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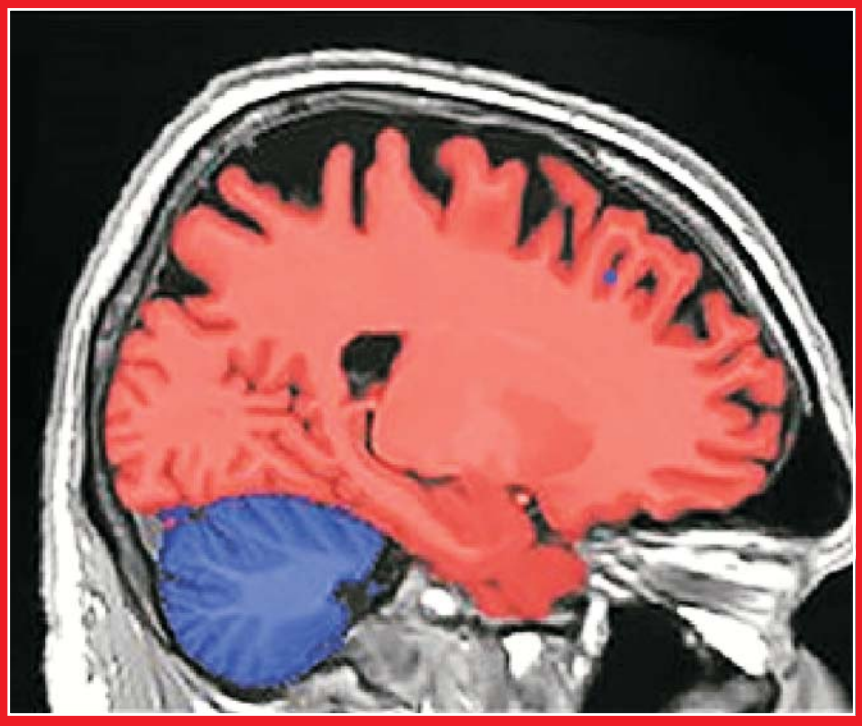

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Fiber type composition of the hip abductor muscles

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Abstract

Objectives: The hip abductor muscles; gluteus medius, gluteus minimus and tensor fasciae latae, play an important role in pelvic stabilization. Morphological changes occur in these muscles as a consequence of chronic musculoskeletal conditions (e.g. osteoarthritis), aging, and following hip joint replacement. Functional studies show unique activation profiles of the different compartments of gluteus medius and gluteus minimus; however, little is known of the fiber type composition of these muscles, which is an important consideration for understanding their functional and metabolic capabilities.

Methods: Eight transverse muscle samples from each compartment of gluteus medius and gluteus minimus, and two samples from tensor fasciae latae were harvested from 11 cadavers, and processed for immunohistochemistry. Fast-twitch muscle fibers were stained with the MY-32 antibody to estimate the proportion of type II fibers comprising the muscles.

Results: Individual muscle fiber composition profiles demonstrated that gluteus medius and gluteus minimus were similar in composition, supporting a predominantly postural function. Tensor fasciae latae had a higher proportion of type II fibers, suggesting a more phasic functional role. No differences were observed between compartments for gluteus medius, but the anterior compartment of gluteus minimus had a significantly higher proportion of type II fibers than the posterior.

Conclusion: This study provides anatomical data for the fiber type composition profiles of the hip abductor muscles, contributing to the understanding of their metabolic and contractile capabilities. These data may be valuable when considering changes that occur at the cellular level in the hip abductor muscles under pathological conditions and with aging.

Keywords: fiber type; gluteus medius; gluteus minimus; skeletal muscle

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Introduction

The contribution of the hip abductor muscles, gluteus medius (GMed), gluteus minimus (GMin) and tensor fasciae latae (TFL), to pelvic and hip stability and movement has attracted increasing interest in recent years, particularly in relation to greater trochanteric pain syndrome,[1–4] hip osteoarthritis,[5–8] and total hip replacement surgery.[9,10] Changes in the morphology of these muscles are evident in individuals with these differing forms of hip dysfunction and following surgery: primarily a loss in muscle volume (atrophy), accompanied by increased intramuscular adiposity (particularly of GMin), with or without a reduction in muscle strength.[3,4,6–10]

The function of the hip abductor muscles has been assessed using a variety of methods including surface electromyography (EMG),[11–14] biomechanical modelling,[14–17] and intramuscular EMG.[13,18–20] Generally, these studies describe GMed as an important stabilizer of the pelvis during weight-bearing, and a powerful abductor of the hip. It is also likely that it contributes to contralateral forward rotation of the pelvis.[19] Likewise, the GMin is an abductor of the thigh, and also contributes to internal rotation of the hip. More recent work has shown that it is also highly active during maximum resisted thigh extension, with the hip in neutral, and at the end of hip extension during the stance phase of the gait cycle.[20] The TFL is also morphologically designed for, and active during isolated hip abduction, and its intensity of activation during mid-stance of gait suggests it assists GMed and GMin to stabilize the pelvis.[12,21–23] The TFL is also active during the initial part of the swing phase where it works with iliopsoas to assist in hip flexion.[12,22,23]

In early EMG studies, each of the hip abductors were considered as a whole muscle,[13,18] which is appropriate for TFL. However, it is now known that GMed and GMin are comprised of compartments which are morphologically[24] and functionally[19,20] unique. Semciw et al.[19,20] established an intramuscular EMG protocol utilizing fine wire electrodes that enabled the collection of data from the compartments of GMed (anterior, middle and posterior) and GMin (anterior and posterior). In healthy, young adults, distinct muscle activation profiles were demonstrated for the hip abductors during specific hip movements and gait. During gait, a compartment-specific activation profile was observed. For GMed, although all three compartments (anterior, middle and posterior) showed two bursts of activity during the stance phase of gait, the anterior compartment activated significantly later than the middle compartment at the first peak (0–20% gait), and both middle and posterior compartments at the second peak (20–60% gait cycle).[19] Comparably, while both anterior and posterior compartments of GMin are co-activated in late mid-stance (peak ~40–50% of gait cycle), posterior GMin is significantly more active during contra-lateral toe-off (~18% of gait cycle) and thus, has been specifically suggested as a major contributor of femoral head stabilization in early stance.[20–24]

Given the dynamic and stabilizing functions of the hip abductor muscles, examining their fiber type composition would provide further insight into their compartmental functions and metabolic capacity. However, despite the numerous gross morphological and functional studies of these muscles, little consideration has been afforded to fiber type. To date, one study has provided data for GMed and TFL, showing the percentage of type II fibers (described as fatigue susceptible fibers with fast-shortening speed[25]) in males was 42% for GMed and 55% for TFL,[26] and another reports on the fiber type composition of GMin.[27] In this study, samples harvested from the anterior and posterior aspects of nine cadaveric GMin muscles exhibited a predominance of type I fibers (described as fatigue-resistant fibers with a slow shortening speed[25]) (range 62% to 74%). However, it is unknown whether there are regional differences between the anatomically and functionally distinct compartments.[11,19,20,24] Such information may be valuable for not only furthering our understanding of the function (i.e. contraction velocity and fatigability[28]) of these muscles but also for providing information relevant to conditions where the morphology of the gluteal muscles is altered.

The aims of this study were to (a) quantify the proportion of type I and type II fibers of GMed, GMin and TFL using immunohistochemistry and stereology and (b) determine the fiber type composition of the different anatomical compartments.

Materials and Methods

Tissue was collected from 15 limbs of 11 cadavers (7 male, 4 female; 7 right, 8 left; mean age at death, 81.9 years, range 66–97 years); both hips from 4 male cadavers were therefore included in our sample.

The cadavers from which samples were taken were embalmed with Crosado Mix.[29] Each specimen was dissected as described elsewhere,[24] and two transverse muscle samples (deep and superficial) of 10 mm in length were taken from the mid-point (proximal-distal, and anterior-posterior) at four areas in each of GMed and GMin, and one area of TFL (**Figure 1**), based on the results of a previous investigation into the compartmentalisation of these muscles.[24] Although initially, the mid-anterior and mid-posterior regions of the GMed and GMin were sampled, after consideration of existing literature and in alignment with recent functional studies,[19,20] the most anterior sample of GMed was considered to be representative of the anterior compartment of GMed, the middle two samples represented the middle compartment and the most posterior sample the posterior compartment of the muscle. For GMin, the two most anteriorly located samples were re-considered to represent the anterior compartment of the muscle, while the two most posterior samples were from the posterior compartment. Following extraction of tissue, samples were immediately immersed in Bouin's solution (saturated aqueous picric acid [250 ml], 37% formalin [250 ml] and acetic acid [50 ml]), at room temperature overnight. Thereafter, samples were kept in 70% alcohol until they were processed and embedded in paraffin wax, oriented to be sectioned transversely across the muscle fibers.

Optimization of Immunohistochemical Methods

The use of Crosado-embalmed cadavers for histology has been shown to be successful and acceptable.[29,30] Mouse and human muscle tissue samples from gluteus maximus and GMed were used to optimize the immunohistochemical protocol to ensure reliable complimentary staining of the mouse monoclonal antibodies MY-32 (Anti-fast skeletal myosin heavy chain MY-32 (catalogue # M4276, Sigma-Aldrich, St. Louis, MO, USA); mouse monoclonal Ab which reacts with type II skeletal myosin (all types)(Dilution 1:200 in tris-buffered saline in 1% bovine serum albumin)) and 1a (Anti-slow skeletal myosin heavy chain NOQ7.1.1A (1a)(gifted by M Duxson); mouse monoclonal Ab hybridoma supernatant specific for type I myosin heavy chain[31] (Dilution 1:100)) (**Figure 2**). Negative control sections were incubated with an equivalent concentration of mouse immunoglobulin (IgG). Initially, both 1a and MY-32 antibodies were used to show

