has been excised off. FDB has been incised at its proximal attachment and reflected distally. ADM has been incised at its distal attachment and reflected laterally. Head of first MT is deviated medially. FHL tendon is over-riding the lateral sesamoid bone under first MT head. Entire LPV is dilated, tortuous and thrombosed. Thrombosis extends to its deep and muscular tributaries. FDB and ADM muscles are discolored by the thrombotic process.

The head of the left first MT was deviated medially, and the two sesamoid bones under the head of the same MT were displaced laterally. The left flexor hallucis longus (FHL) tendon was over-riding the lateral sesamoid bone instead of passing between the two sesamoids. Distinct angulation was noted between the long axis of the proximal phalanx of the left great toe and the long axis of the first left MT. Measurement with the online app OP on the digital image revealed an angulation of 21° between these two axes (Graphic 1).

DISCUSSION

Hallux valgus

Angulation of less than 15° between the proximal phalanx of the great toe and the first MT is considered normal (Hecht and Lin, 2014; McKean and Park, 2022). With an angulation of 21° in the left foot of our cadaveric subject, a diagnosis of HV is reasonable. This is substantiated by the observation of partial over-riding of the great toe on the second toe in the same subject. This was also visible on gross examination of the right foot in our subject, although the angle was not measured on the right foot. HV *per se* is a well-documented entity, with a plethora of references ranging from the 1920s till the twenty first century (McBride, 1928; Hardy et al., 1951; Haines et al., 1954; Piggott, 1960; Inman, 1974; Wilson, 1980; Mann et al, 1981; Hung et al., 1985; Mann et al., 1993; Coughlin, 1995; Einarsdottir et al., 1995; McDonald, 1996; Torkki et al., 2001; Pique-Vidal et al., 2007; Perera et al., 2011; Reina et al., 2013; Hecht et al., 2014; Loveday, 2020; Kohls, 2022; McKean, 2022). HV has been clinically documented to be more common in elderly females (McKean and Park, 2022). Clinically significant HV subjects also have first intermetatarsal (IM) angle of more than 9° (Hecht and Lin, 2014; McKean and Park, 2022), but the circumstances of this cadaver dissection precluded measurement of IM angle in our subject. HV is associated with progressive lateral shift of sesamoid bones under the head of the first MT, due to bowstringing traction effect by the flexor hallucis brevis (FHB) muscle. As a result, the course of the FHL tendon to the great toe also gets deviated laterally. HV is also associated with partial flattening of the medial longitudinal arch of the foot (Moore et al., 2021). This may explain the disproportionately higher plantar pressures on the medial forefoot during gait and stance in HV patients (Plank, 1995; Yamamoto et al., 1996; Bryant et al., 1999).

Plantar venous thrombosis

The venous dissection findings in our cadaveric subject are consistent with the diagnosis of lateral PVT. Isolated PVT has been much less frequently reported than HV, with the exact prevalence still being a moot question. One study documented 78 cases of PVT from 1990 to 2022, giving an average prevalence of 2.6 cases per year (Rastel, 2021). However, another study reported less than 20 cases of PVT before 2013, thereby indicating most case reports began appearing during the last two decades (Karam et al., 2013). All clinical cases of PVT documented in the recent years coincided with advances in foot venous compression imaging techniques ranging from duplex ultrasound (DUS) to MRI (Karam et al., 2013; Czihal et al., 2015; Quinn, 2018; Swellengrebel, 2019; Edwards, 2021; Rastel, 2021, Sheikh, 2022). The most remarkable aspect of PVT is its rarity, and the resultant paucity of its reporting in the contemporary literature (Karam et al., 2013; Rastel, 2021).

Roughly two-thirds of cases of PVT are females (Czihal et al., 2015). Since the medial plantar vein was normal, our subject can be considered a case of isolated lateral PVT. Although a few reports have described medial PVT, lateral PVT has a preponderantly higher frequency, ranging from 30% to 96% in different studies, often extending into plantar arch and metatarsal veins, and a quarter of them extending into deep calf veins (Czihal et al., 2015; Vansevenant and Vanhoenacker, 2015; Quinn, 2018; Edwards, 2021; Sheikh et al., 2022). Prior dissections in this cadaver subject had not revealed any evidence of DVT in the calf.

About half of all cases of PVT are idiopathic, although a few may have occult malignancy, as part of paraneoplastic syndrome, or other hypercoagulable states, commensurate with Virchow's triad (Karam et al., 2013; Czihal et al., 2015; Vansevenant and Vanhoenacker, 2015). Few reports

of PVT caused by physical or mechanical strain or local trauma to the foot or use of orthoses have been mentioned in the literature (Czihal et al., 2015; Vansevenant and Vanhoenacker, 2015; Swellengrebel et al., 2019; Rastel, 2021).

Considering calf DVT in general, factors such as age, gender, footwear, genetic predisposition or mutations have all been postulated to play significant roles in their pathogenesis. Numerous studies have established other risk factors of DVT, namely postoperative recumbency, foot surgery, smoking, cardiac conditions, paralytic stroke, family history, and drug usage, among others (Radl et al., 2003; Peterson et al., 2011; Saragas et al., 2014; Masaragian et al., 2019; Loveday, 2020; Kohls, 2022).

Although our cadaveric subject was known to have died from a stroke, it is difficult to speculate the role of any of these factors in the pathophysiology of isolated lateral PVT in our subject. In the absence of any other sites of venous thrombosis like calf DVT, or obvious etiology of isolated lateral PVT, and not knowing the subject's medical history during her lifetime, analysis of pedobarographic and phlebology literature provided vital clues towards a possible pathophysiological association between HV and lateral PVT in our subject.

Foot phlebology analysis

The foot is drained by a medial and lateral venous network respectively, the latter being larger. The two networks are connected by the first IM perforating vein (Uhl and Gillot, 2010; Vansevenant and Vanhoenacker, 2015). LPV, being the larger of the two plantar veins in the sole of the foot, is the main conduit of venous blood flow from the sole. It drains venous blood from the toes and deep MT veins into posterior tibial Venae Comitantes (VC). LPV follows a course between the FDB and QP muscles, which are fleshy muscles of the first and second anatomical layers of the sole of the foot respectively (Uhl and Gillot, 2010; Moore et al., 2021). According to Uhl and Gillot's 'foot-pump' hypothesis (2010) in their prize-winning seminal phlebology work, these muscles are the principal actuators of the foot-pump, among other intrinsic foot muscles. During various phases of normal walking and standing, venous blood drains sequentially from toes through deep MT veins into the functional 'receptacle' of the LPV, through the latter's physiological distal 'suction pole'. Then the blood is transmitted to the posterior tibial VC through the proximal 'ejection pole' of LPV. This is achieved by the 'milking action' of the intrinsic foot muscles, including the FDB and QP, between which the LPV passes, assisted by normal lateral plantar pressure of longitudinal arch of foot during various phases of gait and stance. The components of the foot-pump are designed to function synchronously and synergistically in normal foot configuration with normal arch supports. In most cases the medial plantar vein is small and does not play a significant role in the foot-pump hemodynamics (Uhl and Gillot, 2010).

Pedobarographic analysis

Pedobarographic studies, which assess foot pressure patterns and distribution during stance and gait, have amply demonstrated abnormal stress patterns on metatarsal heads during various phases of gait in patients with HV. Only one study mentioned increased lateral forefoot pressures during stance and gait in HV patients (Blomgren et al., 1991). Most other studies have recorded increased medial foot pressure patterns, namely significantly higher mean, and peak medial plantar pressures under first three MT heads, especially under first MT head, and increased medial foot contact time in patients with HV. The higher peak pressures under first MT head correlated with higher HV angle and IM angle (Plank, 1995; Yamamoto et al., 1996; Bryant et al., 1999). The slight flattening of the medial longitudinal arch of the foot in patients with HV may explain the higher medial plantar pressures and increased medial foot contact times recorded in these studies (Moore et al, 2021).

Pathophysiological association of HV and PVT

Correlating these phlebology and pedobarographic findings leads us to a possible pathophysiological association between HV and lateral PVT in our subject. Increased medial forefoot plantar pressures are counter-productive to effective functioning of the anatomical and physiological foot-pump (Uhl and Gillot, 2010). Our female ca-

daveric subject with HV would have had partially flattened medial longitudinal arch during her lifetime (Moore et al, 2021). She would have experienced increased medial plantar pressures and increased medial foot contact times during stance and gait (Plank, 1995; Yamamoto et al., 1996; Bryant et al., 1999). It could have led to ineffective functioning of the intrinsic foot muscles, thereby impeding venous return from the toes and deep MT veins into the LPV. Furthermore, inadequate 'milking action' of FDB and QP muscles, between which LPV passes, could have led to failure of functional components of LPV, namely the 'suction pole', 'reservoir', and 'ejection pole' of the foot-pump conduit. Resultant stasis in the LPV could lead to lateral PVT (Uhl and Gillot, 2010). The initiation of lateral PVT may have been from the first perforating IM vein, which connects the medial and lateral plantar venous networks (Vansevenant and Vanhoenacker, 2015; Rastel, 2021). Eventually, lateral PVT may be the precursor of calf DVT in susceptible subjects (Uhl and Gillot, 2010) (Fig. 5).

Gait studies in elderly people with HV have demonstrated temporospatial gait impairment, instability, and risks of falling, especially when walking on uneven surfaces (Menz and Lord, 2005). Physical or mechanical stress on the foot may potentially precipitate PVT in elderly subjects (Vansevenant and Vanhoenacker, 2015; Rastel, 2021). Therefore, it can be postulated that postural factors may have engendered lateral PVT in our cadaveric subject in a secondary way. Encumbered with HV and advancing age, our subject may have been experiencing abnormal mechanical stresses on her foot during her lifetime, leading to lateral PVT.

CONCLUSION

This study proposes a possible pathophysiological association between HV and PVT in an elderly female cadaveric subject. Given the unique coexistence of HV and lateral PVT in this subject, substantiated by a review of the relevant literature, it is our postulation that clinically significant HV in elderly females may alter posture and gait, leading to incompetence of the anatomical and physiological foot-pump postulated by Uhl and Gillot (2010). Since LPV is the main venous conduit of the foot-pump, and intrinsic foot muscles,

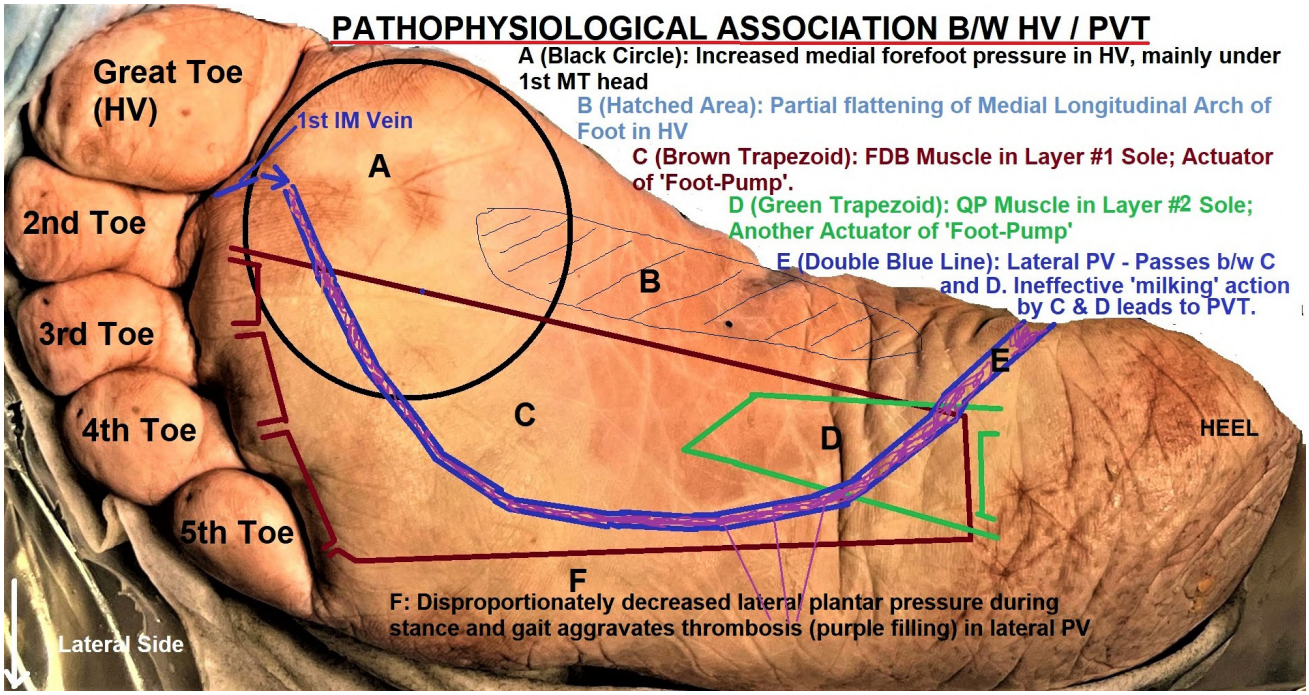


Fig. 5.- Diagrammatic overlay on image of sole of foot to illustrate the 'foot-pump' hypothesis of Uhl and Gillot and the possible pathophysiology association of lateral PVT and HV in this subject. The 'foot-pump' needs properly functioning intrinsic foot muscles, especially FDB and QP in a normally configured and arched foot to propel venous blood effectively through the lateral PV into the posterior tibial VC. HV disrupts the medial longitudinal arch of foot, leads to disproportionate increased medial forefoot pressures, and renders the 'foot-pump' ineffective. This paves the way for PVT and possibly DVT.

especially FDB and QP, are the actuators of the foot- pump, ineffective functioning of the latter can lead to altered venous hemodynamics in foot, leading to lateral PVT.

While pathophysiology of calf DVT and its sequelae have been documented and described *ad infinitum*, the literature is rather sparse in the context of foot PVT and its etiopathogenesis. It is almost nonexistent regarding specific pathophysiological association between HV and PVT, notably because of the relative rarity of both individually, and especially in combination, in the general population. Therefore, more pedobarographic and phlebology studies are required in living subjects with coexisting HV and PVT, for our pathophysiological association postulation to be confirmed.

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Polygastric flexor muscle of the index finger and its clinical implications

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SUMMARY

Although muscle variations in the forearm have been widely reported, the presence of supernumerary muscles in this compartment may be associated with compressive disorders of the nerves of the upper limb. The purpose of this study was to report the finding of a polygastric flexor muscle of the index finger (PFID), a supernumerary muscle associated with the anterior compartment of the forearm, the morphology and pathway of which are closely related to the median nerve. The PFID was found in a routine dissection of an upper right limb. Following a dissection methodology by planes, a narrow, polygastric muscle was identified, formed sequentially and interspersed by four tendons and three muscle bellies, that extended between the common flexor muscle mass of the anterior compartment of the forearm and the index finger. The sixth part of the PFID was partially in the carpal tunnel and established close relation with the median nerve, which was displaced superficially. Knowledge of this and other muscle variations that appear in the forearm and carpal tunnel are relevant when performing a differential diagnosis of carpal tunnel syndrome or in planning surgery on this canal.

Key words: Forearm muscle – Carpal tunnel syndrome – Median nerve – Nerve entrapment – Supernumerary muscle

INTRODUCTION

The muscles of the forearm are located around the radius and ulna, anatomically organized in two anatomical compartments called anterior and posterior. However, clinically three are described considering a lateral compartment, this is relevant for example in compartment syndromes (Fröber and Linss, 1994; Standring, 2016). Of these, the muscles of the anterior antebrachial region have four muscle planes that contain eight muscles (Testut and Latarjet, 1967).

In a recent paper, Wilde et al. (2021) describe in human embryos that forelimb muscles develop in an orderly sequence, from proximal to distal and from superficial to deep. In effect, at Carnegie stage (Cs) 18 (44 days) in the forearm flexor compartment the most superficial muscular layer are distinguishable (pronator teres, flexor carpi radialis, palmaris longus, flexor carpi ulnaris and flexor digitorum superficialis); at Cs 19-20 (46-49

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days), muscles of the deep layers become visible (flexor digitorum profundus). Later on, at Cs 22 (53 days), the intrinsic muscles of palmar region of the hand are detectable, including the thenar, hypothenar and lumbricals muscles. In line with this, in chick and mouse embryos, Tozer et al. (2007) provide evidence that the development of the vascular network precedes and delineates the future cleavage zones in the ventral muscle mass.

A morphological characteristic of most of the forearm muscles is that, at their proximal ends, they are mainly muscular, giving rise to long distal tendons that cross the radiocarpal, carpal, metacarpophalangeal and interphalangeal joints, mobilizing them remotely (Standring, 2016). These muscles can present numerical and morphological variations related to hereditary and evolutionary factors (Testut, 1884), which can have repercussions in aesthetic and functional aspects, and cause clinical disorders. In this sense, among the most frequent muscle variations in the anterior compartment of the forearm is the absence of the palmaris longus muscle (15% of population, Kapoor et al., 2008) and the presence of an accessory fascicle to the flexor pollicis longus (10% of population, Riveros et al., 2015) or flexor digitorum profundus (27% of population, Jones et al., 1997). In this regard, the accessory flexor digitorum profundus of the digiti minimi has been described, which originates in the distal third of the forearm to be inserted in the proximal phalange of the digiti minimi (Wahba et al., 1998), and which might compress the ulnar nerve or impede normal vascularization of the hand. In the same way, the bilateral absence of the flexor digitorum superficialis has been reported, a muscle that, in addition to contributing strength to the palmar-digital grasp, has been used in order to perform tendon transfers (Gupta & Kumar, 2014). Consequently, multiple variations have been described associated with the presence of accessory fascicles, absences as already mentioned, or attachments to other muscles of this compartment (Tountas and Bergmann, 1993; Tubbs et al., 2016).