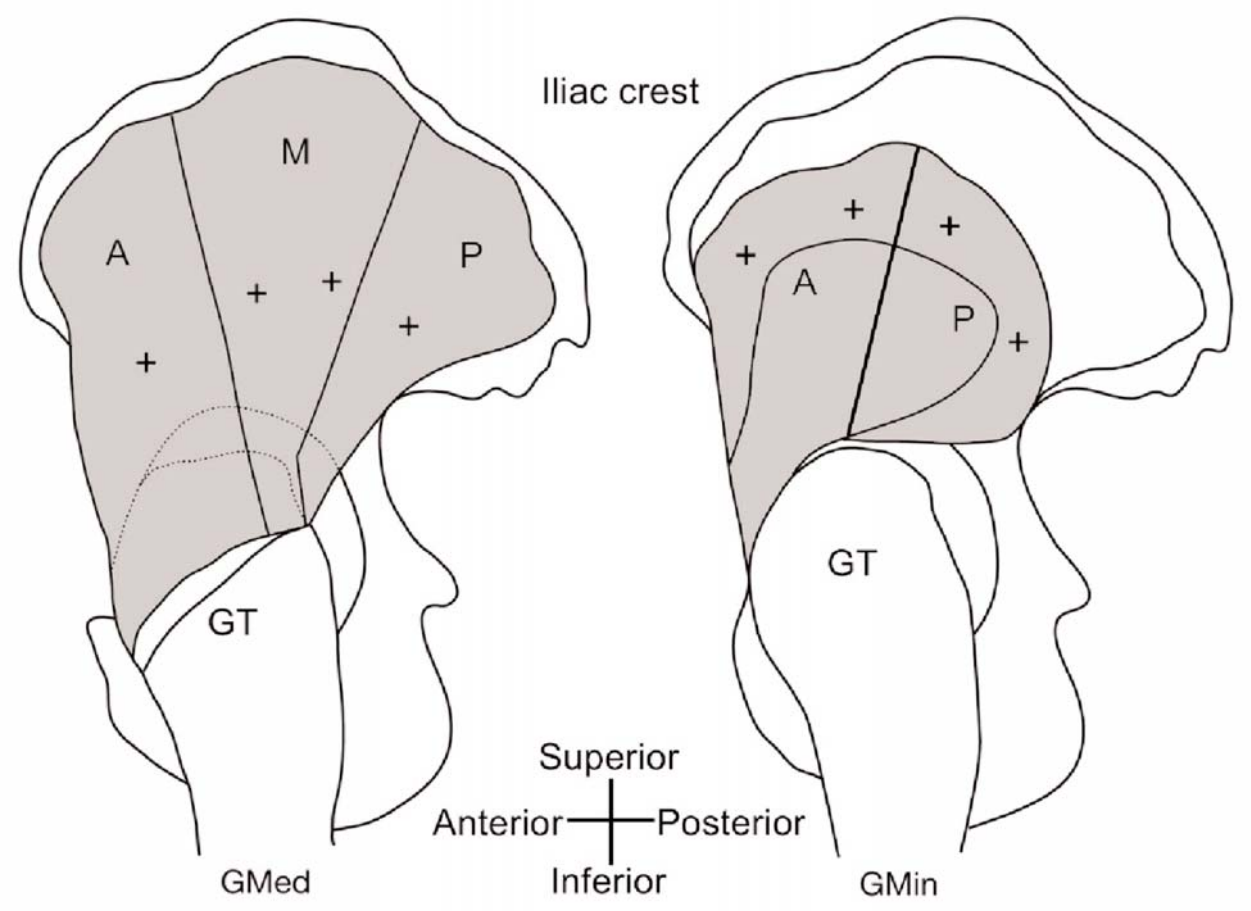

Figure 1. The regions within GMed and GMin from which samples were taken for immunohistochemical fiber typing. Samples taken for staining included a superficial and deep fascicle taken from the areas indicated by "+" in the anatomical compartments of GMed (3) and GMin (2). In total, eight fascicles were taken from each of GMed and GMin. **A:** anterior; **GMed:** gluteus medius; **GMin:** gluteus minimus, **GT**: greater trochanter; **M:** middle; **P:** posterior.

specificity and produce complimentary staining. Subsequently, only MY-32 was used as access to 1a was limited; it was therefore assumed that all non-stained fibers within these sections were type I. Sections of human gluteus maximus were used as positive controls.

Immunohistochemistry

After discarding the first 50 sections (5 µm thickness) (microtome, Leica Instruments, Wetzlar, Germany) of each sample, three serial sections were cut, mounted and left to dry overnight at 37 °C, before being stained using standard immunohistochemical procedures. Briefly, prior to staining, antigen retrieval methods required the sections to be immersed in a 10 mM citrate buffer solution, and heated to 95 °C for 10 minutes. After cooling, an endogenous peroxidase blocking step was carried out (15 minutes, 0.3% hydrogen peroxide) followed by a second blocking step using Donkey serum in 1% bovine serum albumin (catalogue # 85040C- 1K, Sigma-Aldrich, St. Louis, MO, USA) in TBS, for 2 hours, at room temperature. Sections were then incubated with the MY-32 primary antibody (or negative control, mouse IgG) overnight at 4 °C. A Dako biotinylated horseradish peroxidase kit (Dako LSAB2 system-HRP, Dako North Amerika, Inc., Carpinteria, CA, USA) was used for the secondary antibody step. Then, diaminobenzidine (Sigma-Aldrich, St. Louis, MO, USA) was applied to sections for visualization of immunoreactivity, prior to permanently mounting the slides using entellan mounting media (Merck KGaA, Darmstadt, Germany).

Stereology

Whole stained sections were scanned at a magnification of 20× using an Aperio CS2 scanner (Leica Biosystems, Nussloch, Germany) and subsequently viewed in ImageJ

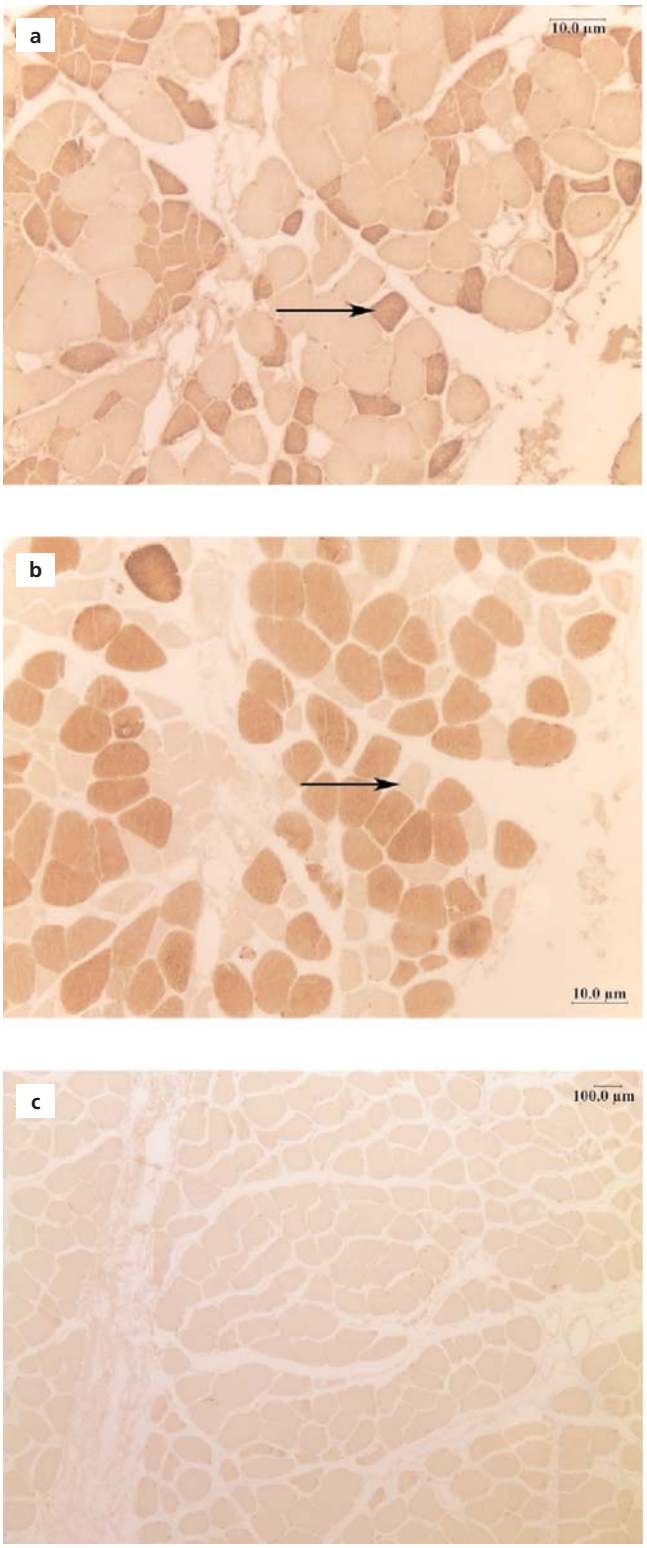

Figure 2. Complimentary staining of Ab MY-32 (type II fibers) and 1a (type I fibers) within GMed. Those fibers that were darkly stained by the MY-32 Ab (**a**), were not stained by the 1a Ab (**b**) (**arrows**). No fibers were stained in the control section (**c**), where a mouse IgG replaced the primary Ab. Magnification: (**a**, **b**) 20×, (**c**) 10×. **Ab:** antibody; **GMed:** gluteus medius; **IgG:** immunoglobulin G.

(NIH, Bethesda, MD, USA, v1.51s) as both a reference for determining counting sample squares and for counting the individual fibers. A grid with squares measuring 20 mm by 20 mm, was laid over the reference image and using a random number generator, selected squares on this grid were chosen for analysis. The number of whole cells within the square, of each fiber type was counted. A total of approximately 100 cells were required to be counted from each section,[32] so depending on the density of cells within each sample square, the number of sample squares that were chosen for counting cells varied (range 5–94). For some sections, it was necessary to count all cells in the section. The mean number of type I and type II fibers was calculated from the two superficial areas, and the two deep areas sampled in the middle compartment of GMed, as were the two areas for the two superficial areas and the two deep areas sampled in the anterior, and posterior compartments of GMin (**Figure 1**). Thus, an average fiber type composition for the superficial samples, and the deep samples, in each of the three compartments of GMed and the two of GMin was attained.

Atrophy Assessment

Each section was assessed for the amount of atrophy present in the sample, using the Goutallier system.[33] Sections with considerable amounts of atrophy (i.e. less muscle than adipose), were excluded from the statistical analysis of the fiber type composition, as data for those sections were insufficient.

Statistics

All data were analysed using Excel (Microsoft Excel for Mac, v16.54, 2021). Descriptive statistics (means, standard errors) of the percentage of type II fibers found in each muscle (GMed, GMin and TFL), and the individual compartments (GMed and GMin only) were determined. A paired Student's t-test was used to determine differences between superficial and deep fascicle fiber types within each compartment of GMed, GMin and TFL (**Table 1**). As no differences were observed, the samples were combined, and the percentage of type II fibers for each compartment was calculated for each muscle; e.g., anterior, middle and posterior for GMed, anterior and posterior for GMin, and the whole of TFL. All samples were then combined to obtain whole muscle type II fiber percentages, for each of the three muscles. Differences across the three muscles were determined using a one-way analysis of variance (ANOVA) as well as to explore differences between the three compartments of GMed. A paired-samples t-test was used for differences between the two compartments of GMin. Significance was taken as $p<0.05$.