Based on the muscle variations described and their clinical relevance, the purpose of the present report was to describe the anatomical aspects of a supernumerary muscle associated with of the anterior compartment of the forearm, which we did not find described in the literature.

CASE REPORT

In this case, we describe a unilateral supernumerary muscle located in the flexor compartment of the forelimb, observed in a routine dissection of an upper right limb of a female cadaver an 82-year-old cadaver. In the anterior compartment of the forearm, a polygastric, narrow muscle was detected, formed sequentially and interspersed by four tendons and three muscle bellies (Fig. 1), making a total length of 342.98 mm. The biometric measurements of width and length are summarized in Table 1. This variation originated independently from the medial epicondyle, extended between the common flexor muscle mass and the index finger, located in the forearm between the flexor digitorum superficialis and the flexor digitorum profundus. In the carpal tunnel, the muscle variation was located superficially to the flexor digitorum profundus, medially to the tendon of the flexor pollicis longus and laterally to the tendon of the flexor digitorum superficialis that goes to the index finger. In the mid-palmar region, the supernumerary muscle was located superficially and laterally to the first lumbrical, ending by adding to the tendon of the first lumbrical (Fig. 2).

With respect to the particularities of this finding, we can emphasize that in the carpal tunnel the distal end of the second muscle belly of this muscle was attached to the tendon of the flexor digitorum superficialis muscle (Fig. 3). From this belly, which entered the carpal tunnel, a tendon originated from which an additional muscle belly emerged, adding a total of three muscle bellies. It is worth mentioning that the third belly was located between two areas, in the carpal tunnel and in the middle palmar region. In the first of these two zones, it had a length of 22.2 mm, where its superficial and lateral location to the tendon that the flexor digitorum superficialis muscle supplies to the index finger and deep to the median nerve stood out. On the other hand, the muscle portion available in the mid-palmar region had a length of 38.93 mm (Fig. 3). According to what was observed, this supernumerary muscle corresponds to a polygastric flexor for the index finger.

The median nerve in the forearm had a superficial trajectory with respect to the polygastric flexor muscle of the index finger and deep to the flexor digitorum superficialis muscle. From the biometric point of view, prior to entering the carpal tunnel, the transverse diameter of this nerve was 3.89 mm and the anteroposterior diameter was 2.13 mm. In the carpal tunnel, at the midpoint between the proximal and distal edge of the transverse ligament of the carpus, its transverse and anteroposterior diameters were 4.54 mm and 1.63 mm, respectively. On leaving the carpal tunnel, the median nerve was located superficially to the third belly of the muscle variation, presenting a transverse diameter of 5.45 mm and an anteroposterior diameter of 2.17 mm (Fig. 2).

Table 1. Biometry of the polygastric flexor muscle of the index finger. Values are expressed in mm.

Portion	Type	Length	Width
1	Tendon	57.38	1.13
2	Muscle	71.12	4.84
3	Tendon	32.97	1.84
4	Muscle	72.22	12.15
5	Tendon	21.82	2.01
6	Muscle	61.13	6.46
7	Tendon	26.34	1.33
Total		**342.98**	

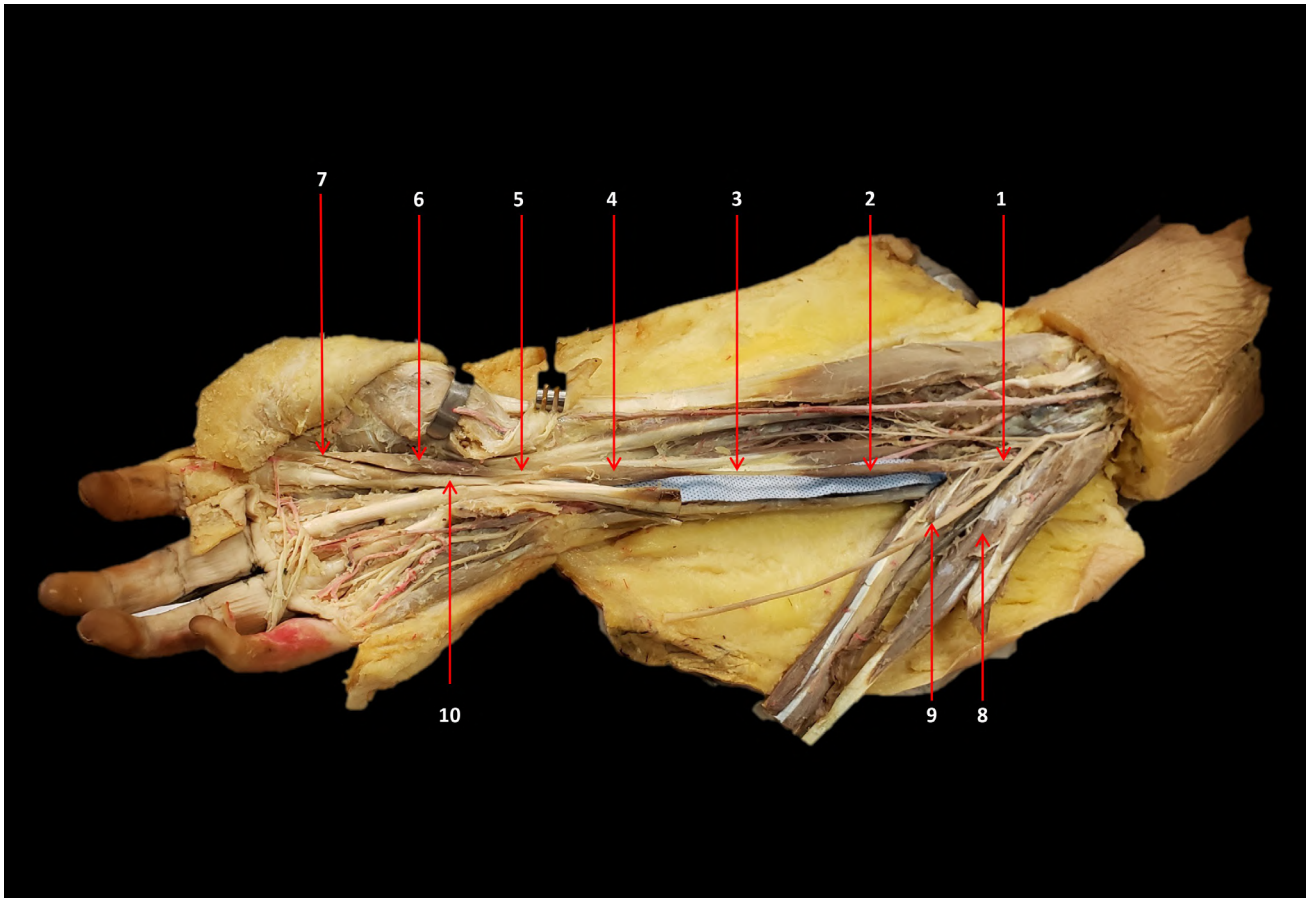

Fig. 1.- Panoramic photograph of the anterior compartment of the right forearm. The muscle is formed by 4 tendons and 3 muscle bellies arranged sequentially: 1. First tendon; 2. First muscle belly; 3. Second tendon; 4. Second muscle belly; 5. Third tendon; 6. Third muscle belly; 7. Fourth tendon; 8. Belly of the flexor digitorum superficialis muscle; 9. Median nerve; 10. Tendon of the flexor digitorum superficialis muscle of the index finger.

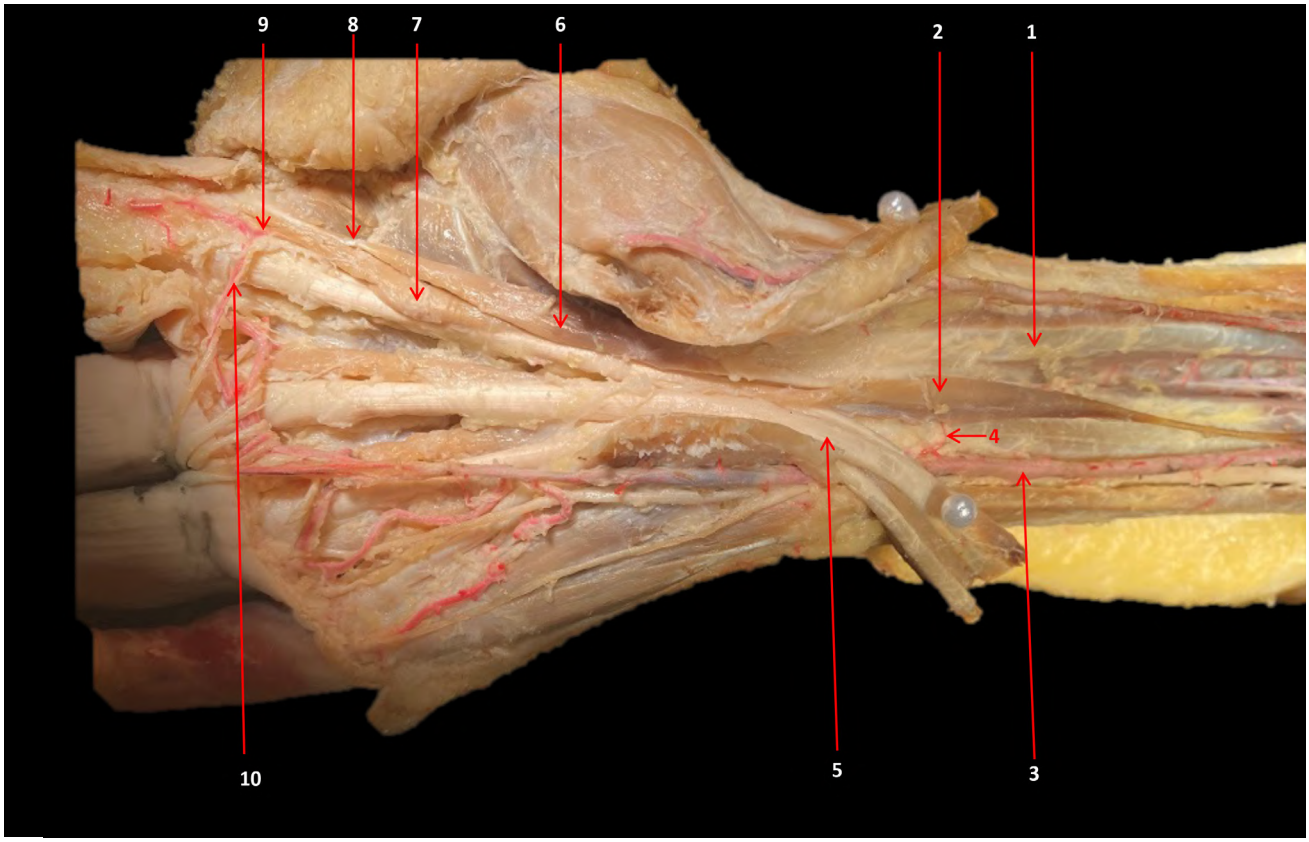

Fig. 2.- Photograph of the right palmar region, palmar aponeurosis moved aside: 1. Flexor pollicis longus tendon; 2. Second muscle belly; 3. Ulnar artery; 4. Muscular branches of the ulnar artery; 5. Flexor digitorum superficialis tendon; 6. Third muscle belly; 7. First lumbrical muscle originating from the flexor digitorum superficialis tendon for the index finger; 8. Fourth tendon; 9. Muscular branches of the radial artery; 10. Superficial palmar arch (radial contribution).

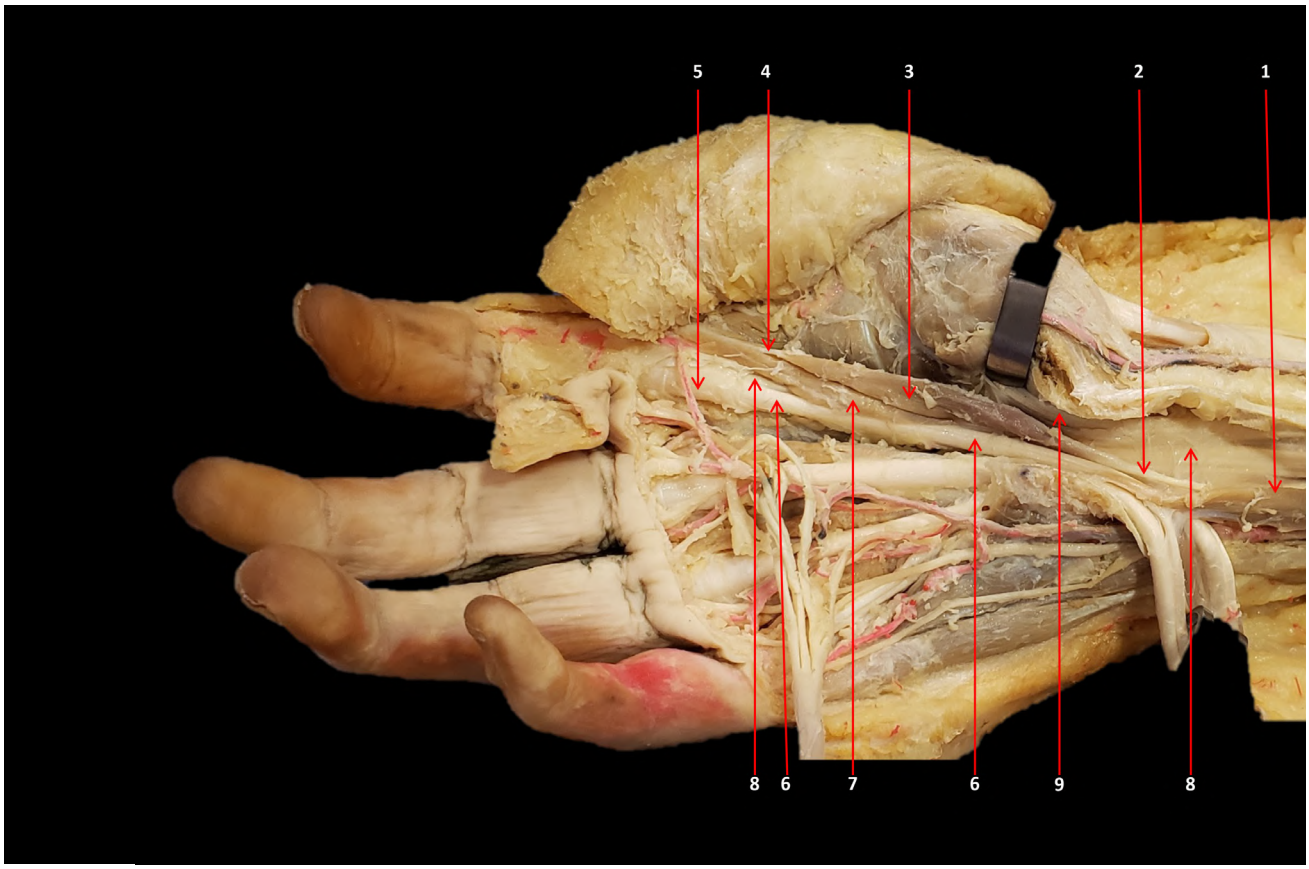

Fig. 3.- Photograph of the right palmar region, the median nerve moved aside: 1. Second muscle belly; 2. Third tendon; 3. Third muscle belly; 4. Fourth tendon; 5. Synovial sheath of the flexor tendons; 6. Flexor digitorum superficialis tendon for the index finger; 7. First lumbrical muscle originating from the flexor digitorum superficialis tendon for the index finger; 8. Flexor digitorum profundus tendon for the index finger; 9. Flexor pollicis longus tendon.

The innervation and vascularization of the polygastric flexor muscle of the index finger was sectorial, differing according to the part analyzed. The first belly of this muscle was innervated by a branch of the median nerve originating in the upper third of the forearm, which entered by the proximal third of the aforementioned muscle belly. On the other hand, it was vascularized by the ulnar artery, which supplied branches to it as it travelled through the deep side of this muscle belly. The second muscle belly also received a branch of the median nerve originating in the distal third of the forearm, which entered by the superficial side of this part. The vascularization for this muscle belly also came from the ulnar artery, which contributed fine branches that medially approached the aforementioned belly. Finally, the third belly of the muscle variation was innervated from a branch of the median nerve originating in the carpal tunnel. This branch entered through the proximal third of this muscle portion. In addition, the irrigation of this muscle belly was provided by the superficial palmar branch of the radial artery (Fig. 2).

DISCUSSION

In the anterior compartment of the forearm, the muscle variants described with greatest frequency include the palmaris longus, flexor pollicis longus and flexor digitorum profundus (Jones et al.,1997; Kapoor et al., 2008; Riveros et al., 2015). In the variations referring to the palmaris longus muscle, this muscle has been described as a variant of the deep palmar muscle, which generally enters the carpal tunnel to be inserted on the deep side of the palmar aponeurosis. This variation, called Palmaris profundus (Reimann et al., 1944), and its clinical implications have been seen on several occasions (Ortiz et al., 2022). Multiple origins have been described for the flexor carpi radialis, as well as variants derived from it, among which the short radial flexor muscle of the carpus stands out: the belly may originate in the medial epicondyle or at the medial edge of the brachial biceps tendon, to be inserted distally in the second metacarpal bone and in the tubercles of the scaphoid bone and trapezium, which could potentially cause compression on the carpal tunnel, as occurs with other muscles in the palm. This variant is characterized as being more present in the Asian population, where it reaches a prevalence of 6.8% (Tubbs et al., 2016; Cheng et al., 2020; Zhou et al., 2020). Regarding the flexor pollicis longus, the presence of accessory fascicles has been reported in 10% of cases, emphasizing the presence of bellies parallel to the flexor pollicis longus, which can pass through the carpal tunnel to enter the palmar region of the hand to be inserted in this finger, which could cause compression on the anterior interosseous nerve, or some of its branches extend to the deep muscles of the anterior compartment of the forearm or of the median nerve itself in the carpal tunnel (Riveros et al., 2015; Gurvich et al., 2022). With respect to the flexor digitorum superficialis muscle, it has been proven that a digastric muscle can emerge from its deep plane, the so-called digastric flexor of the index finger (Chudzinski*,* 1898*)*. In the same way, a case has been described where the entire flexor digitorum superficialis was digastric (Le Double, 1897). A muscle belly derived from this same muscle or directly from the coronoid process has also been reported, which ends in a tendon connected to the tendons of the flexor digitorum profundus or to the flexor pollicis longus, a variant known as the Gantzer muscle (Caetano et al., 2015).

It is well documented that the forelimb muscles develop in a proximal to distal and in a superficial to deep sequence (Wilde et al., 2021); and, according to Tozer et al. (2007), the vascular network precedes and delineates the future splitting of the ventral muscle mass. Considering these facts, we can assume that this supernumerary polygastric muscle in the flexor compartment of the forelimb develop during de embryonic period (*circa* 46-49 days), and the vasculature of this segment participate in it by segregation from the ventral muscle mass.

Regarding the variants mentioned in the forearm, the supernumerary polygastric muscle found in the present work originates independent in the medial epicondyle just like the short radial flexor muscle of the carpus (Tubbs et al., 2016); however, in this case it is located deep to the median nerve. It has three bellies and four tendons,

but does not look like any of those described; in fact, the most similar could be the digastric flexor muscle of the index finger. It has no relation of origin with the flexor digitorum superficialis, however, which also differentiates it from the Gantzer muscle. There are detailed reports on the connections between the superficial and deep planes of the forearm (Ohtani, 1979; Yamada, 1986), in fact, the occasional separation of the bellies of individual muscles has been considered a progressive variation, although very rarely the muscles are digastric (Tubbs et al., 2016).

In the hand, specifically, with respect to the first lumbrical muscle, supernumerary muscles emerge from the flexor digitorum superficialis tendon for the index finger (Wood, 1866; Le Double, 1897). In this case, the third belly of the supernumerary muscle emerged together with the flexor digitorum superficialis tendon of the index finger and was positioned next to the first lumbrical muscle. However, this belongs to a muscle originating independently in the medial epicondyle of the humerus; it does not originate from the flexor digitorum superficialis, flexor digitorum profundus or flexor pollicis longus (Figs. 1 and 3).

The sectorial innervation observed for the belly of this muscle is consistent with that observed in other polygastric muscles. An example of this is the case of the rectus abdominis muscle, which reveals the different myotomes that give rise to the muscle. Consequently, it is to be expected that different roots of the median nerve (C6-T1) come from the segmental innervation described in this case, as occurs with the innervation of the omohyoid muscle (Standring, 2016).

The descriptions of supernumerary or muscles variations in the carpal tunnel are frequent (Henry et al., 2015), and they can be the primary cause of carpal tunnel syndrome (Choo et al., 2017). Its finding during clinical imaging will be useful in surgical planning, improving the surgical results in the long term (Castillo et al., 2018). For this reason, it is important in the imaging studies to include a careful and targeted assessment of the fibro- osseous canals, such as the carpal tunnel, looking for accessory muscle bellies that can produce compressive symptoms (Sookur et al., 2008), both with the use of ultrasound and nuclear magnetic resonance, without forgetting that a simple revision of the carpal tunnel may not be sufficient (Jones, 2006).

CONCLUSIONS

Knowledge of this supernumerary muscle, which we did not find reported in the literature, enhances clinical and surgical practice, highlighting the importance of anatomy in medical practice. With this work it is hoped that there is a contribution to the knowledge of the anatomical variations of the forearm, and to the knowledge and better performance of specialists in attending patients with symptoms in this region.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The body was obtained through the donation program of the Faculty of Medicine at the Pontifical Catholic University of Chile (PUC), which complies fully with the World Medical Association's Declaration of Helsinki and national legal and ethical requirements. Consequently, the study was approved by the MED-UC Scientific Ethics Committee of the Pontifical Catholic University of Chile (No: 190115002).

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A unique case of combined variations of the cystic artery and biliary tree complicating the management of acute cholecystitis

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SUMMARY

Anatomic variations of the biliary tree and/or the vascular supply of the gallbladder pose challenges in the surgical management of diseases and conditions of the liver-biliary tree and the pancreas. A patient with acute cholecystitis underwent imaging investigation preoperatively with computed tomography of the abdomen and magnetic resonance cholangiopancreatography, which revealed a unique combination of variations: the cystic artery originated from the superior mesenteric artery and the right posterior sectoral duct drained at the same point with cystic duct to the common hepatic duct. The patient underwent open cholecystectomy and her postoperative period was uneventful. The surgeon should be aware of these variations in order to avoid intra- or post-operative complications, and the radiologists should report these variations because they could have a significant clinical impact.

Key words: Cystic artery variations – Biliary tree variations – Right posterior duct variations – Surgery – Imaging

INTRODUCTION

Anatomic variations of the biliary tree and/or the vascular supply of the gallbladder pose challenges in the surgical management of diseases and conditions of the liver-biliary tree and the pancreas. The cystic artery typically arises from the right hepatic artery and courses within the cystohepatic triangle to the right common hepatic duct (Andall et al., 2016). It then travels superior to the cystic duct at the gallbladder neck, after which it bifurcates into a deep and a superficial branch to supply the gallbladder and the cystic duct (Andall et al., 2016). The cystic artery may also have origin from nearby arteries such as the left hepatic artery, the gastroduodenal artery, the proper hepatic artery, the celiac trunk, the bifurcation of the proper hepatic artery, the superior pancreaticoduodenal artery, and the superior mesentery artery (SMA) (Andall et al., 2016).

The most common drainage of the right liver lobe ducts is through the right posterior and the right anterior sectoral ducts, the confluence of which forms the right hepatic duct (RHD) (Cucchetti et al., 2011). In the literature, many anatomic variations regarding the anatomy of the bile duct tree have been described. The pattern of

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the biliary tree in the right and left lobe has been classified into several types by some studies (Cucchetti et al., 2011; Chaib et al., 2014).

We present a unique case where a combination of cystic artery and biliary tree variations complicate the management of a patient with acute cholecystitis. The present case report adheres to the CARE checklist for reporting clinical cases.

CASE PRESENTATION

A 52 year-old female patient was admitted to the Department of General Surgery of our Hospital due to acute calculous cholecystitis. The diagnosis was set from her clinical presentation, the abnormal liver function tests, the elevated inflammatory markers and initial imaging with ultrasound examination of the liver and biliary tract. The patient was further investigated with computed tomography (CT) (Fig. 1) of the abdomen due to suspected complicated cholecystitis and with magnetic resonance cholangiopancreatography (MRCP) (Fig. 2) due to suspected stone in the extrahepatic biliary tree. The CT revealed the origin of a sizable cystic artery from the SMA. The MRCP showed that the right posterior hepatic (sectorial) duct (RPHD) drained at the confluence of the cystic duct to the hepatic duct.

She underwent open cholecystectomy due to severe gallbladder inflammation in the ground of these anatomical variations. Her postoperative course was uneventful, and she was discharged on the 2nd postoperative day.

DISCUSSION

There is an average of 24,5% of people who have variant origins of cystic artery, other than the common (75,5%) origin, which is the right hepatic artery (RHA). Although in this review most of the studies found that the main origin of the cystic artery is RHA, there is only one cadaveric study which reports that in 5% of cases the cystic artery originated from the SMA (Bekel, 2020).

In another imaging study of 256 cases, only two cases have been also reported where the cystic artery arose from SMA (Li et al., 2021). In the literature, only one case was also found of a cadaveric study of a cystic artery that arose from SMA, in an 86 years old woman (Yakura et al., 2017). The explanation for those variations in the origin of the cystic artery is found due to the specific developmental pattern of the biliary system. Embryologically, the branching pattern of the gastroduodenal and hepatobiliary vasculature is altered by the growth of both the liver and the pancreas. Four

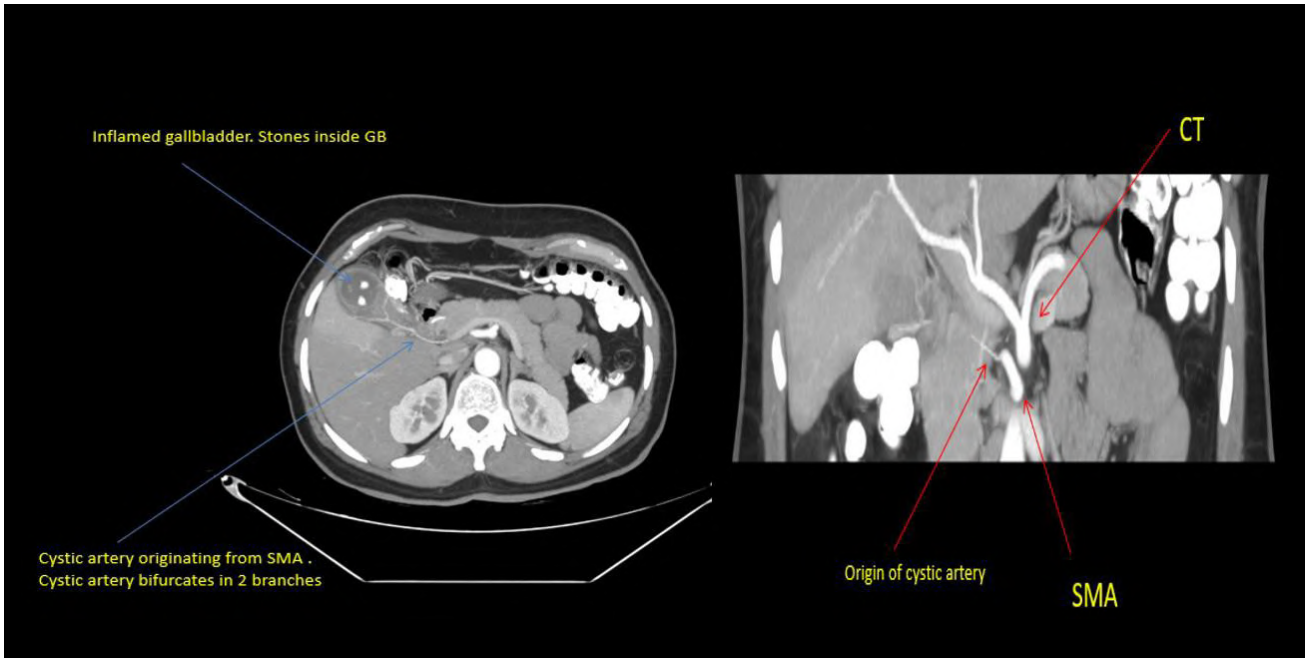

Fig. 1.- Left: CT scan which shows the inflammation of the gallbladder and the stones inside the gallbladder and the course of cystic artery. **Right**: CT scan which shows the origin of the cystic artery from the superior mesenteric artery. SMA: superior mesenteric artery, CT: celiac trunk.

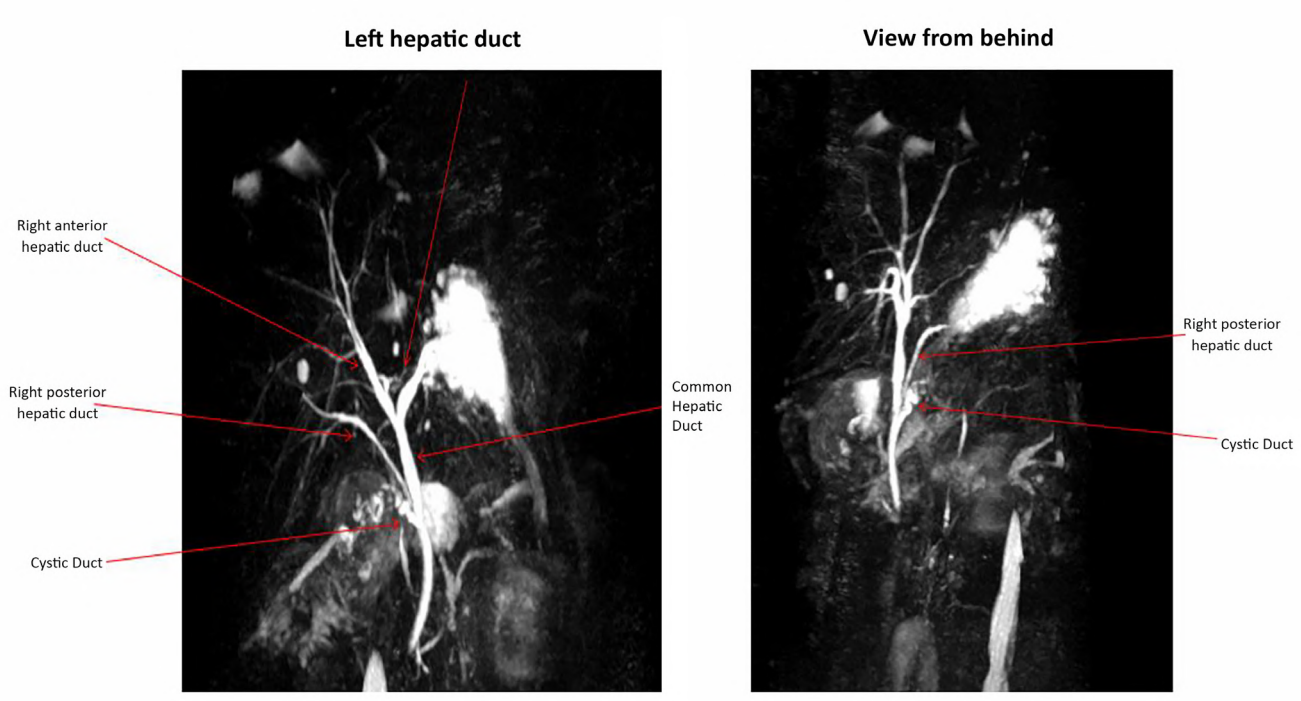

Fig. 2.- Left: MRCP that shows the right posterior hepatic duct draining into the common bile duct in conjunction with the cystic duct. **Right**: MRCP showing the same as in the left image but from a different angle.

primitive splanchnic branches arise from the abdominal aorta, but the central two disappear and the longitudinal anastomosis joins the first and fourth roots. The gastric, common hepatic, and splenic arteries originate at this longitudinal anastomosis. Variety of anomalies can occur from false retention or disappearance of parts of this primitive arterial plexus (Shuang-Qin et al., 2007). Moreover, considering that the liver is derived from a portion of the primitive duct supplied primordially by the celiac and mesenteric arteries, it may receive rami from both of these sources (Loukas et al., 2010). It is really important for the surgeon to be aware of all these variations and also to understand the problems they may cause in a cholecystectomy. Identification of the cystic artery intraoperatively might be challenging, because hemorrhage from an inadvertent injury of the cystic artery might be difficult to control in the ground of an inflamed gallbladder and surrounding tissues and force the surgeon to convert a laparoscopic cholecystectomy to an open one. This was one of the main concerns in our case in order to start the operation not laparoscopically but open.

The knowledge of embryology of biliary tree can explain the variations that exist. At the 5th week, the biliary tree is recognizable; up until the 6th week the common duct and ventral pancreatic bud rotate 180 degrees clockwise around the duodenum. At the 7th week, the bile and pancreatic ducts end in closed cavities of the duodenum, and at that time there is also a stimulation that causes hepatic cells to transfer into another cell type in order to create the duct cells and after all the tubule formation of the biliary tree (Hassan Gamal et al., 2013).

Some variation types may be close to our case, such as Type A5, which has an incidence approximately of 1,6% in an imaging study of 2,032 patients regarding variations in right hepatic duct (Chaib et al., 2014). In another cohort imaging study, ta similar type has been also described (4,5%), where the RPHD join the common hepatic duct after the right anterior hepatic duct (RAHD) and the left hepatic duct (LHD) has merged at the point at which the RPHD may be close to the confluence of the RA and LHD or more distal (Vakili and Pomfret, 2008). Similar also anatomic variation, where the RPHD joins below the confluence of the RAHD and LHD has been described in 8% of patients, in an imaging study of 200 people regarding anatomic variations in biliary tree (Cucchetti et al., 2011). The exact variation we present

where the RPHD, the cystic duct and the common hepatic duct merge at the same point has not been described so far.

The surgeon should be aware of these variations in the biliary tree to avoid an inadvertent injury or ligation to the right posterior duct and subsequent bile leak, or atrophy of the right posterior liver sector, or cause a laparoscopic cholecystectomy to convert to open due to difficulty in understanding the anatomy of the patient. This unique variation was the second reason that the surgeon decided to perform an open cholecystectomy.