Table 1

Mean percentage and differences between means of type II fibers found in superficial and deep regions for all muscles, and each compartment for gluteus medius and gluteus minimus.

	Gluteus medius			
Sample region	Anterior mean (%) SEM n=14	Middle mean (%) SEM n=27	Posterior mean (%), SEM n=12	Difference between compartments (ANOVA)
Superficial	40.8±20.7	41.1±19.4	44.6±18	
Deep	44±27.9	36.8±20.3	38.75±15.7	
Difference	p=0.6	p=0.1	p=0.3	
Combined superficial and deep	42.4±4.6	38.9±2.7	41.7±3.4	$F_{(2,103)}$=0.31, p=0.73
	Gluteus minimus			
Sample region	Anterior mean (%) SEM n=22		Posterior mean (%) SEM n=24	Mean difference between compartments (Paired samples t-test)
Superficial	48.4±25.9		37.4±26.5	
Deep	50.9±26.4		35.7±24.8	
Difference	p=0.3		p=0.5	
Combined superficial and deep	49.7±3.9		36.6±3.7	t(89)=2.5, p=0.02
	Tensor fasciae latae			
Sample region	Whole muscle mean (%) SEM n=12			
Superficial	52.2±17.9			
Deep	55.6±19.6			
Difference	p=0.1			
Combined superficial and deep	53.9±3.8			

Sample size differences between compartments are due to the loss/damage of sections during immunohistochemistry; as more areas were sampled for the middle GMed compartment, and the compartments of GMin, larger sample sizes were available for this compartment. **F:** F-statistic; **SEM:** standard error of means; **t:** t-statistic. Significance taken as p<0.05.

Results

Differences between compartments: **Table 1** shows the mean percentage of type II fibers found within each compartment of GMed, and GMin. There were no statistically significant differences in the percentage of type II fibers across the compartments for GMed ($F_{(2,103)}$=0.31, p=0.73). However, there was a significantly higher mean percentage of type II fibers in the anterior compartment of GMin (49.7±3.9) when compared to the posterior compartment (36.6±3.7, p=0.02).

Differences Between Muscles

The descriptive statistics of the three hip abductor muscles are summarized in **Figure 3**. There was a significant difference between the mean type II fiber type percentage across the three muscles ($F_{(2,219)}$=3.37, p=0.03). Post-hoc analyses using the Bonferroni's correction revealed that there was a significantly higher mean percentage of type II fibers in TFL (53.9±3.8) when compared to GMed (40.5±2.0, p=0.03). No differences were observed between TFL and GMin, nor between GMed and GMin.

Fatty Infiltration

Each specimen showed variable amounts of adipose tissue, but ratings mostly ranged between 0 (normal muscle tissue) and 2 (fat evident, but less fat than muscle),[33] with a few rated 4 (more fat than muscle tissue) for GMin only. For the compartments of GMed, mean fatty infiltration ratings ranged from 0.6 to 0.8 (range 0 to 3), with a median rating of 1 for all three compartments. For GMin, mean fatty infiltration ratings were slightly higher, at 1.6 (anterior) and 1.5 (posterior) (range 0 to 4), with median ratings of 2.0 for both compartments. Little fatty infiltration was observed in TFL, with a mean rating of 0.7, and a median rating of 0 (range 0 to 2) (**Figure 4**).

Although fiber dimensions were not quantified in this study, it was anecdotally observed that the diameters of both muscle fiber types were variable between muscles and

across specimens. There were also differences in size and shape between type I and type II fibers within the same muscle. In general, type I fibers appeared larger and rounder, while type II fibers were smaller and shrunken. Type II fibers also often appeared "spiked" in shape.

Discussion

Insight into the fiber type composition of the hip abductor muscles may contribute to a comprehensive understanding of their function, and provide an anatomical understanding for changes that may occur as a consequence of musculoskeletal conditions such as hip osteoarthritis, greater trochanteric pain syndrome or following hip joint replacement.

The results of this study indicate differences in the fiber type composition of the hip abductor muscles; GMed and GMin are comprised of similar percentages of type II fibers, but contain less than that observed for TFL. Based

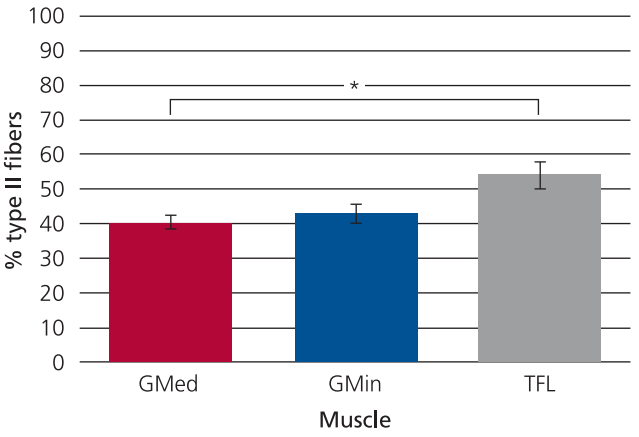

Figure 3. Mean percentage (±SEM) of type II fibers comprising the whole hip abductor muscles: GMed, GMin and TFL. A statistically significant difference in the percentage of type II fibers was observed between GMed and TFL (p=0.03), but not between GMin and TFL nor between GMed and GMin. **GMed:** gluteus medius; **GMin:** gluteus minimus; **TFL:** tensor fasciae latae.

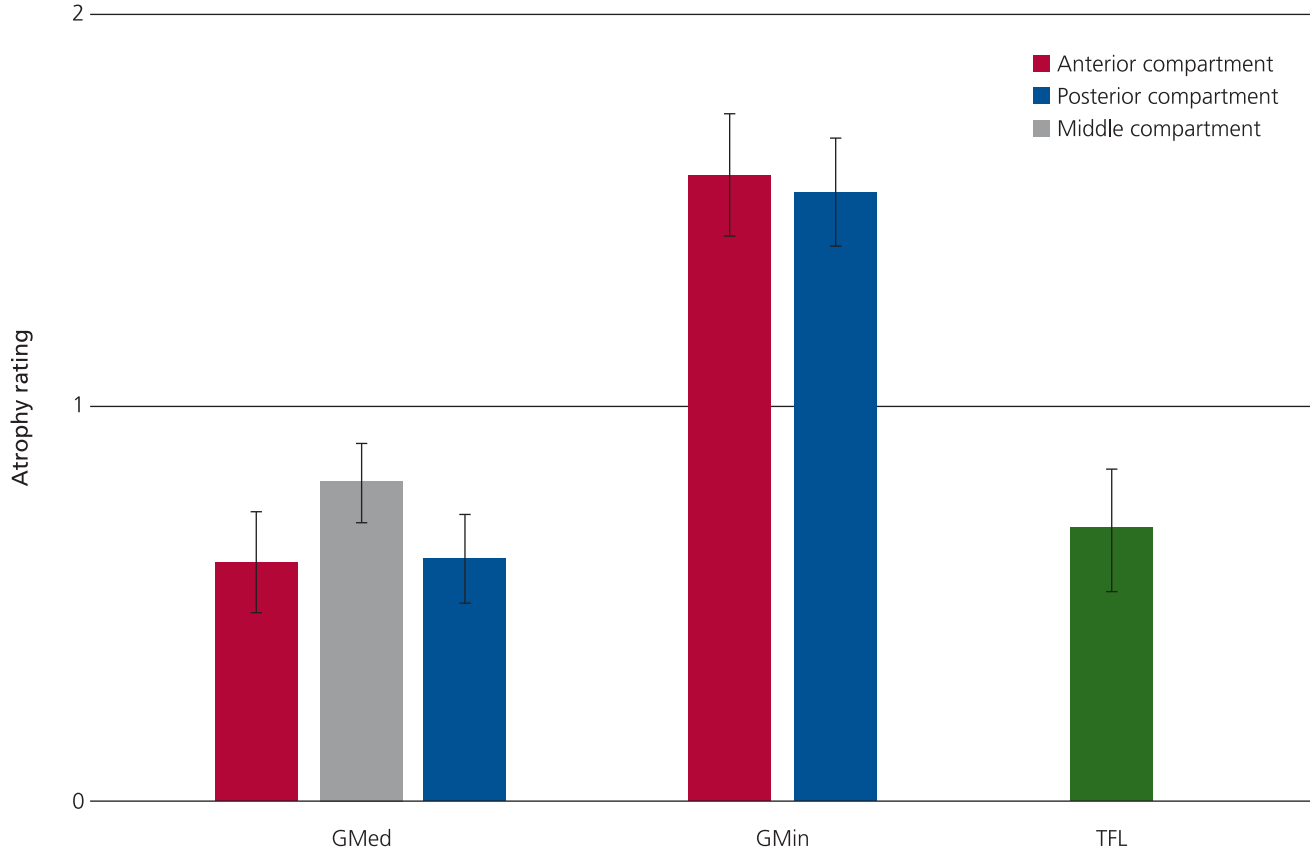

Figure 4. Mean (and SEM) atrophy ratings of each compartment for gluteus medius and gluteus minimus, and for the whole muscle of TFL as determined by using the Goutallier's scoring system. More severe fatty infiltration was observed in sections taken from GMin, with severe atrophy (rated as "4") being found only in sections taken from GMin. **A:** anterior; **GMed:** gluteus medius; **GMin:** gluteus minimus; **M:** middle; **P:** posterior; **TFL:** tensor fasciae latae.

on the metabolic property differences between type I and type II fibers,[34] the lower percentage of type II fibers comprising GMed (40.4±2%) and GMin (42.8±2.7%), and therefore higher percentage of type I fibers, (fatigue-resistant with slow-shortening speed[25]) hints at a more "postural" or stabilising role for these two muscles. In contrast, the higher composition of type II fibers (fatigue susceptible, fast-shortening speed[25]) in TFL (53.8±3.8%) suggests this muscle is potentially involved in more "phasic" activities. These data corroborate those presented by Sirca and Susec-Michieli[26] for GMed and TFL from "normal adult males" (n=11, age range 22 – 44 years), and those data for GMin, as identified more recently by Takano et al.[27]