Either of the variations which presented or the combination of them like in our case, might complicate liver or pancreas procurement and liver transplantation or might complicate liver resections or biliary tract surgery, or a Whipple's operation, or a gastric resection for cancer with D2 lymph node dissection, or most commonly might complicate a simple laparoscopic cholecystectomy, especially when inflammation exists. When present, these variations should be reported by the radiologists when they notice them in imaging studies.

In our case, the patient with acute cholecystitis had a right posterior hepatic duct that drained at the confluence of the cystic duct with the common hepatic duct, and a cystic artery arose from superior mesenteric artery. To the best of our knowledge, no other cases with coexistence of the same anatomic variations have been reported so far to the literature.

CONCLUSION

The surgeon should be aware of these variations in order to avoid intra- or post-operative complications, and the radiologists should report these variations because they could have a significant clinical impact.

Authors' contributions

P.K.: data collection and manuscript preparation. E.L.: original idea and critical review of the manuscript. All the authors read and approved the final manuscript.

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Congenital hand malformations in an anatomical donor: a potential case of brachydactyly type B

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SUMMARY

This study investigates the anatomy of a cadaveric hand presenting with a rare malformation that we identified as a form of brachydactyly. We performed a layer-by-layer dissection of the affected cadaveric hand and documented both the normal and variant anatomical compositions that were present. The osteology revealed complete aplasia of the proximal and middle phalanges of the second, third, fourth, and fifth digits along with truncated distal phalanges of the fourth and fifth digits. The radius, ulna, carpal bones, and the first digit were unremarkable. Neurovasculature followed standard anatomical courses. Normal development of surrounding musculature was observed.

Congenital hand malformations are infrequently observed in the anatomy lab and provide a unique learning opportunity for students and faculty alike. While hand deformities are frequently imaged through noninvasive techniques such as X-rays and CT imaging, they are infrequently dissected. Through dissection, clinicians and anatomists may be able to adopt a more tangible appreciation for the underlying anatomy of this condition.

Key words: Brachydactyly – Anonychia – Clinodactyly – Hand malformations

INTRODUCTION

The upper limb begins developing between weeks four to eight beginning with the formation of two paired limb buds (Guéro, 2018; Simet and Cassidy, 2021). There are several factors that can lead to limb dysmorphologies including but not limited to alternations in signaling biology, environment, and individual genotype (Simet and Cassidy, 2021). Congenital hand malformations occur in approximately 27.2 per 10,000 births (Goldfarb et al., 2017). One of these hand malformations is called brachydactyly. Brachydactyly is a general term that refers to disproportionately short digits in both the upper and lower extremities, resulting from abnormal development of either the metacarpals, phalanges, or both (Tentamy and Aglan, 2008). In this report, we investigated the anatomy

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of a cadaveric hand afflicted with brachydactyly by performing a layer-by-layer dissection to document any unusual findings present. Anatomists have been documenting variations in hand morphology for many centuries, but there are very few reports on the gross anatomy of congenital hand conditions such as brachydactyly (Henle, 1871; Macalister, 1866; Wood, 1866).

Surgical separation of syndactyly, osteotomy for deviated digits or bone grafting for short digits may be indicated in treatment of brachydactyly to enhance function (Stevenson and Hall, 2005). Therefore, there are clinical advantages in studying these limb dysmorphologies through dissection. The knowledge gained from dissecting these limb dysmorphologies provides crucial information of anatomical variation as well as confidence regarding treatment decisions such as surgical separation.

CASE REPORT

We describe a case of a 71-year-old female human cadaver that presented with brachydactyly that is rarely observed within the anatomy lab. The specimen was fixed with an embalming solution of formaldehyde and phenol. The cause of death was documented by the medical examiner as upper gastrointestinal bleeding. A layer-by-layer dissection was performed of the afflicted cadaveric hand and we potentially identified rare anatomical findings. The contralateral hand, and lower extremities presented with normal anatomy. The unskinned hand presented with truncation of second, third, fourth, and fifth digits, clinodactyly (curved finger) of the second and third digits, and anonychia (missing nails) of all digits with the exception of the thumb (Fig. 1). Clinodactyly, although present on the second and third digits, typically occurred in the fifth digit (Goldfarb and Wall, 2015). The inferior portion of the hand had been partially skinned by students for the medical anatomy course before we began this study. The next figure shows the completely skinned hand (Fig. 2). Thenar and hypothenar musculature had standard proximal and distal attachments. The superficial palmar arch and its branches were normal other than being truncated due to the shortness of the fingers. We next removed the thenar musculature and isolated

Fig. 1.- Left handed brachydactyly: The specimen presented with shortening of the second to the fifth digits along with anonychia of the second to fifth digits.

the lumbrical muscles and the tendons of the superficial flexor, flexor digitorum profundus (FDP) and flexor digitorum superficialis (FDS) muscles. All four lumbrical muscles were present but appeared slightly hypertrophic and longer in length than normally observed. Following standard anatomical description, the FDP tendons passed through splits in the FDS tendons, but FDS had a distal attachment on the distal phalanges as opposed to its regular attachment on the sides of the middle phalanges (Fig. 3). FDPs attachments were unremarkable. The lumbricals, FDS and FDP were removed in order to reveal the palmar interossei and the adductor pollicis muscle (Fig. 4). Both transverse and oblique heads of adductor pollicis were present. Finally, all remaining muscles were removed from their attachments in order to isolate the carpals, metacarpals, and phalanges. The osteology revealed complete aplasia of the proximal and middle phalanges of the second, third, fourth, and fifth digits along with truncated distal phalanges of the fourth and fifth digits (Fig. 5). The radius, ulna, carpal bones, and the first digit were unremarkable.

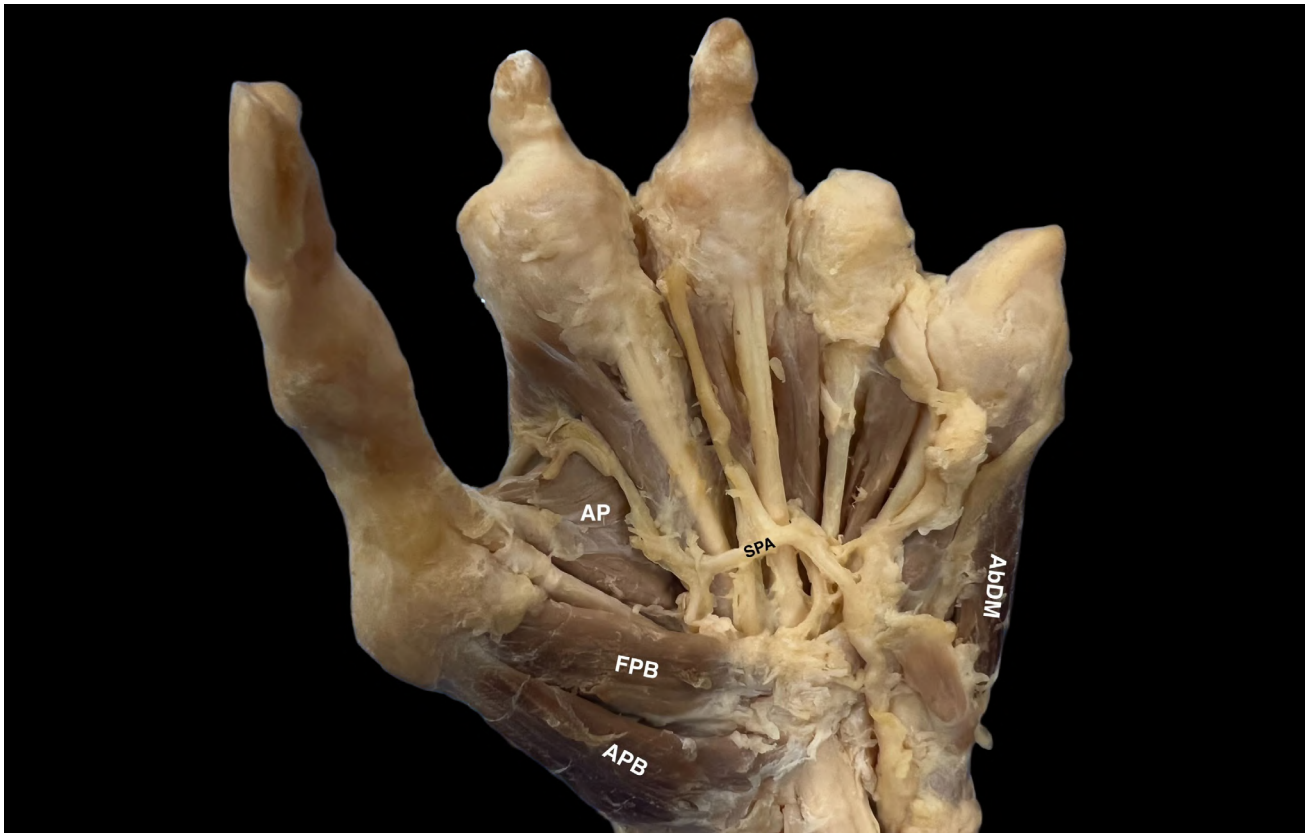

Fig. 2.- Skinned hand: The thenar and hypothenar musculature is shown along with the superficial palmar arch. (FPB; flexor pollicis brevis; AbPB; abductor pollicis brevis; AdP; adductor pollicis; AbDB; abductor digiti minimi; SPA; superficial palmar arch).

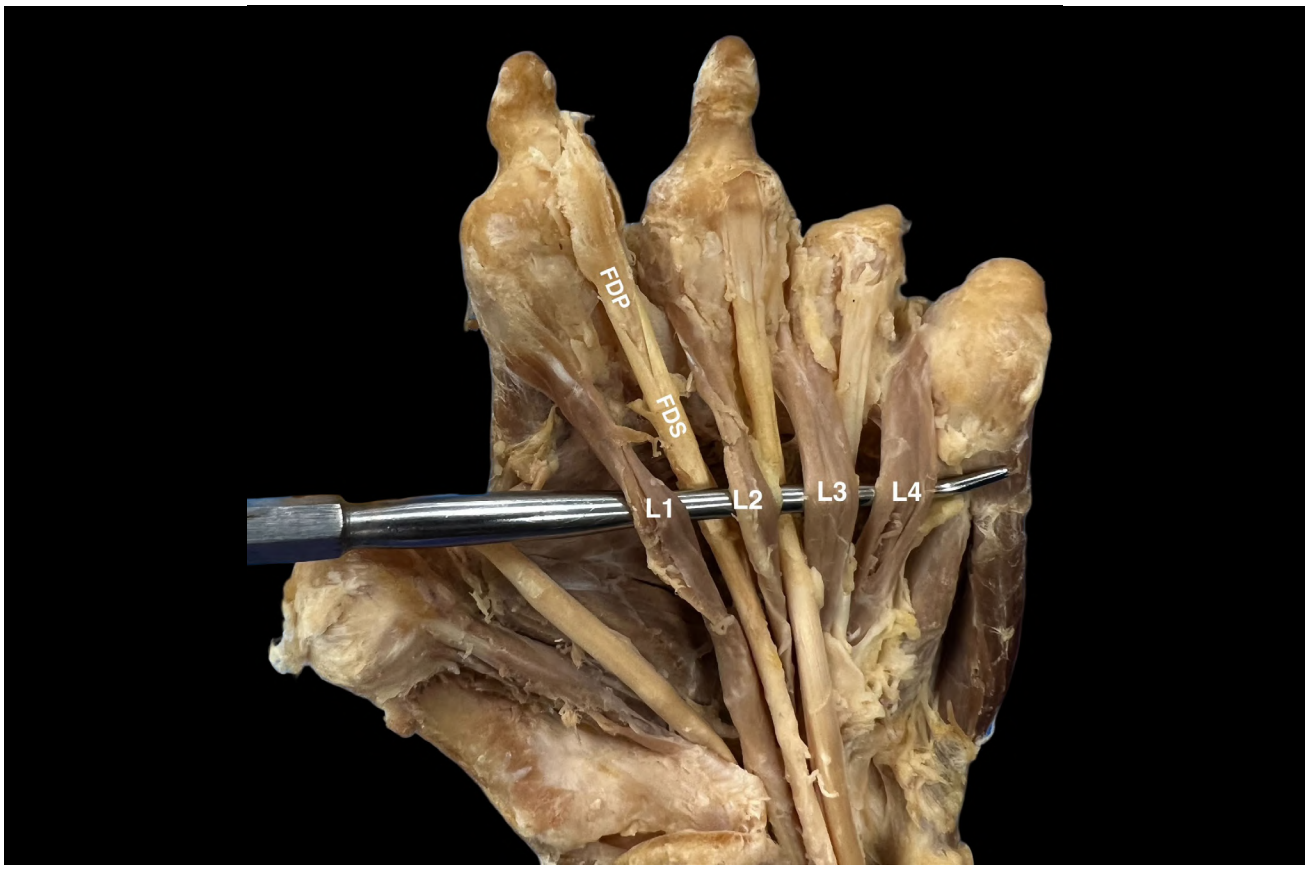

Fig. 3.- Lumbricals and FDS and FDP muscles: The distal attachments of the four lumbricals and FDS and FDP muscles are shown. (L1-L4; lumbricals 1-4; FDS; flexor digitorum superficialis; FDP; flexor digitorum profundus).

Fig. 4.- Adductor pollicis and palmar interossei muscles: The two heads of the adductor pollicis and the deep head of flexor pollicis brevis. (AdP1; transverse head; AdP2; oblique head; FPB; deep head of FPB).

Fig. 5.- Osteology: All proximal and middle phalanges of the second to fifth digits are absent. The distal phalanges of the fourth and fifth digits are shortened.

DISCUSSION

Bell and Temtamy developed a system that is commonly used to classify brachydactyly based on anatomical grounds (Bell, 1951; Temtamy and Aglan, 2008). There are eleven main types of isolated brachydactyly, each characterized by aplasia or hypoplasia of a part of the digit (Temtamy and Aglan, 2008). Fitch's classification provides a comprehensive analysis of each of the main types and also further subdivides Type E (Fitch, 1979). Our findings did not precisely align with any of the categories described in either of the aforementioned systems. Our donor presented with shortening of the 2nd to 5th digits, where all proximal and middle phalanges were absent. Additionally, there was clinodactyly in the 2nd and 3rd digits and anonychia in all digits except the thumb. Our case most closely resembles type B brachydactyly, which is characterized by absence or hypoplasia of the terminal parts of the index to little fingers with complete absence of fingernails (Temtamy and Aglan, 2008). However, the thumb frequently shows variation of the distal phalanges, which was not present in our donor. On the other hand, the case does not appear to match any type of symbrachydactyly either. We hypothesize the congenital variation in the donor to be closest to type IIIA of symbrachydactyly, however a symbrachydactyly is typically associated with ectodermal elements such as nails. Our case lacks this kind of tissue (Goodell et al., 2016). Symbrachydactyly typically results from a lack of blood flow to the tissue during embryological development. In our donor, the digital vessels, and distal median and ulnar nerve branches were unaffected other than being truncated due to the overall shortness of the digits. Overall, based on the osteology findings, we hypothesize that the congenital hand malformation observed in this donor was type B brachydactyly.

CONCLUSION

Brachydactyly is infrequently observed in the anatomy lab as they have an extremely low prevalence, except for the A3 and D classification being roughly 2% (Temtamy and Aglan, 2008). X-rays or CT imaging would provide stronger evidence of the type of brachydactyly present in the patient. Future iterations of similar studies should include acquisition of clinical images prior to anatomical dissection. Even when they are observed, these hand deformities are frequently imaged through noninvasive techniques such as x-rays and CT imaging rather than dissection. Therefore, this case provides a unique learning opportunity of the various patterns of malformation in brachydactyly with the tangible appreciation for the important underlying anatomy of this condition.

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AUTHOR CONTRIBUTIONS

Lin: project development, manuscript writing. *In*: manuscript editing. *Baribeau*: manuscript editing. *Wisco*: manuscript editing, PI.

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Identities and experiences of Anatomists

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SUMMARY

Across the world anatomists are responsible for delivering anatomical education designed to help prepare students in becoming safe and competent medical and allied healthcare practitioners. Despite the critical role that anatomists play in the early stages of student learning, little is known about the identity of anatomists, and how their journeys and experiences have shaped the ways they perceive and embody their role. The aim of this study was to provide anatomists with a reference to take comfort in the shared experiences of other anatomists, to provide individuals and managers with real-life situations that anatomists may come across in their career, and to generate a sense of belonging within the anatomy community. Through a survey data collected from 161 anatomists, it includes demographic characteristics, access to training and support provision, and availability of network and career opportunities. In addition, information was collected that focussed on aspects of wellbeing and lived personal experience in the workplace. The results of this study provide significant evidence for the need to develop a more inclusive, diverse, and supportive environment for anatomists in both the work place as well as within professional societies and at conferences. Self-identifying female anatomists experience more discrimination overall ($p=<0.01$), with specific elements such as barriers to career progression ($p=0.004$) and work-related mental health issues ($p=0.02$). Individuals, teams and managers have a distinct role to play in ensuring that everyone can work and thrive in a culturally safe work environment.

Key words: Gross anatomy education – Medical educators – Anatomists – Professional identity

INTRODUCTION

An anatomist has been defined as someone who studies, researches, or teaches in the anatomical sciences (Anatomy.org, 2021). Anatomists as a group have been surveyed in the past to gain their understanding and viewpoints on a wide range of issues, including attitudes towards different aspects of teaching (Waterston and Stewart, 2005; Moxham et al., 2018), body donation (Anyanwu and Obikili, 2012), sexism in anatomy (Morgan et al., 2016), race in anatomy (Strkalj et al., 2004), use of ultrasound in teaching (Jurjus et al., 2013),

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body painting (Cookson et al., 2017), and twitter (Marsland and Lazarus, 2017). Anatomists have also been investigated as a group to test skills such as spatial ability (Fernandez et al., 2011). Yet surprisingly few studies have focused on the background and workplace experiences of anatomists, and how these shape the delivery of anatomical education. There is also little understanding of anatomists as individuals and how their own unique journeys determine who they are as educators and researchers and their sense of belonging in the anatomy community. This leads to the question: What do we know about anatomists' experiences?

Anatomists in History

An internet search on the term 'anatomist' results in articles outlining the past association of anatomists with the scandals of grave robbing. Historically, it was a requirement that all medical students would dissect and it was the anatomist's responsibility to source bodies (Kaufman, 2005), which resulted in the practice of grave robbing and the Anatomy Act of 1832 (Ellis, 1993). As highlighted in books, such as 'Death, Dissection and the Destitute' (Richardson, 2001), anatomists are associated with cutting up bodies. The negative associations towards anatomists continued in 1933, where German anatomists during the Third Reich were known to have dissected bodies of victims of the National Socialist regime (Hildebrandt, 2009). More recently in the United Kingdom (UK) in the 1980 and 1990s, reports emerged that at Alder Hey Children's Hospital, Liverpool (Hall, 2001), there had been unauthorized removal, retention and disposal of human tissue by pathologists. Although anatomists were not implicated, this malpractice affected public opinion of donation and led to the creation of the Human Tissue Act 2004 (HTA, 2005) in England and Wales. More recently, Gunther von Hagens' 'Body Worlds™' was described by Stone (2011) as 'Dark tourism and the Cadaveric Carnival', bringing Anatomy and Anatomists back into the public domain. Anatomists' connections to body snatching and ethically challenging activities appear to be an association that has been difficult to dispel, and may shape the current role and perception of anatomists, through both the lens of the public and the self-lens of the anatomist.

Career journey of Anatomists

An individual's journey into anatomy rarely follows the same prescribed path. Different individuals may have backgrounds in an arrange of related topics such as gross anatomy, clinical medicine, surgery, biomedical science, histology, archeology and sports science. The Anatomical Society (UK) have highlighted this with examples where career anatomists have backgrounds in Cardiology, Biochemistry, Physiology, Medicine and Neurology (Anatomical Society, 2021). As one anatomist will be quite different from the next, it is important for us to understand this diverse and heterogenous community in order to identify their needs at an individual and community level.

Role

It is not only the career background for anatomists that is varied, but there are also differences in focus within the job role of an anatomist. Three components are commonly described: teacher, researcher, and clinician/surgeon. The different components are played out in an individual's job descriptions, with anatomists employed on a 100% teaching and scholarship pathway, a mixed pathway such as 60% research, 40% teaching, or a 100% research pathway, as well as those who combine anatomy with a clinically focused post. Despite the natural interrelationship between anatomy, clinical practice, research and teaching, different perspectives might result in an unwanted hierarchy, and it is likely that all these factors underpin the complexity of the role of the modern anatomist.

Teacher

The relationship between anatomy and teaching is highly entwined in history. The discovery of anatomical structures and understanding anatomical concepts by anatomists was historically often taught to audiences. One of the most notable anatomy teachers, Andreas Vesalius (1514-1564), advocated the importance of using human cadavers to teach anatomy (Markatos et al., 2020). Anatomy teaching, traditionally, was synonymous

with dissecting and therefore an 'anatomist' was assumed to be and defined as a dissector of dead bodies (Jones, 1997). However, with the advent of electron microscopy in the 1930s, the focus moved away from gross anatomy, and this helped change the antiquated definition of an anatomist. However, the teaching of gross anatomy remained prominent in higher education, particularly focused on medical programmes. Anatomy education continued to develop, and teaching with prosected specimens became seen as an alternative to dissection for some educators (Skidmore, 1995). Meanwhile in the 1990s, the number of hours allocated to anatomy was curtailed to make time in the curriculum for newer subjects such as molecular genetics and a focus on communication skills (McBride and Drake, 2017; Smith et al., 2021). Computer Assisted Learning (CAL) developed around the millennium, and the digital revolution, in addition to further technologies such as Ultrasound (Jurjus et al., 2013) and 3D printing (McMenamin et al., 2014; Smith et al., 17), provided different techniques for the teaching and learning of anatomy. Anatomists, especially those on a teaching-focused pathway, had to adapt and develop new skills and acquire different ways of understanding the human body and incorporate these methods in teaching. Anatomists also had to deliver teaching to ever-increasing numbers of students, along with an expanding breadth of programs that required human anatomy teaching and understanding pedagogical research and practice.

Researcher

Anatomical research encompasses a range of scientific disciples including neurology, developmental biology, anthropology, evolutionary biology, gross anatomy, histology of both human and animal species, and increasingly anatomical education research. The range of case studies provided by Jones et al. (2002) highlights the diversity of anatomical research as applied to sciences and clinical practice. As in other disciplines, the availability of funding can be a driver in determining what research is carried out in the field of anatomy (Jones et al., 2002). Research also underpins teaching, anatomists are perhaps seen as 'discoverers' and as Jones et al. (2002) suggest, staff may be required to undertake both in what is commonly known as a 'mixed' pathway.

Clinician / Surgeon

Similar to the relationship between anatomy and teaching, the association between surgery and anatomy is historical, dating back to the Greek anatomist and surgeon Herophilus in 335BC (Howard and Hess, 2002). The identity of a 'surgeon-anatomist' continues and is highlighted in the plight of anatomists (Mall, 1907) in the journal Science. The President of the Journal explains "that an individual has safely passed the pioneer stage in the development of a scientific profession in America". Mall (1907) continues to explain that anatomy then over time fell into disrepute, and that the conception of anatomy as a "mere maid-servant of surgery is still entertained by some". It is not clear if this opinion still exists, but Phitayakorn and Lachman (2015) explain that there is a need for both to work together, especially in the development of procedural skills training, innovation and advancing surgical techniques and assessment. In the United Kingdom, it was reflected that a Chair in Anatomy was always a stepping stone to that of surgery, and that under these conditions the quality of teaching was rarely good, with many surgeons focusing on private practice in London (Ellis, 1993).

Skill set of Anatomists

Like academics in other disciplines, the skill set of anatomists is of course broader than the three identities described above. As anatomists progress through their career as academics, they are required to have developed a broad range of transferable skills in addition to some very precise ones, such as the art of prosecting. As for most academics, anatomists are required to have an up-to-date appreciation of new knowledge, the ability to apply technological advances, the aptitude to adapt to changing teaching and learning requirements, e.g., during Covid-19 (Brassett et al., 2020; Evans et al., 2020; Longhurst et al., 2020; Pather et al., 2020). Anatomists may deliver education within a range of courses and therefore also have skills in curriculum planning, manage-

ment and leadership, and contribute towards specific activities of the institution, e.g., assessment. In addition, anatomists need to have a good understanding of the clinical or scientific implications of their teaching, which often intersect with other disciplines such as pathology or radiology. Anatomists need to know and abide by the laws that govern body donation and dissection in their country, they need to manage Health and Safety requirements, and they need to have an understanding of engineering and laboratory design (Trelease, 2006). Anatomists have also been described as being entrepreneurial by nature. In the 1700s, there were advertisements in newspapers offering courses in anatomy for anyone who was willing to pay (Guerrini, 2004). This is not that dissimilar to today when, due to ever increasing budget restrictions, income generation is important and the increasing number of laboratories supplementing their income with surgical courses and training. Therefore, it can be said that due to the nature of the discipline, anatomists are a highly adaptable and a highly trained group of people who operate within the higher education setting, with niche skills and attributes unique to this group of people.

Requirement for Anatomists

Perhaps the most cited research to date centers around the necessity for them in higher education and the concern over the decreasing number of qualified and experienced anatomists and the need for more anatomists in many institutions throughout the world (Eldred and Eldred, 1961, Blevins and Cahill; 1973; Bird, 1979; Santana, 2003, Schaefer et al., 2019; Wilson et al., 2019). In 2002, it was projected that there would be a shortage of anatomy educators, with 65% of Anatomy Heads of Departments indicating that they would have moderate to great difficulty in hiring anatomy educators over the next five years. Wilson et al. (2019) reported that 21% of posts between 2017 and 2018 were not being filled. The reasons postulated for this shortage include the rise in molecular-based PhDs creating a shift in the training paradigm. Another cause cited was the economic downturn in the 2000s (Wilson et al., 2019) and the reduction in contact teaching hours (McBride and Drake, 2017). It was also suggested that as medical schools moved to interdisciplinary and applied learning approaches, this led to a severe shortage in anatomists (Pathiraja, 2014). To address the shortage, some institutions have called for sessional teachers to fill the gaps (Caruth and Caruth, 2013; Lachman et al., 2013; Rhodes et al., 2018). Evidence from the United Kingdom (UK) suggests that the shortage in anatomists is being compensated for by increasing the number of posts known as Demonstrators' (Smith et al., 2021).

In summary, it is clear that there is a need to better understand the role and experiences of anatomists as a community. This study started as a symposium for the International Federation of Anatomy Associations World Congress meeting in August 2019, where Prof. Smith and Prof. Finn led a symposium entitled '#mylifeinanatomy'-authors (except RM, LB) presented at the symposium. The aim was to provide a candid discussion to celebrate, and critique, the opportunities and barriers facing career anatomists today. During the discussion it became clear that little research had been conducted into this specific group of people and their experiences. Therefore, this study continued over 12 months to reach anatomists at differing career stages across the globe to gain a better understanding of their day-today experiences within their roles and of their career in anatomy so far.

Research Aims

This project aims to understand a range of facets that make up what it means to be an anatomist today. These include demographic characteristics, access to training and support provision, and availability of networking and career opportunities.

Research Questions

1. What is the range of demographics that make up the population of anatomists?
2. How do anatomists access and receive training and mentorship?
3. What support is available to anatomists?
4. How do anatomists feel about their workplace culture?

5. Have anatomists experienced any issues relating to harassment or bullying, especially related to any protected characteristics?
6. Are there issues specific to mental and physical health that are related to being an anatomist?

MATERIALS AND METHODS

Study Design

This quantitative study used a survey design. The questionnaire employed by Brighton and Sussex Medical School (BSMS) as its annual staff survey was used as the starting point for the survey and further questions were then developed based on trends in the literature about medical educators and educators in higher education. A draft survey was pilot tested by Resident Medical Officers at BSMS and refinements were made in light of its responses. The final survey (Appendix A) comprised 51 questions. The survey was hosted on the University of Sussex Qualtrics XM survey software platform (Qualtrics Labs Inc., Provo, UT). Ethical approval for this study was granted by Hull York Medical School in 2019.

Participants

There is no international database of anatomists, so this research study utilised both convenience sampling and purposeful sampling to recruit anatomists through the following strategy.

1. International Federation of Associations of Anatomists (IFAA) World Congress 9-11th August London Excel Docklands. A paper survey was distributed to participants in their conference bags and during the '#mylifeinanatomy' workshop and associated symposia. Secure return boxes (one for consent and one for the survey to ensure anonymity) were located at the reception desk.
2. Invitation to participate through the membership lists of anatomy societies via email with link to Qualtrics Survey (where gatekeeper permission was given).
3. Invitation to participate through professional social media platforms e.g. Twitter with link to Qualtrics Survey.

Data were extracted from Qualtrics into Microsoft Excel® (Microsoft Corp., Redmond, WA) in November 2020 and were analyzed using IBM SPSS statistical software, Version 26.0 (IBM Corp., Armonk, NY). Free text comments were analyzed using thematic analysis (Braun and Clarke, 2012), which was undertaken by one researcher (CS) who coded each response and then grouped the codes to provide key themes. The themes were then checked by another researcher (GF). The number of initial exported data lines was 237. Data cleaning removed lines where no responses had been provided to generate n=161 final responses. Chi Square tests were used to explore relationships between certain factors, such as gender.

RESULTS

Demographics of participants

The demographics of the participants are presented in Table 1. A number of key factors are highlighted that make this sample representative. The professional level of participants that responded might reflect the constitution of an anatomy department, with Assistants (40%), Associates (25%) and Professors (26%). There was an even spread of career level with 32% reporting early career, 36% mid-career, and 32% established. There was a higher percentage in continuous employment (66%), with 87% being employed full time. There was no significant difference in relation to gender and mode of working, e.g., Full time or Part time. When asked if participants had a flexible working agreement in place, 84 anatomists (54%) replied that they did. A Chi Square test showed a statistically significant relationship between gender and having flexible working ($p=<0.00$), with more males having this (56%). Under half of the participants (42%) reported having any caring responsibilities – there was a statistically significant relationship between this and gender ($p=<0.00$), with again more males (59%) reporting they had caring responsibilities. Within the respondents, there was a strong focus (60%) on education pathways, as defined by spending more than 60% of their time teaching.

APPENDIX A. Original Survey.

About You	Circle/Tick Appropriate Option		
1. Please select which grade you are	Support/Technician		
	Lecturer/Teaching Fellow/Assistant Professor		
	Senior Lecturer/Senior Teaching Fellow/Associate Professor		
	Professor		
	Prefer not to say		
	Other: please state		
2. Are you clinically qualified?	Yes	No	
3. What sort of contract do you have?	Permanent		
	Fixed Term		
	Prefer not to say		
4. Please select your age range	Under 20		
	21-30		
	31-40		
	41-50		
	51-60		
	61-70		
	70 and over		
5. Please select at what level you consider to be in your career	Early-Career		
	Mid-Career		
	Established-Career		
6. Is your role Full Time or Part Time?	Full Time	Part Time	
If Part Time what percentage?			
7. What percentage of your role is teaching/research? Mark where you are			
0% Teaching 100% Research----------50% Teaching 50% Research----------100% Teaching 0% Research			
8. Do you have a flexible working agreement in place?	Yes	No	
9. Are you currently studying for a qualification?	Yes	No	
If Yes please provide details of the qualification.			
10. What gender do you identify as?	Male		
	Female		
	Neither		
11. Does your gender identity match your sex?	Yes	No	Prefer not to say
12. Do you have caring responsibilities for dependents	Yes: Under 18		
	Yes: Adult dependants		
	Yes: both of the above		
	No		
	Prefer not to say		
13. To which ethnicity to do identify as? (You are welcome to mark more than one) (There is no international standard classification, the UK classification has been adopted and includes the FDA, USA 2016 guidelines- we recognise this may appear different to one you are used to and apologise if there is a group not included- please add this in for us under 'Other')			
Arab	Asian or Asian British- Bangladeshi	Asian or Asian British- Indian	
Asian or Asian British- Pakistani	Other Asian Background	Chinese	
Black or Black British- African	Black or Black British Caribbean	Other Black background	
Mixed- White and Black African	Mixed- White and Asian	Mixed: White and Black Caribbean	
Other Mixed background	White	Aboriginal and/or Torres Strait Islander	
American Indian or Alaska Native	Gypsy or Traveller	Hispanic or Latino	
Native Hawaiian or other Pacific Islander	Other	Prefer not to say	
14. What national societies do you belong to? (please tick all those that apply)			

Anatomical Society	American Association of Clinical Anatomists
American Association for Anatomists	Argentine Association of Anatomy
Anatomical Society of India	Australia and New Zealand Association of Clinical Anatomy
Anatomical Society of Nigeria	Anatomische Gesellschaft
Anatomical Society of Southern Africa	Brazilian Society of Anatomy
British Association of Clinical Anatomists	Chinese Society of Anatomical Sciences
Czech Anatomical Society	Dutch Anatomical Society
Hungary Anatomical Society	Institute of Anatomists
Indonesian Anatomists Association	Korean Association of Anatomists
Portuguese Society of Anatomy	Pan-American Association of Anatomists
Polish Society of Anatomy	Russian Scientific Medical Society of Anatomists, Histologists and Embryologists
Serbian Anatomical Society	Società Italiana di Anatomia e Istologica
Other Please State:	

Training and career progression 1=Strongly Disagree, 2= Disagree, 3=Neither, 4=Agree, 5=Strongly Agree					
15. Do you feel you have received adequate training to be able to undertake your role effectively?					
At current institution	1	2	3	4	5
At previous institutions 1	1	2	3	4	5
At previous institutions 2	1	2	3	4	5
At previous institutions 3	1	2	3	4	5
Please detail the training that you feel has been most valuable					
16. Do you feel career opportunities are available to you?					
At current institution	1	2	3	4	5
At previous institutions 1	1	2	3	4	5
At previous institutions 2	1	2	3	4	5
At previous institutions 3	1	2	3	4	5
Please detail the career progression opportunities that you feel have been most valuable					

17. Do you feel your career progression has been actively blocked at any point?	Yes	No
If Yes is/was this by		
A Manager		
A Head of School/Faculty		
Another individual		
Institutional based issues		

18. I am actively encouraged to take up career development opportunities	1	2	3	4	5
19. Staff who work part-time or flexibly in my current institution are offered the same career development opportunities as those who work full-time.	1	2	3	4	5