Despite these observations, the relative percentages of type I and type II fibers within each muscle are not dissimilar, especially when compared with muscles recognized as having a predominantly postural function, such as the thoracolumbar transversospinal muscles (mean 88.6% type I)[35] or the palmaris brevis (72.2% type I).[25] Similar heterogeneity is observed in a number of other muscles within the body and reflects the ability of the skeletal muscle to adapt to a variety of functional demands.[36] Physiologically, GMed, GMin and TFL probably participate in both tonic activity (to maintain posture) as well as phasic activity (creating movement of joints).[37] This hypothesis is supported by the functional-based literature which states that both gluteal muscles are important stabilisers of the pelvis,[11,12,16,18,21,38,39] and also have the ability to move the lower limb through hip abduction and internal rotation.[11,14,15,38] Similarly, while TFL is considered to be involved in contributing towards flexion and abduction of the hip joint,[11,12,14,15,22,39] some authors attribute to it a role in pelvic stabilization[21,22,39] especially during the stance phase of the gait cycle.[23]

As has been previously reported, the fiber type composition of a muscle can vary depending on where the sample is taken (i.e. superficial vs deep,[37] or between anatomically distinct compartments[28]). The current study observed statistically significant compartmental differences for the percentage of type II fibers comprising GMin, but the same was not observed for GMed. As the functional profiles of the different compartments of GMed and GMin are unique, we anticipated that there would be differences between compartments, for both muscles. However, the results of our study support this hypothesis, particular to GMin only. Functionally this makes sense based on the extended length of time for which GMin posterior is required to provide stabilization through the early and midstance phases of gait,[20] it is expected that the characteristics of this region of the muscle support a slower maximum shortening velocity and are more resistant to fatigue, and thus, would contain a higher proportion of type I fibers. However, it is also likely that the observed difference in fiber type composition between compartments of GMin is attributable to the atrophic changes that appear to affect GMin preferential to GMed,[6,7,10,24,27] explaining why we did not observe a similar difference for the larger, more active muscle of GMed. Although it is known that the individual compartments of the GMed are activated at different times during gait and isolated hip movements,[19,20] the overall metabolic capacity of the different regions of the muscle may be too similar to detect a difference.

The current study also observed a tendency towards the predominance of fatty infiltration (and thus atrophy) of the muscle in GMin compared to GMed and TFL, corroborating observations made in previous studies.[6,7,10,24,27] As shown by Semciw et al.[19,20] GMin is an important pelvic stabilizer, so the predominance of atrophy in this muscle could significantly affect hip stability during gait and standing. However, the current study did not indicate that fatty infiltration was constrained to anterior GMin as shown in recent morphological studies.[7,24,27] It is possible that the advanced age of the specimens in the current study (mean age, ~81 years) can explain this absence. It has been recently observed that the preferential location of fatty muscular atrophy in GMin could be dependent upon age; individuals younger than 70 years of age are more commonly observed to have atrophic changes located in the anterior compartment of GMin, while those older more commonly experience changes throughout the whole muscle (i.e. in both compartments).[40]

Although atrophy of individual muscle fibers and the muscle overall was not quantitatively determined, the descriptions afforded to its appearance and occurrence may be important in understanding the pathology of these muscles. In the present study, type II fibers appeared smaller and less rounded in shape, compared to type I fibers. This change in shape may indicate that type II fibers undergo selective atrophy. A selective decrease in the size of type II fibers or type II fiber area,[26,40,41] as well as changes in shape,[41] attributed to aging, have been previously described in a number of different muscles including vastus lateralis, GMed, gluteus maximus, and TFL. Additionally, photographs published in some of these studies[26,41] showed a similar histological appearance to the fibers observed in the present study. Furthermore, Lexell et al.,[41] and Sirca and Susec-Michieli,[26] both observed an alteration in size and/or shape of type II fibers (angulated and atrophic type II fibers) in the older participants (aged between 70 and 80 years), when compared to younger par-

ticipants (aged 19–44 years). The mean age of the cadaveric specimens used in the current study is similar to those of the older participant groups in these studies, so it is possible that the observations of atrophy can be explained in the same way. The evidence outlined above, supports the suggestion that the atrophy observed in the current study is due to aging, but in the current study TFL was shown to have more type II fibers than both GMed and GMin, but it was the least atrophied muscle. The impact that use, or rather, disuse of these muscles also needs to be considered when trying to explain the disparity between atrophy of the different muscle fiber types. Further quantitative analysis on fiber type dimensions are needed to provide conclusive information for GMed, GMin and TFL.

Limitations

It is generally accepted that the aging process affects the fiber composition of a muscle,[42] but how and to what extent is still largely unknown. Historically, there was agreement that with age, there was a preferential atrophy of type II fibers.[26] However, with advancements in histological methods and the understanding of co-expressions of different MHC isoforms and thus muscle fiber characteristics, this "preferential atrophy" theory is being contested, especially for the elderly.[43] It is also difficult to ascertain the full amount to which age plays a role in the changing characteristics of the muscle fiber as physical activity also impacts on fiber type composition,[26] and different muscles may behave differently (i.e. gastrocnemius versus soleus) with aging.[43] As there is no existing information addressing a changing fiber type composition specifically for GMed, GMin and TFL, with age or activity, and we also do not have the data from a younger sample to compare results, we cannot comment on to what extent these factors may have influenced our data, if at all.

Unfortunately, the limited sample size utilised for the current study did not allow analysis for differences between males and females. Within the existing studies that have investigated sex difference in fiber type composition, no data for the hip abductor muscles are available, and results for other muscles are variable. Some studies have found males to have a higher proportion of type II fibers than females (e.g. vastus laterals, biceps brachii[44] (but statistical analysis was not undertaken), some report the opposite,[45] and others show no differences (e.g. longus colli and multifidus[46]). This possibly indicates that the composition of fiber types is influenced in a number of ways. For example, fiber composition may be muscle-dependent, affected by age, physical activity levels and hormones, or there are methodological limitations such as the use of fresh or fixed tissue and the subsequent histological investigation that can be used.[37,43] The current study is further limited by the lack of medical history information that is provided as part of the bequest programme at the University of Otago. Further work to address these limitations and provide a comprehensive overview of the existence of sex differences in fiber type composition is advised.

Differentiation was made between type I and type II muscle fiber types but not between the sub-types of type II fibers. Identification of these fiber sub-types in the hip abductor muscles could contribute to a better understanding of the functional capabilities of GMed, GMin and TFL. As the MY-32 monoclonal Ab does not differentiate between fiber sub-types,[47] the ATPase method of detection would need to be employed, for which, the acquisition of fresh tissue is necessary. Additionally, investigation into the diameter size of these muscle fibers in this age group and a quantification of differences would help to explain any unexpected differences in fiber type composition, and contribute to the understanding of what might happen to different fibers comprising the hip abductor muscles as the aging process occurs.

Conclusion

The hip abductor muscles are considered to play an important role in pelvic stabilization during gait and abduction and rotation of the hip. This study has provided an account of the fiber type composition of each of the hip abductor muscles, using immunohistochemistry. Our findings suggest in general, that there are unequal distributions of type I and type II fibers within GMed, GMin and TFL, suggesting a more postural role for GMed and GMin (slower contraction, more fatigue resistant) and a more phasic role for TFL (faster contraction, more prone to fatigue), although it is likely that all three muscles participate in both actions. Furthermore, this study has shown differences in fiber type composition between the anterior and posterior compartments of GMin. Overall, such knowledge is of significance when addressing the functional capabilities of these muscles; these data provide anatomical evidence for the verification of the functions of these muscles, and a comparison for what changes might occur under pathological conditions.

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Conflict of Interest

The authors declare that there are no conflicts of interest to report.

Author Contributions

NAMSF: Protocol/project development, data collection or management, manuscript writing/editing; SJW: Protocol/project development, data analysis, manuscript writing/editing; HDN: Protocol/project development, data analysis, manuscript writing/editing.

Ethics Approval

All cadavers were from a New Zealand European population and had been bequeathed to the Department of Anatomy, in accordance with the New Zealand Human Tissue Act (2008). Ethical approval was granted by the Department of Anatomy, University of Otago, Dunedin, New Zealand. As the undertaking of this study was prior to the establishment of a university-governed ethical approval process for the use of cadavers in research, internal approval for the use of cadavers in this research project was granted by the Department of Anatomy, University of Otago, Dunedin, New Zealand in 2008 and 2014.

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The relationship between the mastoid triangle and localization of the Asterion

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Abstract

Objectives: The relationship between the mastoid triangle and the localization of the Asterion can be used in craniotomy and posterolateral surgical approaches. Therefore, we aimed to identify the relationship between the localization of the Asterion and mastoid triangle in dry skulls and its effect on surgery.

Methods: Our study was performed on 93 adult skulls obtained from bone collections of the Anatomy Departments of Necmettin Erbakan University and Akdeniz University. The mastoid triangle, Asterion and linear distances between them were measured for to determine the localization of the Asterion.

Results: The Asterion was located just above the Frankfurt horizontal plane on the left sides of the skulls in 54 (58.1%) specimens and on the right sides of the skulls in 71 (76.3%). It was located below the Frankfurt horizontal plane on the left sides of the skulls in 39 (41.9%) specimens; and on the right sides of the skulls in 19 (20.4%). There was a positive correlation between the distance of Asterion to apex of the mastoid process (r=0.832).

Conclusion: The relationship between the mastoid process and the Asterion can be used for determination of the dural venous sinuses and neighboring neurovascular structures, in retrosigmoid posterolateral surgical approaches.

Keywords: anthropometric measurements; Asterion; craniometry; mastoid triangle; skull; surgical landmarks

Anatomy 2021;15(3):189–197

Introduction

Surface landmarks are useful in detecting the venous sinuses and neurovascular structures in neurosurgical approaches directed to reach the posterior fossa and posterolateral cranial base.[1] The mastoid area of the skull is particularly resistant to physical injury due to its compact structure and anatomical location. Thus, it may stay intact in otherwise damaged and fractured skulls.[2] The mastoid triangle (MT) is an essential surgical zone for transmastoid cisternoscopy, and surgical approaches directed to cerebellopontine triangle, mastoid antrum and dural venous sinuses. Therefore, anthropometric measurements of MT and nearby surgical landmarks, such as mastoid process (MP), should be considered in surgery to prevent damage to the auricular branch of the lesser occipital nerve, great auricular nerve, emissary vein, sigmoid and transverse sinuses.[3–5] Another surgical landmark is the Asterion which located at the junction of transverse and sigmoid sinuses, frequently used for posterolateral surgical approaches.[1,3,5,6] The position of the Asterion and other prominent anatomical landmarks provide orientation for clinical and surgical interventions.[7] Various researchers have investigated the anatomical variations related with the MP, MT and Asterion according to ethnicity, sexual

This study was an oral presentation at the16th National Anatomy Congress on 11–14 September 2014, Malatya, Turkey.

dimorphism and sex determination.[8–11] However, the correlation between the MT and the location of Asterion is still needed to be investigated in more details. Therefore, in this study, we aimed to identify the relationship between the localization of Asterion and MT in dry skulls and its surgical significance.

Materials and Methods

Measurements were performed on 93 adult Turkish dry skulls with unknown age and sex obtained from bone collections of the Anatomy Departments of Necmettin Erbakan University and Akdeniz University. Skulls with any pathologies, fractures and deformities were not included to the study. Both measurements were recorded bilaterally using an electronic digital caliper (INCA, DCLA-0605, 0.6–150 mm, USA). Same researchers performed the measurements and repeated them twice to ensure measurement reliability and minimize individual variability.

The following measurements were performed on both sides (**Figures 1a**, **b**, **2a**, **b** and **3b**):

- The length of mastoid process (L-MP): The distance between the Frankfurt Horizontal Plane (FHP is the horizontal plane extending between the uppermost point of the external acoustic meatus and the infraorbital margin) and the apex of the MP.
- The mediolateral diameter of the mastoid process (MLD-MP): The width between the medial and lateral surface of the MP.
- The anteroposterior diameter of the mastoid process (APD-MP): The width of the MP in the anteriorposterior direction.
- The distance between Asterion and the root of the zygomatic arch (A-ZA).
- The distance between Asterion and the apex of the mastoid process (A-AMP).
- The distance between Asterion and suprameatal spine (A-SS).
- The distance between Asterion and porion (A-P).
- The distance between the Porion and the apex of the mastoid process (P-AMP).
- The distance between Opisthion and the apex of the mastoid process (O-AMP).
- The transverse distance between the apex of the mastoid process (WBM).
- The area of the mastoid region (AMR).

Heron's Mastoid Triangle Area Formula (A) was calculated as[8,10,11] (**Figure 3a**):

$$A=\sqrt{(s(s-a)\,(s-b)\,(s-c)} \quad s=(a+b+c)/2$$

a: The distance between Asterion and Porion; **b:** The distance between the Porion and the apex of the mastoid process; **c:** The distance between Asterion and the apex of the mastoid process

The localization of the Asterion in reference to the FHP was evaluated between 0–2 (0: at the same level; 1: above the FHP; and 2:below the FHP). The data were analyzed using SPSS (Statistical Package for Social Sciences) for Windows (Version 21, Chicago, IL, USA). The data were expressed as number, percentage, mean±standard deviation (SD), maximum and minimum

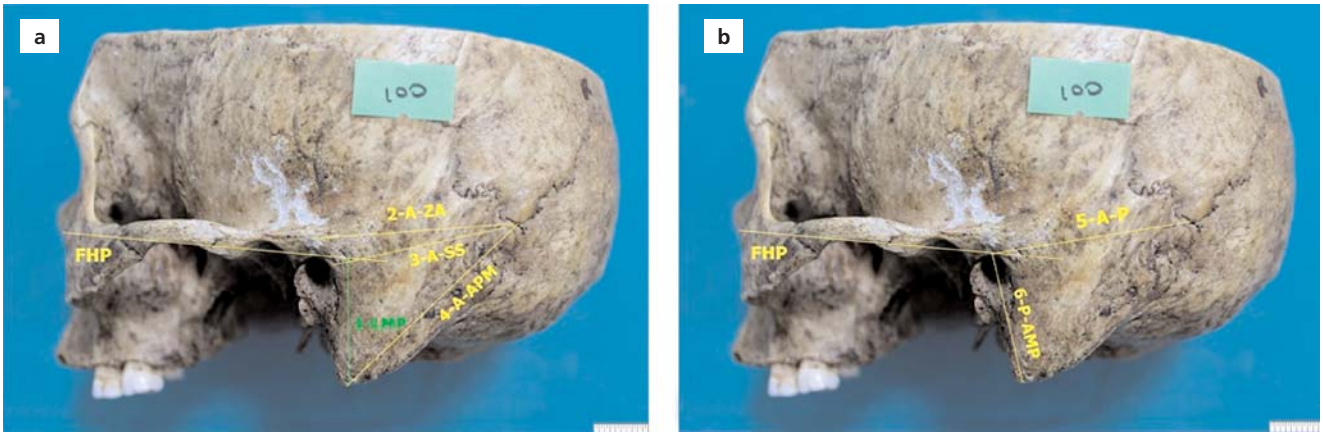

Figure 1. Morphometric measurements for to determine mastoid triangle. (**a**) **1-LMP:** length of the mastoid process; **2-A-ZA:** distance between Asterion and the root of the zygomatic arch; **3-A-SS:** distance between Asterion and suprameatal spine; **4-A-AMP:** distance between Asterion and the apex of the mastoid process; **FHP:** Frankfurt horizontal plane. (**b**) **5-A-P:** distance between Asterion and Porion; **6-P-AMP:** distance between Porion and the apex of the mastoid process.

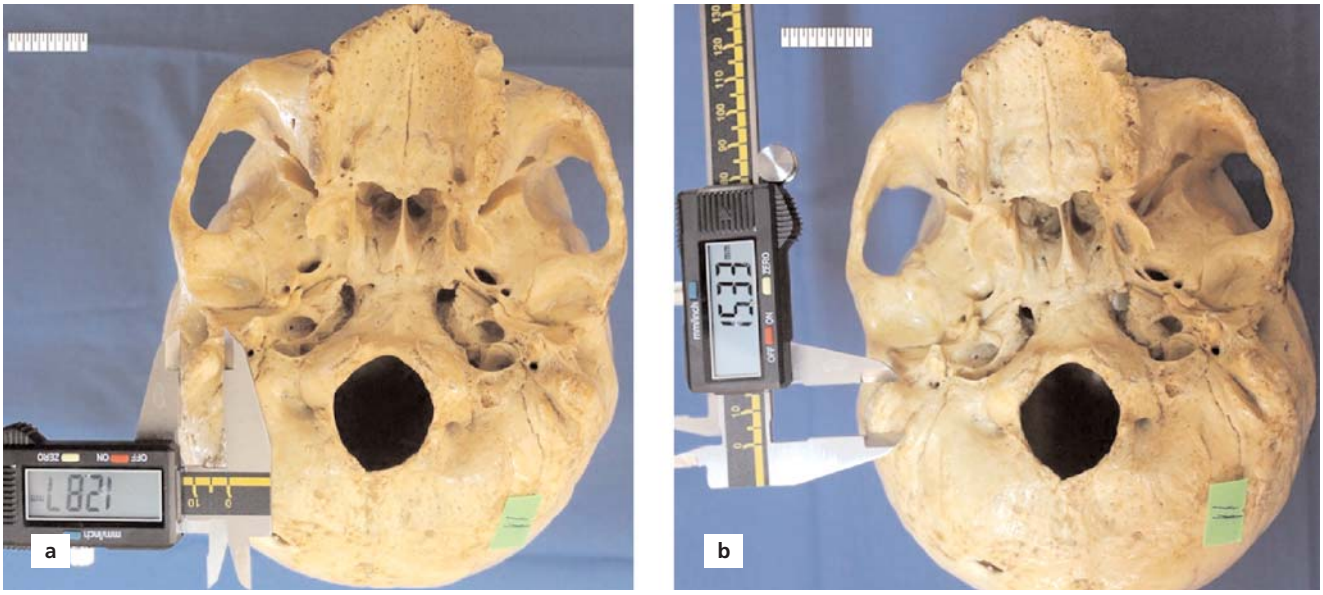

Figure 2. (**a**) Measuring the medio-lateral diamater of mastoid process; (**b**) measuring the antero-posterior diamater of mastoid process.

values. The relationship between the parameters was analyzed by paired sample t-test (for to evaluate the parameters of MT and MP on both sides) (**Tables 1** and **2**), chi-square analysis (for localization of the Asterion) (**Table 3**) and Pearson correlation test (for determining the correlation between the parameters) (**Table 4**). For all analyses; $p<0.05$ was considered as statistically significant.

Results

The findings showed that the length of mastoid processes (MP) on the right side was 25.50±5.49 mm and 25.82±4.35 mm on the left. However, there were no significant differences among sides (**Table 1**). The mediolateral diameters (MLD) of the MP were 12.70±4.29 mm on the right side

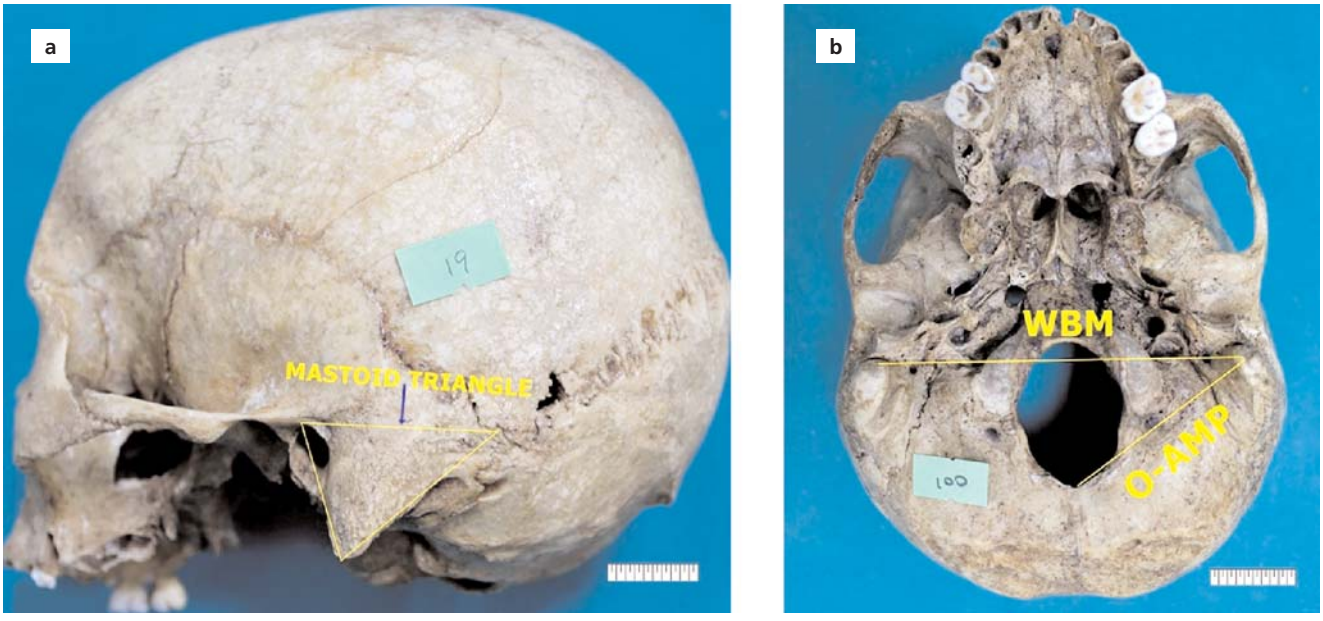

Figure 3. (**a**) Mastoid triangle; (**b**) **O-AMP:** distance between Opisthion and the apex of the mastoid process; **WBM:** The transverse distance between the apex of the mastoid process on both sides.