20. My institution provides me with (Select all that apply)	A helpful annual appraisal/review
	Time to undertake development opportunities
	Useful mentoring opportunities
	Useful networking opportunities
	Funding to undertake development opportunities
	Other opportunities please state:
21. My professional society provides me with (Select all that apply)	Useful mentoring opportunities
	Useful networking opportunities
	Funding to undertake development opportunities
	Other opportunities please state:

22. I understand the promotion process and criteria at my institution	Yes	No
23. When were you last promoted? Please provide Year and Month		

24. In the past, I have moved institution to gain promotion that would not be possible if I had remained at the institution			Yes	No		
25. My institution values the full range of an individual's skills and experience (e.g., research, pastoral work, outreach work, teaching, administration and technical support) in the following:						
When carrying out performance appraisals/reviews			Yes	No		
When considering promotions			Yes	No		
26. Please add any further comments about training or career progression.						
Support						
27. I am supported in my teaching role by: Select All that apply						
Head of Department/School		Line manager				
Director of teaching		Teaching office				
Your named mentor		A critical friend				
PA/Admin assistant		Other, please state:				
28. I am supported in my research role by Select All that apply						
Head of Department/School		Line manager				
Director of Research		Research office				
Your named mentor		A critical friend				
PA/Admin assistant		Other, please state:				
29. What other sources of support would you like to see at an institutional level?						
30. What other sources of support would you like to see at a national or international level?						
Activities 1=Strongly Disagree, 2= Disagree, 3=Neither, 4=Agree, 5=Strongly Agree						
31. I am encouraged to represent my institution externally (e.g., on committees/boards, panels, as chair or speaker at conferences).			1	2	3	4 5
32. I participate in external committees			Yes		No	
33. If yes, please provide details on the type of committee(s) you are involved with		Research	Teaching	Clinical	Other	
	Local					
	Regional					
	National					
	International					
	Other					
34. I supervise PhD students		Yes	No			
Workplace Culture 1=Strongly Disagree, 2= Disagree, 3=Neither, 4=Agree, 5=Strongly Agree						
35. I feel well-integrated with other colleagues in my department.			1	2	3	4 5
36. I feel well-integrated with other colleagues across my institution.			1	2	3	4 5
37. I feel well-integrated with other colleagues across the national anatomy sector.			1	2	3	4 5
38. I feel well-integrated with other colleagues across the international anatomy sector.			1	2	3	4 5
39. Work-related social activities at my institution, such as networking events, are likely to be welcoming to all staff, regardless of ethnicity or gender (e.g., consider whether venues, activities and times are appropriate).			1	2	3	4 5
40. Work-related social activities within the anatomy sector, such as networking events, are likely to be welcoming to all staff, regardless of ethnicity or gender (e.g., consider whether venues, activities and times are appropriate).			1	2	3	4 5
41. My institution makes it clear that inappropriate images that stereotype people in relation to ethnicity or gender are not acceptable (e.g., in calendars, newspapers and magazines, on computers and mobiles).			1	2	3	4 5

42. The anatomy community makes it clear that inappropriate images that stereotype people in relation to ethnicity or gender are not acceptable (e.g., in calendars, newspapers and magazines, on computers and mobiles).	1	2	3	4	5
43. My institution uses a range of staff regardless of ethnicity or gender as visible role models (e.g., in staff inductions, as speakers at conferences, at recruitment events).	1	2	3	4	5
44. The anatomy community uses a range of staff regardless of ethnicity or gender as visible role models (e.g., in staff inductions, as speakers at conferences, at recruitment events).	1	2	3	4	5
45. Please add further comments about workplace culture here if you would like to.					
Equality and Diversity 1=Strongly Disagree, 2= Disagree, 3=Neither, 4=Agree, 5=Strongly Agree					
46. Within in my institution I have undertaken training in equality and diversity.	Yes: Online				
	Yes: Course or Workshop				
	No				
	Don't Know				
47. Within my institution I have undertaken training in understanding unconscious bias.	Yes- Online				
	Yes- Course or Workshop				
	No				
	Don't Know				
48. My institution has made it clear to me what its policies are in relation to gender equity (e.g. on discrimination, parental leave, career leave, flexible working).	1	2	3	4	5
49. Please add further comments about equality, diversity and inclusion here if you would like to.					
Harassment and Bullying 1=Strongly Disagree, 2= Disagree, 3=Neither, 4=Agree, 5=Strongly Agree					
50. I am aware of, or have knowledge of my institution's policy on the Prevention of Bullying and Harassment.	Yes	No			
51. I would know who to go to if I wanted to report an incident of bullying or harassment at my institution	Yes	No			
PTO					
52. I am confident that my line manager/supervisor would deal effectively with any complaints about harassment, bullying or offensive behavior.	1	2	3	4	5
53. I have experienced a situation(s) where I have felt uncomfortable because of my ethnicity or gender. Note: the next question asks about specific discrimination	Yes	No			
54. I have experienced discrimination because of my ethnicity	Yes	No: Go to next Question			
If yes, was this at your institution, at a national anatomy event or at an international anatomy event or other location?					
Would you consider the perpetrator to be more senior or junior to you?					
If this has occurred more than once, please provide a rough estimate					
Please expand if you wish					
55. I have experienced discrimination because of my gender	Yes	No; Go to next Question			
If yes, was this at your institution, at a national anatomy event or at an international anatomy event or other location?					
Would you consider the perpetrator to be more senior or junior to you?					
If this has occurred more than once, please provide a rough estimate					
Please expand if you wish					
56. I have experienced discrimination because of my sexual orientation	Yes	No: Go to next Question			
If yes, was this at your institution, at a national anatomy event or at an international anatomy event or other location?					
Would you consider the perpetrator to be more senior or junior to you?					
If this has occurred more than once, please provide a rough estimate					
Please expand if you wish					

57. I have experienced discrimination because of my age	Yes	No- Go to next Question				
If yes, was this at your institution, at a national anatomy event or at an international anatomy event or other location?						
Would you consider the perpetrator to be more senior or junior to you?						
If this has occurred more than once, please provide a rough estimate						
Please expand if you wish						
58. I have experienced discrimination because of another 'protected characteristic' or 'protected class or group' (As classed by the UK Equality Act 2010: age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex, sexual orientation	Yes	No				
If yes, was this at your institution, at a national anatomy event or at an international anatomy event or other location?						
Would you consider the perpetrator to be more senior or junior to you?						
If this has occurred more than once, please provide a rough estimate						
Please expand if you wish						
Flexibility and Working Hours 1=Strongly Disagree, 2= Disagree, 3=Neither, 4=Agree, 5=Strongly Agree						
59. Meetings in my institution are completed in core hours to enable those with caring responsibilities to attend.	1	2	3	4	5	
60. Meetings that I participate in for external bodies/societies are completed in core hours to enable those with caring responsibilities to attend.	1	2	3	4	5	
61. My line manager/supervisor is supportive of requests for flexible working (e.g., requests for part-time working, job share, compressed hours).	1	2	3	4	5	
62. Please add further comments about flexible working						
Wellbeing 1=Strongly Disagree, 2= Disagree, 3=Neither, 4=Agree, 5=Strongly Agree						
63. I feel that my institution cares about my well-being at work.	1	2	3	4	5	
64. I feel my institution is a great place to work for:						
Women	1	2	3	4	5	
Men	1	2	3	4	5	
65. I feel the anatomy community at a national level is a great place to work for:						
Women	1	2	3	4	5	
Men	1	2	3	4	5	
66. I feel the anatomy community at an international level is a great place to work for:						
Women	1	2	3	4	5	
Men	1	2	3	4	5	
67. I have experienced mental health issues that I can attribute to my work.	Yes	No				
If yes, was this related your institution, at a national anatomy event or at an international anatomy event or other location? Please expand if you wish						
68. I have experienced physical health issues that I can attribute to my work	Yes	No				
If yes, was this related to your institution, at a national anatomy event or at an international anatomy event or other location? Please expand if you wish						
69. Please add further comments about well-being here if you would like to.						
Future						
70. I would like to see active progress made by the anatomy sector in relation to ensuring balance. Please explain in what area and any suggestions of how this might be achieved.						
71. There are no further survey questions. If you have any further comments on the topics covered, please add them here:						

Table 1. Demographic information of participants.

Grade	
Professor	41(26%)
Associate Professor/Senior Lecturer	40 (25%)
Assistant Professor/Lecturer	65 (40%)
Technical/Support	7 (4%)
Other	6 (4%)
Prefer not to say	2 (1%)
Clinically Qualified	
Yes	53 (33%)
No	108 (67%)
Contract	
Fixed Term	48 (30%)
Permanent	106 (66%)
Prefer not to say	6 (4%)
Age	
21-30	26 (16%)
31-40	50 (31%)
41-50	34 (21%)
51-60	23 (14%)
61-70	16 (10%)
70 and over	12 (8%)
Level of career	
Early	51 (32%)
Mid	58 (36%)
Established	51 (32%)
Full Time/Part Time	
Full Time	139 (87%)
Part Time	20 (13%)
Gender	
Female	87 (54%)
Male	70 (44%)
Neither	3 (2%)
Ethnicity	
Arab	1 (0.5%)
White	115 (67%)
Hispanic and Latino	8 (5%)
White Hispanic and Latino	1 (0.5%)
Asian or Asian British	2 (1%)
Other Asian	11 (7%)
White American Indian or Alaska Native	1 (0.5%)
Chinese	6 (4%)
White Other	3 (2%)
Asian or Asian British Bangladeshi	2 (1%)
Asian or Asian British Indian	5 (3%)
Other Asian Background	5 (3%)
White Aboriginal and or Torres Strait Islander	1 (0.5%)
Black or Black British	2 (1%)
Mixed White and Asian	1 (0.5%)
Prefer not to say	4 (2%)
Other	4 (2%)

Training, Support and Career Progression

Exploring the membership of professional societies, the majority of respondents were members of the Anatomical Society UK (n=57), followed by the American Association for Anatomists (n=51). A total number of 217 memberships were reported, with 28 different societies represented, reflecting the fact that many anatomists belong to more than one society (Table 2). In response to feeling that anatomists have received adequate training at their current institution to undertake their role efficiently, 67% (88) strongly agreed or agreed. This number decreased when asked about previous institutions, with 58% (53), 60% (30) and 42% (12) for their first, second and third institutions respectively, indicating that training has improved slightly over time or that individuals have moved to an institution with better training. A similar trend was observed when asked about the career progression opportunities that were available with 54% (71) at their current institution, then 40% (32), 41% (17), 34% (8) for their first, second and third institutions respectively. When anatomists were asked if they felt they had had their career progression blocked, 52% (69) said yes and 48% (65) (n=134) said no. In exploring if this had a correlation to gender, a Chi Square test revealed a positive relationship (p=0.00), with females (66%) being more affected. On the question of career opportunities, 59% (78) reported they were encouraged to take up career opportunities, but only 39% (49) said that part-time staff were offered the same opportunities. When asked about understanding of the promotion process, 82% (11) said they did. However, 39% (49) revealed they had moved institution to gain promotion. Sadly, only 64% (79) of anatomists felt that their institution valued their full set of skills when considering promotion.

Inclusivity

Anatomists were asked at departmental, institutional, national and international levels as to how integrated they felt with other colleagues. The full details are in Figure 1, however overall integration was reported to be higher 68% (78) at departmental level, dipped at institutional level 44% (54) and national level 30% (35) but rose at

Table 2. Learned Society Membership.

Society	Number *
Anatomical Society UK	57
American Association for Anatomists	51
American Association for Clinical Anatomists	20
Dutch Anatomical Society	13
British Association of Clinical Anatomists	11
Societa Italiana di Anatomic e Istologica	9
Australia and New Zealand Association of Clinical Anatomy	8
Institute Anatomical Sciences	8
Sociedad Anatómica Española	6
Anatomische Gesellschaft	5
Russian Scientific Medical Society of Anatomists, Histologists and Embryologists	3
Human Anatomy and Physiology Society	2
Mexican Society of Anatomy	2
Anatomical Society of Nigeria	2
Anatomical Society of Southern Africa	2
Anatomical Society of Argentine	2
Turkish Anatomical Society	2
Sociedad ecuatoriana de ciencias Morfo funcionales	1
Korean Association of Anatomists	1
Chinese Society of Anatomical Sciences	1
Polish Anatomical Society	1
Czech Anatomical Society	1
Society of Clinical and Experimental Anatomy Nigeria	1
American Society of Andrology	1
Anatomical Society of India	1
Specific Clinical Societies	4
Medical Education Societies	1
American Physical Therapy Association	1
Total Membership of Societies	217
*Many individuals belong to more than one society	

international level 46% (52). When asked about work-related social activities at institutional and sector level, such as networking events, to ascertain if they were likely to be welcoming to all staff regardless of ethnicity or gender (e.g. whether venues, activities and times are appropriate) there was very strong disagreement. At institutional level only 14% (16) agreed, and 65% (78) disagreed. At a sector level this was lower, with 6% (8) agreeing and 66% (76) disagreeing. In asking "My institution makes it clear that inappropriate images that stereotype people in relation to ethnicity or gender are not acceptable (e.g., in calendars, newspapers and magazines, on computers and mobiles)", 70% (82) disagreed. Similar trends were seen when referring to the anatomy sector with 65% (76) disagreeing. In exploring if their institution uses a range of staff regardless of ethnicity or gender as visible role models (e.g., in staff inductions, as speakers at conferences, at recruitment events), 56% (66) disagreed. At a national level the trend was the same, with 53% (63) disagreeing. In exploring training, 39% (46) had not completed any training on unconscious bias. Eighty percent (97) were aware of their institutional policy on bullying and harassment, and 85% (102) knew to whom they could go to report any such incidents. However, only 61% (72) were confident that their line manager/supervisor would deal effectively with any complaints about harassment, bullying or offensive behavior.

Protected Characteristics

Sixty seven percent of participants identified as 'white'. Due to the small percentages of other groups, it was not possible to perform any statistics aligned to ethnicity (Table 1). Thirty five percent (41) of anatomists reported that they had felt uncomfortable because of their ethnicity or gender, with 11% (13) reporting that they had experienced discrimination because of their ethnicity. Of these individuals, 50% (6) reported that the perpetrator/s was senior to them, and 42% (5) reported that the perpetrator/s included those who were senior and junior. When asked if anatomists had experienced discrimination because of their gender, 36% (43) had done so. There was a statistically significant difference between experiencing discrimination because of gender ($p=<0.00$). Females were more affected, with the perpetrator frequently being more senior to them (82% of those who experienced discrimination because of gender were female). In response to whether anatomists had experienced discrimination because of their sexual orientation, only 2% (3) reported this to be the case. Discrimination because of age was reported by 25% (30) anatomists. In response to "I have experienced discrimination because of another 'protected characteristic' or 'protected class or group' (as classed by the UK Equality Act 2010: age, disability, gender reassignment, marriage and civil partnership, pregnancy and mater-

nity, race, religion or belief, sex, sexual orientation), 7% (9) had done so.

In exploring how institutions support those with caring opportunities, 62% (74) felt that meetings occurred within core hours to enable those with caring responsibilities to attend. Similarly, 51% (56) felt the same when working with external bodies/societies. When asked about flexible working, 67% (79) felt their line manager/supervisor was supportive of requests for flexible working (e.g., requests for part-time working, job share, compressed hours).

In response to " I feel my institution is a great place to work for women", 52% (58) agreed compared to 81% (75) in response to the same question answered by men. At a national level, 70% (73) felt anatomy was a great place for women, compared to 81% (86) for men. Internationally as an anatomy sector, the trend continues with 65% (69) for women and 80% (84) for men.

Physical and Mental Health

Exploring if anatomists have experienced issues related to their physical and mental health, 41% (49) had experienced mental health issues that were attributable to work. A statistically significant relationship (P=<0.02) was identified between mental health and gender, with females more likely to experience this (68% of participants who experienced mental health issues related to work were female). Thirty percent of participants (36) had experienced physical health issues that were attributable to work.

DISCUSSION

The findings of this study suggest that anatomists have experienced a number of issues common to the sector. These include discrimination, health and wellbeing issues as a result of work, and a lack of defined training and progression.