Table 1

The mean, standard deviation, minumum, maximum values of paramaters according to sides (mm).

	Right					Left				
Parameters	**n**	**Mean**	**SD**	**Min.**	**Max.**	**n**	**Mean**	**SD**	**Min.**	**Max.**
LMP	93	25.50*	5.49	10.90	38.25	93	25.82*	4.35	15.33	38.79
MLD	93	12.70*	4.29	6.72	25.39	93	11.39†	2.18	7.05	20.88
APD	93	15.71*	2.76	10.31	23.02	93	15.26*	3.04	9.42	24.27
A-ZA	93	42.75*	4.90	25.65	57.27	93	44.05*	7.15	32.79	64.91
A-AMP	93	49.58*	5.31	36.42	66.50	93	49.24*	5.06	38.23	64.72
A-SS	93	42.40*	7.21	2.11	53.67	93	42.80*	4.45	34.38	66.18
A-P	93	49.50*	4.59	32.10	62.52	93	48.86*	4.61	29.12	60.54
P-AMP	93	33.14*	4.22	23.30	55.36	93	32.41*	4.69	23.92	57.74
O-AMP	93	58.00*	4.36	44.93	71.19	93	57.74*	5.35	28.71	69.21
AMR	93	737.55*	134.40	420.77	1152.33	93	718.34*	142.16	371.44	1273.80

Note: Values in the same row which are not sharing the same subscript are significantly different on each side ($p<0.05$). Cells with no subscript are not included in the test. Tests assume equal variances. Tests are adjusted for all pairwise comparisons within a row of each innermost sub-table using the Bonferroni correction. **A-AMP:** distance between asterion and the apex of the mastoid process; **AMR:** area of the mastoid region; **A-P:** distance between asterion and porion; **APD:** the antero-posterior diamater of mastoid process; **A-SS:** distance between asterion and suprameatal spine; **A-ZA:** distance between asterion and the root of the zygomatic arch; **LMP:** length of mastoid process; **MLD:** medio-lateral diamater of mastoid process; **n:** number of the specimens; **O-AMP:** distance between opisthion and the apex of the mastoid process **P-AMP:** distance between porion and the apex of the mastoid process; **SD:** standard deviation. *The difference between mean values on each side is not statistically significant.

and 1.39±2.18 mm on the left. The difference in between both sides was statistically significant ($p<0.005$) (**Table 1**). The bimastoid width was 103.37±6.62 mm (**Table 2**).

Asterion was classified into three types in reference to the FHP (**Table 3**). Accordingly, in Type 1; Asterion was at the same plane as the FHP. In Type 2; Asterion was just above the FHP, and in Type 3; it was below the FHP. In 54 of the specimens (58.1%) Asterion was just above the FHP, and in 39 (41.9%) below the FHP on the left sides of the skulls. In 3 of the specimens (3.2%) Asterion was at the same level as the FHP, in 71 (76.3%) just above the FHP, and in 19 (20.4%) below the FHP on the right

Table 2

The mean, standard deviation, minimum and maximum values of bimastoid width (mm).

	n	**min.**	**max.**	**mean**	**SD**
WBM	93	79.25	116.36	103.3797	6.62375

n: number of the specimens; **SD:** standard deviation; **WBM:** transverse distance between the apex of the mastoid process of the both sides.

Table 3

Classification of Asterion in reference to the FHP.

		Right		Left				
		n	**%**	**n**	**%**	**X^2**	**df**	**p**
AS_FHP_TYPE	Type 1 (at the same level with FHP)	3	3.2%	0	0.0%	12.21	2	0.002
	Type 2 (above the FHP)	71	76.3%	54	58.1%			
	Type 3 (below the FHP)	19	20.4%	39	41.9%			

n: number of specimens; **χ^2:** chi-square value; **df:** degree of freedom.

Table 4
Correlation between mastoid triangle and mastoid process.

Parameters		AMR	WBM	O-AMP	P-AMP	A-P	A-SS	A-AMP	A-ZA	APD	MLD	LMP	SIDE
Side	r	-.070	.b	-.027	-.082	-.070	.034	-.033	.107	-.078	-.189*	.033	1
	p	.345	.000	.712	.266	.339	.649	.656	.147	.288	.010	.659	
LMP	r	.594*	.361*	.230*	.619*	.126	.137	.480*	.381*	.401*	.499*	1	
	p	.000	.000	.002	.000	.086	.061	.000	.000	.000	.000		
MLD	r	.151†	.076	.086	.162†	.006	.038	.142	.264*	.453*	1		
	p	.040	.468	.245	.027	.936	.603	.053	.000	.000			
APD	r	.361*	.205†	.069	.385*	.118	.107	.283*	.302*	1			
	p	.000	.049	.348	.000	.110	.148	.000	.000				
A-ZA	r	.462*	.250†	.211*	.201*	.538*	.443*	.539*	1				
	p	.000	.016	.004	.006	.000	.000	.000					
A-AMP	r	.832*	.478*	.442*	.475*	.743*	.581*	1					
	p	.000	.000	.000	.000	.000	.000						
A-SS	r	.458*	.461*	.269*	.163†	.630*	1						
	p	.000	.000	.000	.027	.000							
A-P	r	.681*	.428*	.402*	.274*	1							
	p	.000	.000	.000	.000								
P-AMP	r	.843*	.224†	.171†	1								
	p	.000	.031	.020									
O-AMP	r	.359*	.678*	1									
	p	.000	.000										
WBM	r	.399*	1										
	p	.000											
AMR	r	1											

*Correlation is significant at the 0.01 level (2-tailed); †Correlation is significant at the 0.05 level (2-tailed). **r:** spearman correlation coefficient.

side of the skulls. This localization of the Asterion was statistically significant among sides (χ^2=12.21, p=0.002) (**Table 3**). Moreover, the correlation between parameters A-AMP and AMR (r=0.832), A-AMP and A-P (r=0.743), A-P and AMR (r=0.684), P-AMP and AMR (r=0.843), O-AMP and WBM (r=0.678) was statistically significant (**Table 4**).

Discussion

Evaluation of the relationships between the bony landmarks on dry skulls are still gold standard to determine ideal surgical navigation for surgeries directed to various structures within the skull. MT is such a landmark area being formed by connecting the imaginary lines between Porion, Asterion and mastoid end-points. The posterosuperior angle of this dimorphic triangle is formed by Asterion.[6] Previous studies in the literature have been conducted to determine the relations in between these bony landmarks.[5,6] Galindo-de León et al.[5] used the root of the zygomatic arch, suprameatal spine, the apex of the MP, external occipital protuberance and FHP to define a safe zone in neurosurgical approaches. In addition to provide surgical landmarks, these morphometric points and areas can also be used for sex determination.[9,10,12] However, Kanchan et al.[11] stated that MT was a poor predictor of gender and had limited value without a population reference. We also aimed to contribute to the literature by evaluating the correlation between the MT and Asterion.

The relation of Asterion to the MT have been conducted in previous studies.[1–3,5–7,13,14] The distance between Asterion and the apex of the mastoid process (A-AMP) was revealed as 49.20±4.68 mm by Day et al.,[13] 49.70±4.80 mm by Martinez et al.,[14] 47.89± 3.72 mm for the right side and 47.62 ± 2.87 mm for the left side by Mwachaka et al.,[3] 49.1±5.4 mm by Ucerler and Govsa,[1] 51.53±4.97 mm by Galindo-de Leon et al.,[5] 43.65±6.75 mm for the left side and 45.01± 6.04 mm for the right side by Akkaşoğlu et al.,[6] 50.2±0.58 mm for the right side and

48.7±0.56 mm for the left side by Çalışkan et al.[7] in various populations. However, Kemkes and Göbel[15] found the A-AMP as 49.4±5.1 mm (right), 49.4±5.5 mm (left) in females, and 50.2±4 mm (right), 50.5±4.8 mm (left) in males in German population. Yilmaz et al.[16] reported the A-AMP distance as 5.06 cm (right), 5.07 cm (left) in males, and 4.89 cm on both sides in females. Moreover, they concluded that the parameters were nearly the same on both sides for both genders.[16] Passey et al.[2] determined A-AMP distance as an average of 50.00±9.75 mm in males and 49.84±6.97 mm in females over 100 radiographs ($p<0.001$). Helmy et al.[17] revealed that the A-AMP distance was 5.21 cm (right), 5.24 cm (left) in males, and 4.72 cm (right), 4.80 cm (left) in females. Consistent with the literature, our study showed the A-AMP distance was 49.58±5.31mm (right) and 49.24±5.06 mm (left) in Turkish dry skulls. These findings suggest that A-AMP distance has a consistent and symmetrical distribution regardless of the ethnicity. Moreover, we found a positive correlation between the A-AMP and AMR ($r=0.832$), A-AMP and A-P ($r=0.743$). Correlation between Asterion and the measurements related with MT indicates that the MT is affected by the localization of the Asterion. These parameters may also vary depending on ethnicity.

The root of the zygomatic arch and the apex of the mastoid process can be used to determine the localization of the Asterion. Mwachaka et al.[3] reported that the distance between Asterion and the root of the zygomatic arch (A-ZA) was 59.06±2.72 mm (male) and 58.75±2.02 mm (female) ($p=0.060$). Moreover, their findings showed that A-ZA were 58.44±2.12 mm on the left and 58.85±2.25 mm on the right side ($p=0.065$). Çırpan et al.[18] determined A-ZA as 55.11±3.86 mm (right) and 54.37±4.35 mm (left). Furthermore, it was reported to be 43.95 ± 7.02 mm and 43.97±7.37 mm in a study by Akkaşoğlu et al.[6] The data obtained from our study were compatible with the studies of Akkaşoğlu et al.,[6] while it was less than the findings of previous studies. **Table 5** summarizes the previous studies that evaluated the distances of the Asterion to the various bony landmarks and their relations.