Identity and professional registration

Literature from around the mid-1600s describes the granting of Royal Charters to Anatomy Schools in the United Kingdom, indicating that there were lots of 'unofficial' anatomy schools as well as those who had been deemed to meet a defined level (Michell, 2016). Anatomists as individuals were referred to as being 'incorporated', and these were the only anatomists who could legally

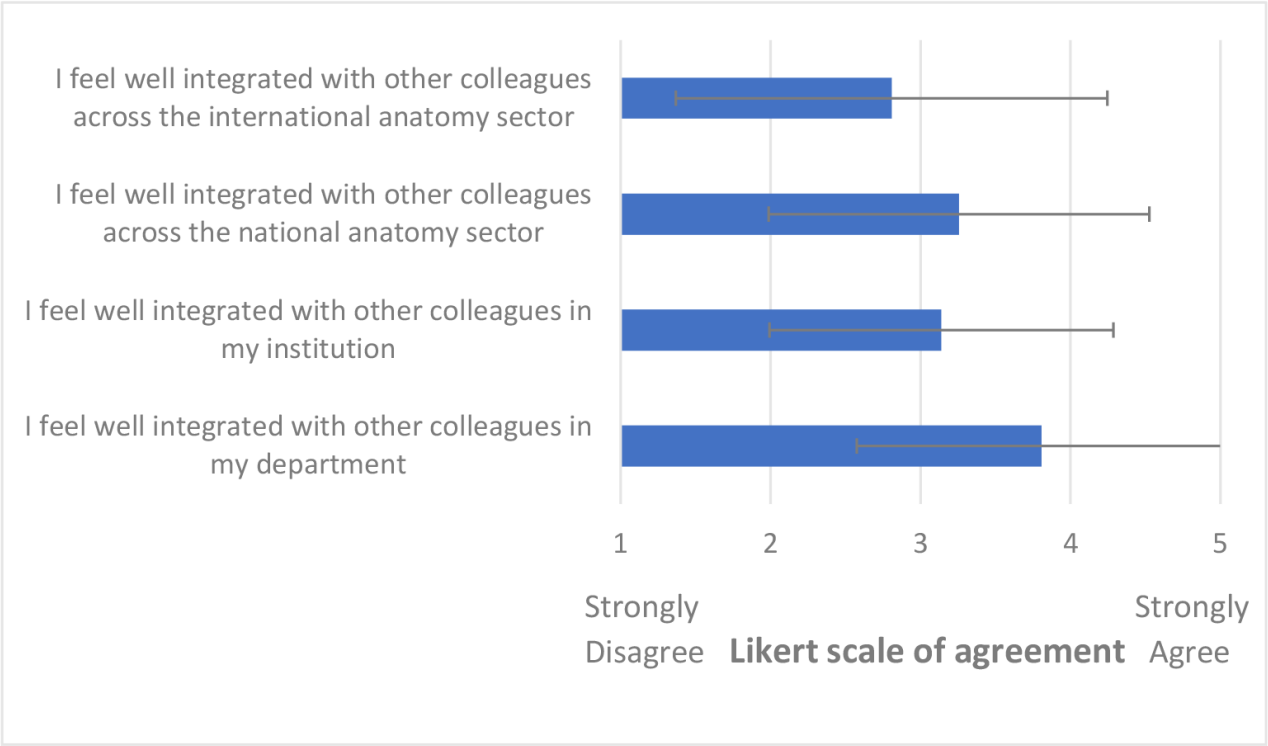

Fig. 1.- Integration at department, institutional, national, and international level.

receive bodies. However, in the 18th Century there was an increase in private hospitals and thus the number of 'unincorporated' anatomists increased (Ward, 2015). In the 18th and 19th centuries, the definition of a qualified anatomist became more straightforward as it was linked to legislation around the use of human bodies. This connection with legislation remained until 2004. In the United Kingdom prior to the Human Tissue Act (HTA), an anatomists could be 'licensed' as an individual by Her Majesty Inspector of Anatomy, but with the establishment of the Human Tissue Authority, an Institution is licensed with named individuals on the license. A component that has changed is that the term 'anatomist' can now encompass a variety of professional activities, including research, teaching and technical work. Only some of these may use specimens from human bodies and therefore have a need to work under regulations. The individuals in the study were predominantly involved in teaching anatomy and therefore were likely to be or have been involved in dissection. Dissection echoes back to the historical identity of anatomists, previously seen as taboo and condemned by society (Dangerfield, 2002). However, there is little information available today on the perception of anatomists by the general public. In recent years, one anatomist (Gunther von Hagens), creator of the controversial Body Worlds exhibition, has influenced the public's perception of anatomy, and has been cited as an anatomist in the old-fashioned sense, motivated by the beauty of anatomy, rather than the science (Jones and Whitaker, 2009). There are also intricate ties to the past in the link between anatomy and art and the beauty of anatomy, as, for example, the anatomist Emily Evans (Emily Evans, 2022) who, as an anatomist, has also developed a successful arts collection. The identity of anatomists today appears to be as broad as ever.

The issue of identity of anatomists is probably compounded by the lack of a clear definition of an anatomist. It may also be attributable to the heterogeneity within the anatomy community, possibly also linked to a lack of sense of belonging and therefore perceived support worldwide. This issue is also probably exacerbated by there being only one or two anatomists per institution, with the overall numbers who work in the discipline being relatively small compared to other biomedical sciences. With the emergence of new disciplines and a shift in focus towards communication skills within medical education, anatomy as a discipline has experienced a severe reduction in the allocation of teaching hours (Smith et al., 2021). This has doubtless affected the number of anatomists, with retired faculty members not being replaced, even while there were not enough anatomists to fill advertised posts (Topp, 2004; Fraher and Evans, 2009; Wilson et al., 2020). It could be argued that within the discipline, the historical perception that anatomists are not needed continues to pervade the sector.

Although anatomists frequently work in a laboratory-based environment and contribute towards key preclinical training, they are also key players in assisting medical students to develop the 'professional knowledge' domain of the Outcomes for Graduates (General Medical Council, 2018). Despite this, they are not considered to be part of the same professional bodies to which their colleagues who are doctors and allied health professionals belong, such as the General Medical Council. While such organizations are primarily focused on protecting patients, it can be also argued that the knowledge imparted by anatomists informs future patient care, which raises the question of professional registration for anatomists. The various learned societies that exist to support anatomists and other biomedical scientists have no legal jurisdiction. The study highlighted that anatomists mostly felt integration at the department level, but this was not so at the national or societal level, albeit this perception did increase again at the international level. The reasons for these differences are unclear, but may relate to whether anatomists feel welcomed and included.

Qualification

The number of qualified anatomists has been raised as a concern (Sugand et al., 2010), but interestingly the literature does not specify what constitutes a 'qualified anatomist'. There have been a number of improvements that provide a qualification for anatomists in the past 10 years. These include the Anatomical Society Anato-

my Training Programme in collaboration with the American Association for Anatomy (Fraher and Evans, 2009), a graduate model of training with the Anatomy Education Research Institute (O'Loughlin and Husmann, 2019), and an apprenticeship-style model at the University of Kentucky (Richardson-Hatcher et al., 2018). In the UK, there are dedicated Master's degrees in human anatomy and education, such as those offered by the University of Sheffield and Hull York Medical School.

There has been in recent years an emphasis on 'teaching-focused' anatomists, and it is therefore unsurprising that the majority of anatomists in this survey were 'teaching-focused'. There has been previous debate over the value of a teaching credential (Rizzolo and Drake, 2008). In the UK and Australia, the Advance HE fellowship (Advance HE, 2020) structure is promoted and recognized in the Teaching Excellence Framework (TEF) (TEF, 2020), so that it is likely that most anatomists in these countries who have a significant teaching role have accredited fellowship status, as this is a common requirement for employment and promotion.

Training and professional development

The identification of Early Career Anatomists (ECA) has occurred. However, ECAs may find navigation of the higher education landscape a complex task, especially in anatomy with novel pedagogies. Kramer et al. (2020) explains that it is an international challenge to create anatomists of the future and initiatives such as Early Career Networks are an important tool in supporting junior anatomists. With new generations of students entering anatomy as a discipline there must be support in place to help ECAs progress into established careers while training new ECAs. Schaefer et al. (2019) suggests weaknesses in education-focused postdoctoral training due to the undervaluing of teaching and to the fact that other forms of postgraduate training may be more suitable, and this reflects the level of an ECA. It is also worrying to see that there is less focused support for mid and late career anatomists, with this study reporting that individuals (39%) have had to move institution to gain promotion. Just over half of participants (52%) felt they had their career progression blocked, which may be due to prejudice or unconscious bias.

Discrimination

It is clear that discrimination exists in anatomy, especially in relation to gender, ethnicity, and age. It is perhaps surprising, in this study, that males report having a higher amount of flexible work and caring responsibilities. It is not surprising that the study indicates a detrimental effect to individuals based on their ethnicity and on their identification as female. This echo's patterns in the literature on clinical academic careers (Finn et al., 2022). Gender inequality is also highlighted by the marked difference in whether individuals feel "their place of work is great", with 52% for women compared to 81% for men. This trend continues across the international anatomy community, with 65% for women and 80% for men. These may reflect issues of power imbalance and hierarchy, which both affect the sense of belonging and the ability to speak out and have your voice heard.

Health and Wellbeing

Historically, one of the risks of being an anatomist was disease transmission. In the winter of 1848-49 in Scotland, records showed that 33 out of 38 bodies had died from cholera, a known infectious disease. The risk to anatomists of catching cholera or tuberculosis was mainly during the period between death to arrival in the medical school (Kaufman, 2005). However, this occupational hazard was reduced with the advent of embalming, although the chemicals used in embalming are still harmful to human health, especially formaldehyde (Skisak, 1983; Pabst, 1987; Mirabellor et al., 2011; Waschke et al., 2019). From the survey it would appear that the modern anatomist is less at risk of physical health problems and more so impacts on one's mental health. From the survey it was reported that anatomists who identify as female are more likely to experience poor mental health related to work than those who identify as male. This could be related to the rate and incidence of discrimination against female anatomists in the workplace that was observed in the survey results.

CONCLUSION

Anatomists are fulfilling vital roles in the education of medical, allied health and science-focused individuals. Collectively educational institutions, the learned societies, and anatomists themselves need to take collective action to ensure that individuals are treated with dignity and respect. Anatomists should be offered appropriate training and development opportunities. A career in anatomy should be rewarding, prosperous and embedded within a positive culture of inclusion and equality. It is hoped that the results from this study provide anatomists at all stages of their career with a sense of belonging within their discipline. It is also hoped that the issues identified within this study encourage anatomists to speak out against adversity within their institution and societies, in a hope to drive progressive changes towards creating a more forward-thinking culture within the discipline of anatomy.

RECOMMENDATIONS

1. This study acts as a call to arms to explore further the experiences of anatomists and to develop better support systems for colleagues.
2. National Societies should continue to work collaboratively to develop training opportunities for anatomists at all stages of their career (early, middle, late).
3. International and National Societies should develop and implement policies to promote inclusion in the anatomy community.
4. Everyone should work to develop a culture of change to provide allyship to all members of the anatomy community and to challenge inappropriate behavior.
5. Establish an attitude and policy of zero tolerance on any aspect where a protected characteristic of an anatomist is treated with discrimination.

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Enhancing the Embryology teaching-learning experience in the medical curriculum: a faculty & student lookout

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SUMMARY

It has been identified that most medical students are dissatisfied with current embryology teaching, and they often find embryology learning difficult. The present study was conducted to evaluate the perception of faculty and undergraduate medical students regarding the existing teaching-learning practices in embryology. The present cross-sectional study involved faculty, undergraduate, and postgraduate students engaged in embryology teaching-learning. The study was conducted in two steps. In the first step, the undergraduates were provided with a semi-structured questionnaire that addressed the practices of embryology teaching-learning in the current medical curriculum. The responses were recorded using a Likert scale. In the second step, the participants were invited to answer an open-ended question on improving the teaching-learning practices of embryology. The study involved 50 faculty, 232 medical undergraduates, and 15 postgraduate students. Most participants (76.1%) agreed that human embryology is essential in understanding anatomical variations, congenital anomalies, and clinical ailments.

Although embryology is interesting to study, it is not easy to comprehend, as stated by most students (52.24%). They also felt that embryology is often neglected while learning Anatomy (70.73%). Ways to improve the embryology teaching-learning practices assessed in step two identified the following themes: image and video-assisted learning, experiential learning, 3D-models assisted learning, case-based learning, specimen-based learning, assessment-based learning, and small-group teaching. Embryology teaching-learning is an integral part of the Anatomy curriculum. Therefore, there is a need to reform the existing methodologies of embryology teaching-learning to enhance student engagement. Seeking students and faculty's perceptions about the current practices of embryology teaching and its impact on their learning becomes useful. This study intents to utilize the feedback gained in improving the process of imparting embryology knowledge and will assist in a positive learning experience for the students.

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INTRODUCTION

Human Embryology is integral to basic science teaching in the medical curriculum. Understanding the mechanisms and causes of the embryo's normal and abnormal development is essential. In addition to exploring the incredible process of making a human being also provides a better orientation of gross anatomy to medical students. The knowledge (learning outcome) of embryology also finds its applications in various fields of Medicine, such as surgery, pediatrics, obstetrics, and gynecology (Moxham et al., 2016; Dinsmore et al., 1999). Further, as infertility is a growing problem in the current generation, it also enables the students to stay abreast with the recent advances in in-vitro fertilization, embryo implantation, and cryopreservation of embryos. Interestingly, embryonic stem cells are gaining importance in treating various diseases. The knowledge of embryology is also helpful in dealing with stem cells and cloning (Hamilton and Carachi, 2014; Aversi-Ferreira et al., 2012; Carlson, 2002; Vermeulen et al., 2019).

Students often find embryology challenging to understand and tend to lose interest in its learning. The method of imparting embryology knowledge to the student could be one of the reasons.

The traditional teaching method believes that the didactic lecture is the most effective method for conveying information to the student (Butler, 1992). Most medical colleges in India teach embryology using blackboard or PowerPoint presentations. As embryology is a dynamic subject, these teaching modalities may fail to give a 3D orientation of the embryo/embryogenesis to medical students in their early years of learning. Therefore, the students find it challenging to understand and comprehend the concepts. They may even fail to reproduce the same in their assessments (Aversi-Ferreira et al., 2012; Halasz, 1999). Thus, embryology is often neglected from the curriculum by most students.

Implementing the Competency-Based Medical Curriculum (CBME) by the National Medical Council (NMC) of India has shifted the focus from traditional didactic lectures to self-directed learning or a flipped classroom approach. Different modalities of small group teaching/learning and hybrid learning modes have evolved since (UG Curriculum-NMC, 2021; Kerdijk et al., 2013). It has further warranted a revision and reformation in teaching-learning (T/L) practices in anatomy, including embryology.

The students' and faculty's perceptions and viewpoints are paramount while revising the T/L practices and exploring the methodologies best suited for embryology (Jaiswal et al., 2015).

Therefore, the present study aims to seek the perceptions of medical undergraduate, postgraduate students, and the faculty in Anatomy about embryology T/L practices. The feedback obtained can be utilized to improve the embryology T/L experience for the students.

MATERIALS AND METHODS

The present cross-sectional study was carried out in the year 2021. It included undergraduate (both first and senior years) students, anatomy postgraduates, and faculty involved in embryology teaching-learning. The undergraduate students of senior years were engaged in embryology learning in their first professional year. All the students were exposed to the same teaching-learning methods during their embryology teaching-learning sessions. The students were exposed to didactic lectures, small group discussions using embryology models, video-based and case-based learning sessions.

The Institutional Ethics Committee approved the study. All the participants were allowed to participate or decline participation in the study. Informed consent was taken from the participants who agreed to participate in the study.

A two-step approach was followed in conducting the study.

Step 1:

In step 1, the undergraduate (including only first-year) students who willingly consented to participate in the study were given a close-end-

ed structured questionnaire (Annexure 1). The questionnaire components addressed the current practices of embryology teaching and its impact on their learning. The questionnaire was administered online through Microsoft teams (Microsoft, One Microsoft Way, Redmond, Washington, U.S.).

Data analysis: Quantitative analysis

The responses to the close-ended questions were recorded using a Likert scale (1-5: strongly disagree-strongly agree). Some of the close-ended questions also had 'yes,' 'no,' and 'don't know/may be' types of responses. The results were expressed in frequency and percentages. Paired

Annexure 1. Questionnaire on the first-year undergraduate student's perception of the current practices of embryology teaching and its impact on their learning.

	Strongly agree(%)	Agree	Neutral	Disagree	Strongly disagree
Human embryology is essential in understanding gross anatomy					
The current syllabus of embryology is relevant for acquiring knowledge					
The study of human embryology is an important and necessary part of medical training					
Knowledge of human embryology is essential in understanding other subjects such as physiology, medicine, surgery, obstetrics, Pediatrics, etc					
Knowledge of human embryology helps me to better understand certain clinical ailments better					
Knowledge of human embryology is essential in understanding gross anatomy					
The lessons learnt in human embryology can be used practically as a health care professional					
I find the subject of human embryology interesting					
I find the subject of human embryology difficult to understand					
Embryology should go hand in hand with the relevant topics in gross anatomy.					
Teaching more slowly (i.e., at a slow pace) than the other gross anatomy lectures helps me follow embryology better					
The concepts of embryology taught in the lecture classes are adequate and understandable					
I find answering exam questions on human embryology more stressful than answering those on gross anatomy topics					
I personally would like to have more human embryology incorporated into the anatomy lab (more demonstration sessions)					
I personally would prefer to not be required to learn human embryology in medical school					
The concepts of embryology taught in the lecture classes are adequate and understandable					
	Yes		**No**	**Don't know/may be**	
Are you satisfied with the present time allotted to teach embryology in the current CBME curriculum?					
Small group teaching is required to understand embryology					
Do you feel embryology is often neglected while learning Anatomy?					
Given the amount of reading embryology requires, do you feel the percentage of marks allotted for embryology in the examinations is sufficient?					

T-test was used to compare the differences in the observations between the male and female undergraduate students.

Step 2

In step 2, we extended the study to all participants. In this step, the undergraduate (including first and senior-year students), postgraduate students, and faculty of anatomy were involved. The faculty engaged in teaching embryology with an average teaching experience of 8-30 years were considered. The study participants were invited to answer an open-ended question. Herein the participants were encouraged to opine on the measures required to improve the teaching-learning practices of embryology.

Data analysis: Qualitative analysis

The responses to the open-ended question were reviewed and subjected to qualitative analysis, and themes were identified. Thematic analysis was performed. The authors coded the material after reading and rereading the participants' replies. The codes were then examined to find the pattern, and the themes were identified. An inductive and semantic technique was used.

RESULTS

The present cross-sectional study involved the following:

Step 1: 222 first-year medical undergraduates (108 male and 119 females)

Step 2: 222 first-year medical undergraduates (108 male and 119 females), ten senior undergraduates (8 males and two females), five anatomy postgraduate (one male and four females) students, and forty faculty members (11 males and 30 females) in anatomy. The faculty involved in teaching embryology, with an average teaching experience of 8-30 years, were considered.

Step 1: First-year undergraduate students (N=222) perception of the current practices of embryology teaching and its impact on their learning

The fact that the knowledge of human embryology is essential in understanding gross anatomy was agreed upon by 67% of the study participants. Nearly 11% of the participants disagreed with this fact, and 21 % were neutral.

Most of the study participants agreed that the current syllabus of embryology is relevant for acquiring knowledge (69%). The same was disagreed by 9% of the participants, while 22% were neutral.

The rest of the responses to the close-ended questions are presented in table 1. Paired T-test revealed no significant difference between the observations in males and females.

When asked about the T/L methods suitable for embryology, the following were the collective responses obtained:

- Lecture class with blackboard teaching: 22.6%
- Lecture class with PowerPoint presentations (PPTs): 29.2%
- Lecture class with models/ videos: 73.9%
- Case scenario-based learning (problem-based learning): 32.7%
- Small group teaching: 42%

When asked to specify the other options available, the following were the responses obtained:

Use original fetal specimens, clay models, animation-based learning, and embryology learning videos incorporated into PPTs.

Step 2: Participants' views on the measures required to improve the T/L practices of embryology

Step 2 involved 222 first-year medical undergraduates (108 males and 119 females), ten senior undergraduates (eight males and two females), fifteen anatomy postgraduate (11 males and four females) students, and forty faculty members (11 males and 30 females) in anatomy.

The response to the open-ended question 'how can embryology T/L be made more interesting and effective in the current CBME curriculum' was reviewed. The themes identified are presented in table 2.

Table 1. First-year undergraduate student's perception of the current practices of embryology teaching and its impact on their learning.

	Strongly agree (%)	Agree	Neutral	Disagree	Strongly disagree
The study of human embryology is an important and necessary part of medical training	53(23.87)	120(54.05)	41(18.46)	8(3.6)	4(1.8)
Knowledge of human embryology is essential in understanding other subjects such as physiology, Medicine, surgery, obstetrics, Pediatrics etc	26(11.71)	81(36.48)	81(36.48)	28(12.61)	10(4.5)
Knowledge of human embryology helps me to understand certain clinical ailments better better	48(21.62)	124(55.85)	43(19.36)	6(2.7)	5(2.2)
Knowledge of human embryology is essential in understanding gross anatomy	39(17.56)	113(50.90)	47(21.17)	20(9.0)	7(3.15)
The lessons learned in human embryology can be used practically as a healthcare professional	22(9.90)	79(35.58)	92(41.44)	22(9.90)	11(4.95)
The concepts of embryology taught in the lecture classes are adequate and understandable	19(8.55)	107(48.19)	67(30.18)	24(10.81)	9(4.05)
I find the subject of human embryology interesting	30(13.51)	82(36.93)	60(27.02)	37(16.66)	17(7.65)
I find the subject of human embryology difficult to understand	37(16.66)	79(35.58)	66(29.72)	34(15.31)	10(4.50)
I find answering exam questions on human embryology more stressful than answering those on gross anatomy topics	35(15.9)	107(47.7)	35(15.9)	30(13.6)	15(6.8)
I study only a few selected topics in embryology from an examination point of view rather than the entire syllabus.	80(36.4)	97(43.2)	20(9.1)	10(4.5)	15(6.8)
I would prefer not to be required to learn human embryology in medical school	11(4.95)	21(9.45)	53(23.87)	104(46.84)	37(16.66)
Embryology should go hand in hand with the relevant topics in gross anatomy.	73(32.88)	116(52.25)	25(11.26)	8(3.60)	4(1.80)
Teaching more slowly (i.e., at a slow pace) than the other gross anatomy lectures helps me follow embryology better	43(19.36)	91(40.99)	56(25.22)	24(10.81)	11(4.95)
I would like to have more human embryology incorporated into the anatomy lab (more demonstration sessions)	45(20.27)	91(40.99)	60(27.02)	18(8.10)	12(5.40)
	Yes		**No**	**Don't know/Maybe**	
Are you satisfied with the time allotted to teach embryology in the current CBME curriculum?	81(36.48%)		95 (42.79%)	50(22.52)	
Small group teaching is required to understand embryology	169(76.12)		23(10.36)	34(15.31)	
Is embryology often neglected while learning Anatomy?	157(70.72)		31(13.96)	36(16.21)	
Given the amount of reading embryology requires, is the percentage of marks allotted for embryology in the examinations sufficient?	155(69.81)		43(19.36)	28(12.61)	

DISCUSSION

The present study reiterates that the knowledge of human embryology is essential for understanding the basic concepts of Anatomy. Being an integral part of the anatomy, understanding the intricacy and notion of the organization of the human body requires knowledge of fundamental pre-clinical medical topics such as embryology. Further, it also aids in providing a proper understanding of physiological and pathological processes, both normal and abnormal occurring in different diseases or disorders of the human body (Zaletel et al., 2016). Student responses recorded in the current study have documented the same.

Although embryology is interesting to study, it is challenging to comprehend, as stated by most students (52.24%) in the current study. Studies in the past also opined the same. They further added that many students find it challenging to see and comprehend embryology and to understand and reproduce it in a theory exam (Moraes and Pereira, 2010).

Table 2. Participant responses on 'how can embryology teaching-learning be made more interesting and effective in the current CBME curriculum' and the themes identified.

Quote	Theme
"With animated pictures and videos of the events occurring. Also, by including the embryology models in teaching" **(First year undergraduate 1)** "*Embryology teaching- learning can be made more interesting in CBME curriculum by using 3D teaching videos. Such videos help students to grasp faster and to make learning easier*" **(Postgraduate 1)** "*Chalk and board explanation mainly and assisted by schematic videos and clinical pictures is helpful*" **(Senior undergraduate student 1)**	Image and Video assisted learning
"*First of all, you have to take the students to an imaginary world where they visualize the entire events. More use of picture sequences. Animated videos are the most important teaching aids in learning embryology. First round of teaching should be very simple sequences. Once they understand the simple sequences then add details. We need to prepare simple flow charts either with words or with diagrams - as flash cards to revise the embryology*" **(Faculty 1)** "*Teaching it at a slower pace compared to the current pace as it is very interesting subject which is made disinteresting by the current teaching pace*" (**First year undergraduate student 2)**	Experiential learning
"*Use of more videos and 3D models rather than passive descriptive lectures. Visualization of structures makes learning and understanding better. Digital 3D models being made available or resources for such being made aware among students*" **(Faculty 2)**	3D models assisted learning
"*Real life photos of anomalies and it's cause, case-based discussions, models making can be activity and explaining those to their peers as an exhibit may help them remember very well*" **(Faculty 3)**	Case based learning
"*Embryology is the subject in which more specimen learning helps rather than theory lectures. What I believe is that for embryo, specimen and diagrams are very important to know better than just mug it up*" **(First year undergraduate student 3)** "*Showing them live demonstration in clinical embryology department. Zebra fish embryos are transparent and can be used as an interesting tool for explaining*" **(Faculty 4)**	Specimen based learning
"Small part to be covered in a single lecture. Use of videos, 3D models to explain facts. Reinforcement of the lectures in small group. Assessment drives learning. so, quizzes can be conducted. Model and chart making competition can be conducted" **(Faculty 5)**	Assessment-based learning
"*Small group discussion is helpful. As per CBME, ECE sessions with cases of congenital abnormalities, then a description of the basic science will help. Use of models concomitantly will increase the understanding.*" **(Faculty 6)**	Small group teaching

The present study also observed that the students found answering exam questions on human embryology more stressful than answering those on gross anatomy topics (63.6%).

Since the subject is given such little weight in theoretical tests, most students typically only focus on a few topics from an exam perspective. Very few students fully grasp the subject and its application in the clinical field (Moraes and Pereira, 2010).

Similar observations were made in the current study, with nearly 79.6% vouching that they study only a few selected topics in embryology from an examination point of view rather than the entire syllabus. It is because the weightage of the embryology content was less compared to the gross anatomy topics in the theory examinations. Therefore, the students tend to study only a few selected topics in embryology from an examination point of view, and some others just skip the subject altogether.

Although embryology learning is complex, students still find it highly relevant. Only a tiny percentage of the students prefer not to be required to learn human embryology in medical school (14.4%). It further evokes the need to explore the measures that would make embryology teaching-learning exciting and easy for the students.

As a remedy to permit an easy understanding of topics in embryology, most students opined that embryology should go hand-in-hand with the relevant topics in gross anatomy (85.13%). Students also preferred incorporating more human embryology topics into the anatomy lab/demonstration sessions for better understanding (61.26%). It was also found that teaching embryology slowly compared to the other gross anatomy topics helped to follow the concepts better (60.35%).

However, when asked whether the students were satisfied with the present time allotted to teach embryology in the current CBME curriculum, 36.48% agreed, and 42.79% denied. The remaining 22.52% were neutral.

Previously it has been claimed that it is possible to cover the entire embryology curriculum for undergraduates in two hours with successful results. But this observation is highly subjective, controversial, and impossible to adapt to the current scenario (Kazzazi and Bartlett, 2017).

Students find studying embryology frustrating because of the short teaching hours and difficulty of the subject. According to reports, medical students find learning about embryology complex and lack confidence in understanding. Additionally, they believe it was poorly taught to them during their college studies (Hamilton and Carachi, 2014; Scott et al., 2013).

It could also be one of the reasons for the students feel that embryology is often neglected while learning Anatomy (70.73%). Students also opined that given the amount of reading embryology requires, the percentage of marks allotted for embryology in the examinations is not sufficient (89.17%)

The impact of severely limited hours of embryology teaching on students' understanding warrants further research. Additionally, newer measures need to be taken to implement effective embryology teaching-learning practices in a restricted time frame and make them more inclusive in Anatomy learning.

Demonstrating fast, three-dimensional changes occurring macroscopically and microscopically has always been challenging in embryology teaching (Moraes and Pereira, 2010). Therefore, there is a need to identify and implement appropriate teaching-learning methods to improve the understanding of embryology.

Lecture classes incorporated with embryology models and videos (73.9%) and small group teaching (42%) were identified as good teaching-learning methods for embryology in the current study. Exploration of how to improve the embryology teaching-learning practices revealed the following themes: image and video-assisted learning, experiential learning, 3D models assisted learning, case-based learning, specimen-based learning, assessment-based learning, and small group teaching.

According to the conventional teaching method, the most effective method for conveying information to students is through a didactic lecture. However, it needs to provide adequate time for more profound learning activities (Al-Neklawy, 2017).

A study in the past revealed that didactic lectures were least preferred (32.8%) in learning. On the contrary, the students liked video lectures (41%) to learn and understand rare signs and cases (Papanna et al., 2013).

Some universities have practiced collecting clinical histories with pertinent pictures and videos, applying this method to impart embryology, and using photographs of newborns with abnormal embryos. Using images of normal and abnormal embryos, fetuses, and newborns helps people comprehend the issues being discussed (Moraes and Pereira, 2010). Specimen-based learning also adds to it.

When taught using clinical examples and management in instruction, embryology helped students comprehend and apply the ideas. It further elevated their level of satisfaction (Scott et al., 2013). It was also found that including clinically oriented multiple-choice questions (MCQs) at the end of the class was helpful (Hasan et al., 2018). It was also found that two-phased teaching would be highly beneficial. In this model, the basics of embryology are taught in the class, and their relation to clinical cases and scenarios would be introduced in the clinical setting, i.e., pediatric/neonatal surgery units of the hospitals (Hasan et al., 2018).

It would be an advancement in teaching techniques to use three-dimensional models and multimedia to assist students in visualizing the changes and processes within fetuses (Koscinski et al., 2019). It helps in experiential learning, as observed in the present study.

Studies have opined that the association of complementary pedagogic methods with movies and drawings related to embryology permits the optimization of embryo teaching (Koscinski et al., 2019). The present study also stated that such practices' association with routine didactic lectures could make embryology teaching learning effective and further enhance student engagement.

Previous studies have also affirmed that learning embryology through model construction is more effective than traditional embryology teaching (Aversi-Ferreira et al., 2012).

It is also observed that the creation of models encourages active learning and gives students a 3D perspective of different dynamic developmental changes in embryology with high recall memory. Materials such as play dough were stated as excellent materials for model construction (Patil, 2020). Similar observations were made in the current study.

Assessment is a central feature of teaching and the curriculum. It is one of the most potent influences/methods to assess the student's learning experience (Liu and Carless, 2006). Including more formative assessments in the form of quizzes and poster/model-making competitions can enhance embryology learning, as suggested in the present study.

A medical student's weight assigned to a subject in the overall evaluation plan has a direct impact on how motivated oneself to study that subject (Wormald et al., 2009). Considering the relevance of embryology in understanding anatomy, more weightage needs to be given to it, as noted in the present study.

As observed in the present study, student engagement and learning in embryology can be further improved by incorporating small group teaching (SGT). It has been found that SGT provides a friendly learning environment. It optimizes learning, especially compared to didactic lectures, particularly in healthcare. Students' knowledge is improved by actively building on their understanding and peer interactions. Additionally, SGT gives students a chance to collaborate and fosters teamwork abilities. To work in healthcare environments, you must possess specific skills (Burgess et al., 2020).

Shankar & Roopa, in their study, opined that traditional didactic lectures followed by modified team-based learning (TBL) sessions were better than conventional teaching methods (Shankar and Roopa, 2009). As observed in the present study, problem-based learning (PBL) can also be used in embryology.

Self-directed learning (SDL) can also be considered an alternate form of education (Pai et al., 2014). It has been found that retention of knowledge was better with SDL. It can further lead to collaborative learning and peer-to-peer interactions, enhancing embryology learning and retention.

Previously, it was discovered that 97% of students believed that peer teaching boosted their retention of the knowledge they had taught to their peers, and 100% of students agreed that peer teaching experience improved their grasp of the topics they had prepared (Krych et al., 2005). Similar practices can be utilized in embryology learning. This form of collaborative learning can be an effective educational strategy to promote peer collaboration in enhancing teamwork and communication skills (Glynn et al., 2006). It, in turn, would make the students more involved in learning embryology.

Al-Neklawy (2017), in their study on 100 Egyptian medical students, presumed that online anatomy teaching using learning management systems is an additional learning tool in the teaching-learning of anatomy. Herein the students can learn and understand concepts at their own pace. This kind of hybrid and flipped classroom approach may be applied in embryology learning and is beneficial. It has also been found that virtual reality tools further enhance embryology education when assessed both subjectively and objectively (Arendale, 2014).

All in all, the following measures can be taken to make embryology teaching-learning effective:

In the beginning, basic concepts of general embryology (i.e., topics such as gametogenesis, ovarian cycle, ovulation, fertilization, cleavage, implantation, placenta formation, etc.) should be taught leisurely and at a slow pace using models, 3D movies emphasizing clinical applications rather than describing the entire process.

Systemic embryology should be taught alongside gross anatomy sessions. During the sessions, less importance should be given to the entire formation process, and emphasis should be laid on the most common clinical applications.

Embryology can be made interesting to learn and easy to retain if it is taught with more clinical applications and a less detailed explanation of the entire process (as seen in current practice). Further, the TBL, PBL, and SDL sessions can be designed based on clinical applications, using the basic knowledge of embryology. These teaching-learning methodologies ensure that the students acquire the general and specific learning competencies in embryology. These methods are equally appropriate for both recent and experienced students.

CONCLUSION

Embryology is an essential component of anatomy and medical education. Therefore, there is a need to reform the existing methodologies of teaching-learning embryology to enhance student engagement, as identified in the present study. Seeking students and faculty's perceptions about the current practices of embryology teaching and its impact on their learning becomes vital, as observed in the present study. Utilizing the feedback gained in improving the process of imparting embryology knowledge will result in a positive and active learning experience for the students. Further, the integration of the following practices, i.e., "Why teach embryology?" followed by "What and how should it be taught?", and then "When and where should it be taught?", will make embryology teaching-learning an enriching and rewarding experience for both students and faculty.

RECOMMENDATIONS AND FUTURE RESEARCH DIRECTIONS

The impact of enhanced practices of embryology teaching-learning on students' performance can be assessed, analyzed, and further improvised. Its effectiveness can be evaluated by comparing it with the academic results. This measure can further instigate the policy makers or members of the respective board of studies to bring about further reforms in embryology's duration and teaching-learning practices.

DISSEMINATION HISTORY

The current work was presented in part as a speech to the 68th National Conference of Anatomical Society of India- NATCON-2022 organized by the Department of Anatomy, King George's Medical University, UP, Lucknow, from 28th -30th January 2022. The first author won the best paper award on this occasion.

ETHICAL APPROVAL AND CONSENT

The KMC (Kasturba Medical College) and KH (Kasturba Hospital) Institutional ethics committees approved the conduct of the study. The study was performed following the ethics committee's relevant guidelines and regulations. The study participants were recruited after obtaining their written informed consent.

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