The size of the MT may be an indicator of gender and/or the position of the Asterion. It was reported that the total MT area was 1447.70 mm^2 or larger in the skulls belonging to males, and less than or equal to 1260.36 mm^2 in the skulls belonging to females (95% confidence).[19] In German population, Kemkes and Göbel[15] found the total MT area as 1434.3 mm^2 in males and 1315 mm^2 in females. The same area was revealed as 1418.9 mm^2 in males and 1209.1 mm^2 in females in the Portuguese.[15] In another study, Galdames et al.[10] stated that the total MT areas were 1389.55 mm^2 in males and 1296.22 mm^2 in females. In the present study, the findings showed that the total area of the MT was 1455.89 mm^2. Considering the correlation between the MT and the Asterion, we suggest that MT can be used in localization of the Asterion.

The Asterion has been proposed as a major landmark combined with petrosal approaches to the cranial base.[1] Furthermore, determining the junction of the transverse-sigmoid sinus according to the localization of Asterion is essential for posterolateral surgical approaches. Mwachaka et al.[3] determined the location of Asterion at the junction of the transverse-sigmoid sinus in 72 (80%) skulls. Moreover, they stated that in only one case (1.1%), it was just below junction.[3] Fang et al.[4] reported that 44 (68.75%) Asterion was located at the junction of the transverse-sigmoid sinus. Moreover, they concluded that the root of the zygomatic arch and the apex of the mastoid process could be used to determine the exact position of Asterion.[4] However, the same type was found in 11 (55%) according to the Çırpan et al.[19] A study by Galindo-de Leóne et al.[5] revealed that the intersection of the transverse and sigmoid sinuses was at the level of Asterion in 82.4% of cases, above the Asterion in 12.5% of the cases, and below it in 5.1% . The most common type in respect of the location of Asterion was Type 2 in Turkish dry skulls. Our measurements confirmed that the Asterion were located just above the FHP in majority of the cases (**Table 3**). The localization of the Asterion may differ in populations depending on ethnicity, and it may be affected by epigenetic, embryological or environmental factors.

Previous studies have revealed that the localization of the Asterion varies depending on cephalocaudal orientation.[1] Since the Asterion is usually positioned close to the transverse–sigmoid sinus junction, the burr hole on the Asterion may directly impact the sinus, causing injury and bleeding.[1] It has also been reported that the first trephine should be positioned 15 mm below the Asterion to limit the potential damage to the transverse sinus.[5] At about 50 mm posterior to the suprameatal spine and 11.5 mm inferior to the FHP, a retrosigmoid transtemporal approach can be performed.[1] According to Çırpan et al.,[19] surgical approaches through the 10 mm superior or inferior to the Asterion have a significant risk of damaging the sigmoid and transverse sinuses. Therefore, Asterion can be consistently determined using the parameters in relation with the MT.[3] Approaches directed to posteroinferior side of the Asterion are the safest methods to prevent lacerating the transverse-sigmoid sinus complex. Therefore, the burr hole must be located posteroinferior to the Asterion for posterolateral approaches.[14] The result of our study showed that the Asterion was 42.6 mm behind the suprameatal spine, 49.42 mm above the MP, and 17.5 mm

Table 5

Comparison of our measurements with other researchers.

Researchers	Samples	A-AMP	A-ZA	A-P	P-AMP 7
Day et al.[13]	100 dry skulls	49.20±4.68	53.88±5.09	-	-
Martínez et al.[14]	25 skulls of adult cadavers	49.70±4.80	55.42±4.92	-	-
Ucerler and Govsa[1]	16 skull bases, 24 half-skull bases, 17 fixed male cadaver heads and 10 fixed male half cadaver heads	49.1±45.4	54.6±5.5	-	-
Kemkes and Göbel[15]	97 skulls (German forensic medicine sample)	Female R: 49.4±5.1 Female L: 49.4±5.5 Male R: 50.2±4 Male L: 50.5±4.8	-	Female R: 46.3±3.7 Female L: 46.2±4.4 Male R: 48.6±3.3 Male L: 48.4±3.5	Female R: 28.9±3.6 Female L: 29.2±3.4 Male R: 30.9±2.6 Male L: 30.9±3.1
Kemkes and Göbel[15]	The Portuguese cemetery sample consisted of 100 skulls	Female R: 45.8±4.6 Female L: 46.0±4.3 Male R: 49.5±5.2 Male L: 49.2±4.9	-	Female R: 45.1±2.9 Female L: 44.9±3.6 Male R: 47.7±3.8 Male L: 47.1±3.3	Female R: 28.4±2.6 Female L: 27.8±2.8 Male R: 31.5±3.7 Male L: 30.9±3.7
Galdames et al.[10]	81 human skulls of Brazilian individuals	Female R: 48.34±3.87 Female L: 50.17±5.18 Male R: 50.21±4.96 Male L: 50.22±4.95	-	Female R: 46.74±3.30 Female L: 47.53±3.80 Male R: 47.45±3.46 Male L: 47.1±3.46	Female R: 27.55±2.78 Female L: 29.74±4.14 Male R: 30.72±2.73 Male L: 29.22±2.73
Mwachaka et al.[3]	50 adult dry skulls	R: 47.89± 3.72 L: 47.62 ± 2.87	R:58.85±2.50 L:58.44±2.12	-	-
Saini et al.[9]	138 adult skulls (104 male, 34 femlae)	Male: 47.83±4.06 Female: 43.00±4.32	-	Male: 47.89±3.17 Female: 44.69±3.75	Male: 31.77±3.07 Female: 27.98±3.47
Galindo-de León et al.[5]	88 dry skulls	R: 43.65 ± 6.75 L: 45.01± 6.04	54.74±4.46	-	-
Kanchan et al.[11]	118 dry skulls (69 male, 49 female)	Male: 48.68±4.66 Female: 47.16±4.74	-	Male: 43.97±3.24 Female: 42.31±3.74	Male: 27.43±3.05 Female: 25.73±2.54
Gangrade et al.[24]	100 dry skulls (50 male, 50 female)	Female R: 49.06±3.02 Female L: 48.51±3.27 Male R: 52.39±4.32 Male L: 52.4±5.46	-	Female R: 46.98±2.98 Female L: 46.59±2.88 Male R: 49.02±4.07 Male L: 49.25±4.08	Female R: 28.47±2.16 Female L: 28.28±2.31 Male R: 31.53±3.20 Male L: 30.48±3.56
Jain et al.[25]	100 dry skulls	R:4.95±0.81 L:4.92±0.81	-	R: 4.59±0.71 L: 4.60±0.71	R: 3.13±0.53 L: 3.10±0.51
Yilmaz et al.[16]	CT images of 140 individuals (70 men, 70 women)	Female R: 4.89±0.32 Female L: 4.89±0.32 Male R: 5.06±0.46 Male L: 5.07±0.46	-	Female R: 4.61±0.35 Female L: 4.60±0.31 Male R: 4.93±0.38 Male L: 4.98±0.38	Female R: 2.89±0.24 Female L: 2.90±0.24 Male R: 3.12±0.29 Male L: 3.13±0.29
Fange et al.[4]	CT angiography images of 32patients	R: 49.10±3.56 L: 48.70±2.23	R:54.6±5.50 L:54.1±5.42	-	-
Sukre et al.[26]	132 dry human skulls (80 male, 52 female)	Male:48.33±0.64 Female:42.59±1.12	-	Male: 44.96±0.57 Female: 40.46±1.03	Male: 29.86±0.41 Female: 25.12±0.69
Akkaşoğlu et al.[6]	20 dry skulls	R: 45.01± 6.04 L: 43.65 ± 6.75	R: 43.95±7.02 L: 43.97 ±7.37	-	-
Madhumathi et al.[27]	30 human skulls	R: 45.63± 5.22 L: 44.49±5.18	-	R: 40.93± 5.29 L: 40.45±5.77	R: 23.26±4.52 L: 23.01±4.15
Çırpan et al.[19]	172 human skulls	R: 48.00± 5.04 L: 47.63±5.15	R: 55.11±3.86 L: 54.37±4.35	-	-
Caliskan et al.[7]	20 skulls and 18 hemi skulls	R: 5.02±0.58 cm L: 4.87±0.56 cm	-	-	-
Passey et al.[17]	110 human skulls (55 male, 45 female)	Male: 50.00±9.75 Female: 49.84±6.97	-	Male: 44.11±6.82 Female: 39.72±5.72	Male: 21.21±2.15 Female: 31.66±3.21
Helmy et al.[18]	CT images of 132 adult Egyptian patients (66 male, 66 female)	Female R:4.72±0.55 Female L:4.80±0.54 Male R:5.21±0.56 Male L:5.24±0.59	-	Female R: 4.50±0.40 Female L: 4.62±0.38 Male R: 4.88±0.44 Male L: 4.97±0.43	Female R: 2.88±0.30 Female L: 2.88±0.38 Male R: 3.24±0.39 Male L: 3.15±0.40
Our study	93 dry skulls	R: 49.58±5.31 L: 49.24±5.06	R: 42.75±4.90 L: 44.05±7.15	R: 42.4±7.21 L: 42.8±4.45	R: 33.14±4.22 L: 32.41±4.69

A-AMP: distance between asterion and the apex of the mastoid process; **A-P:** distance between asterion and proion; **A-ZA:** distance between asterion and the root of the zygomatic arch; **P-AMP:** distance between porion and the apex of the mastoid process (double-digit numbers are in mm, single-digit ones are in cm).

above the FHP in Turkish dry skulls. Therefore, it can be suggested that the burr hole can be positioned at least 17.5 mm inferior to the Asterion to prevent a potential damage to the transverse sinus. The optimal drilling position for a retrosigmoid approach was previously suggested to be at the halfway between the mastoid apex and the Asterion.[20] A 2 cm diameter hole centered on this site proved effective for exposing the associated structures in the cerebellopontine angle. In the retrosigmoid approach, the optimum implant location was suggested to be 1.9±0.1 cm posterior, 1.7±0.1 cm inferior to the Asterion and 3.3±0.2 cm posterior, 2.1±0.1 cm superior to the mastoid notch.[21] Meningiomas which develop at the junction of the sigmoid and transverse sinuses can be removed without major risks.[22] The results of this study suggests aa safe zone posteroinferior to the Asterion and posterosuperior to the MP (and MT) in posterolateral surgical approaches.

The limitation of this study is that this study was conducted on only Turkish dry skulls, and the gender of the skulls were unknown. Further studies should be conducted to investigate the relationship between the Asterion and MT with 3D imaging modalities.

Conclusion

The relationship between the mastoid process and the Asterion can be used for determination of the dural venous sinuses and neighboring neurovascular structures, in retrosigmoid posterolateral surgical approaches. The differences coming from ethnicity and gender should also be kept in mind before planning the surgical approach.

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Conflict of Interest

None.

Author Contributions

ADAK: project development, data collection, data analysis, writing manuscript; DAS: project development, data collection; MB: project development, data collection; MS: project development, data collection; EO: project development, data collection, writing manuscript; MTY: data analysis; GS: project development, data collection.

Ethics Approval

The present study was approved by the Ethics Committee of Necmettin Erbakan University with protocol ID:2015/160.

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Analysis of the thymus in different age groups using multidedector computed tomography

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Abstract

Objectives: The aim of this study was to assess the morphological properties of the thymus in different age groups.

Methods: 306 multidedector computed tomography (MDCT) images were retrospectively evaluated between 2014–2017 and 181 images (mean age: 51.093±18.631).

Results: The mean volume of thymus in males was significantly higher than in females ($p<0.05$). The arrowhead shape was the most frequent type (71.27%). The thymus was mostly located at the level of T4–5 vertebrate (44.20%). The thymus tend to be more inferiorly located with an increase in age, being at T6–7 vertebrate level. The thymus was most frequently located left to the midsagittal plane (74.03%). Volume of the thymus was noticed to increase with age; however, it was noted to decrease after 50–59 years of age.

Conclusion: In majority of the cases, the thymus was observed to be located left to midline the at the T4–5 vertebrate level. The volume of the thymus tend to decrease after age of 50 and tend to have a more inferior position.

Keywords: anatomy; morphology; multidetector computerized tomography; thymus

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Introduction

Thymus is a soft and spongy tissue located anteriorly at the superior and inferior mediastinum. It develops from the 3rd pharyngeal arch. It usually extends up to the fourth costal cartilage.[1,2] It plays an important role in the development of cells in the immune system.[3] Organogenesis of the thymus starts during the early stages of fetal development. It starts to develop at the 7th and 14th gestation weeks and shows lineer growth throughout the fetal development.[4] At the 9th week of pregnancy, lymphocytes and haematopotic cells are seen in the thymus. Evaluation of the thymus size has played an important role in determining immunological conditions before and after birth.[5]

The name of the thymus gland is derived from the Greek word "thumos", which means "soul", and for centuries, it was believed that the soul was localized in this part of the body. Galen was the first who noted that the thymus diminishes as the organism ages.[6] The thymus grows from birth to 2–3 years of age, then it reaches its maximum weight (30–40 gr), and then begins to shrink in the period of adolescence because of the influence of sex hormones present in the bloodstream.

The age intervals at which thymus stops development has been a debate in previous studies. It is common belief that the thymus grows until puberty after which the cortical lymphocytes and epithelial cells gradually atrophies and is replaced with adipose tissue.[7] Nutritional deficiency, infections and increase in body temperature are known to cause thymic atrophy. While Roitt[7] reported that the thymus continues to grow until puberty, Hasselbalch et al.[8] concluded that the size of the thymus continually increases at the first months and then gradually reduces after the 6th month of age. Dervişoğlu[9] suggested that

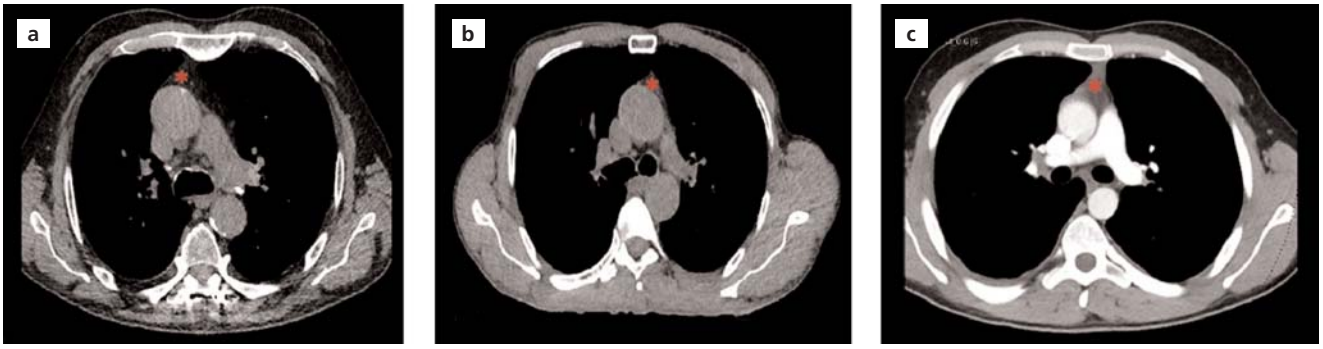

Figure 1. Determination of thymus type on axial images. *Thymus; (**a**) arrowhead type; (**b**) round type; (**c**) bilobal type.

changes in thymus size according to age has an important impact on autopsies.

The variations regarding the size, shape and localization of the thymus has been a subject of various studies in addition to its changes with age.[10–13] The aim of this study was also to assess the morphological properties of the thymus according age of the participants in a large series by multidetector CT and contribute to literature.

Materials and Methods

In this cross-sectional large-scale study, multidetector computed tomography (MDCT) (Siemens Somatom Sensation, Erlangen, Germany) thoracic images of 306 patients were examined between 2014 and December 2017. The images were randomly selected from Division of Radiology, Selçuk University Hospital. Images of 125 cases were excluded from the study due to some technical problems or pathological conditions affecting the anterior mediastinum. Thus, 181 images (96 males and 85 females) without any known thymic malformation were included in the study. The acquired data was later on processed at a workstation in axial plane and VRT (volume rendering technique) format to acquire volumetric and subvolumetric images. These cases were grouped according to age intervals (**Table 1**). Morphological and morphometrical analyses of thymus was done on axial images. All analyses and measurements were conducted by the same person.

Table 1
Groups according to age and the number of participants.

Group	Age (years)	n
1	≤29	29
2	30–39	26
3	40–49	19
4	50–59	38
5	60–69	41
6	>70	28

The shape of the thymus were classified into 3 groups as previously described in the literature[14] according to its appearance in the axial images. Accordingly, the shape of the thymus was described as; arrowhead (**Figure 1a**), bilobal (**Figure 1b**), and round (**Figure 1c**). The localization of thymus tissue in relation to the midsagittal plane was described as midline, or predominantly right or left-sided (**Figure 2**). The widest anteroposterior (verti-

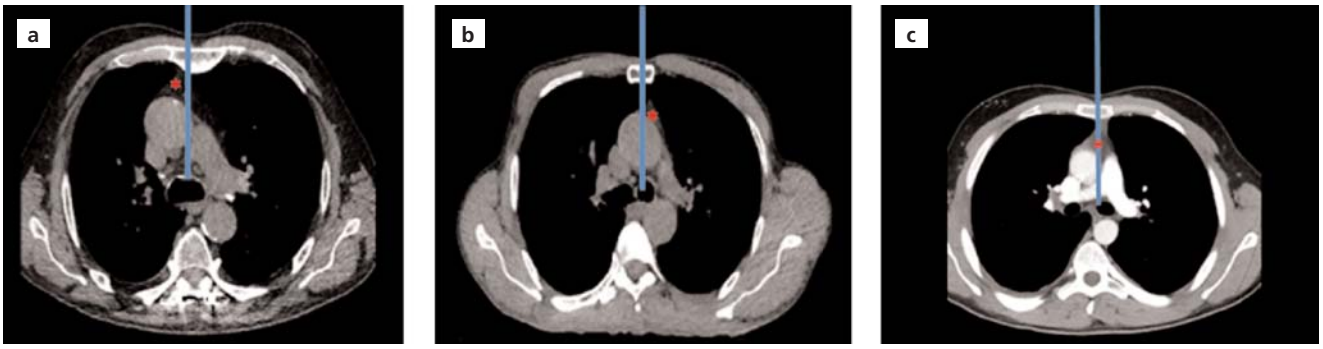

Figure 2. The localization of thymus according to its relation with midsagittal plane on axial images. *Thymus; (**a**) left to the midsagittal plane; (**b**) right to the midsagittal plane; (**c**) at the midsagittal plane.

cal) and the widest transverse diameter of thymus was measured (**Figure 3**). The thymus volume was measured by following the contour of the thymus manually on each slice on the workstation screen, with automatic workstation calculation in cm^3 (**Figure 3**). The density of the thymus was classified under 5 types according to its solid tissue component as; Type 1 (10–25%), Type 2 (25–50%), Type 3 (50–75%), Type 4 (75–100%), Type 5 (100% d).[14] (**Figure 4a–e**).The position of the thymus was determined according to the level of vertebrae on the VRT images (**Figure 5a–d**).

The data were expressed as number, percentage, mean±standard deviation (SD), maximum and minimum values. The relationship between the parameters was analyzed by independent sample t-test for to analyze whether or not there were differences in the mean vertical and transverse diameter, volume and density in respect of the gender of the participants. The relationship between grouped variables according to age was calculated with one-way Anova test. In the groups that had significant difference, post-hoc tests were used to determine the source of the difference. Variance homogeneity showed that the variance of vertical diameters and volume of the thymus was not homogeneously distributed. So that, Tamhane's T2 test was used in the post-hoc comparisons of these variables. The data obtained in the study were analyzed using SPSS (Statistical Package for Social Sciences) for Windows (Version 22, Chicago, IL, USA). For all analyses; $p<0.05$ was considered as statistically significant.

Results

The mean age of the participants in our study was 51.093±18.631 in males (range: 17–86 years) and 51.635± 18.631 in females (range: 19–86 years). The most frequent shape of the thymus was arrowhead in 129 (71.27%); and bilobal in 41 (22.65%); round in 11 (6.08%). In males; thymus was arrowhead shaped in 77 (42.54%), bilobal in 16 (8.84%), round in 3 (1.66%), whereas in females arrowhead in 52 (28.73%), bilobal in 25 (13.81%) and round in 8 (4.42%).

Thymus was located at the middle of the midsagittal plane in 35 cases (19.34%); left to the midsagittal plane in 134 cases (74.03%) and right to the midsagittal plane in 12 cases (6.62%).

When the location of thymus evaluated according to the gender, it was seen that thymus was located at the middle of the midsagittal plane in 20 females (11.05%), on the right in 5 females (2.76%) on the left in 60 females (33.15%). Whereas in 15 males (8.29%) it was located at the middle of the midsagittal plane, in 7 males (3.87%) on the right and in 74 males (40.88%) on the left of the midsagittal plane. Overall, thymus was dominantly located left to the midsaggital plane in majority of the cases (**Table 2**).

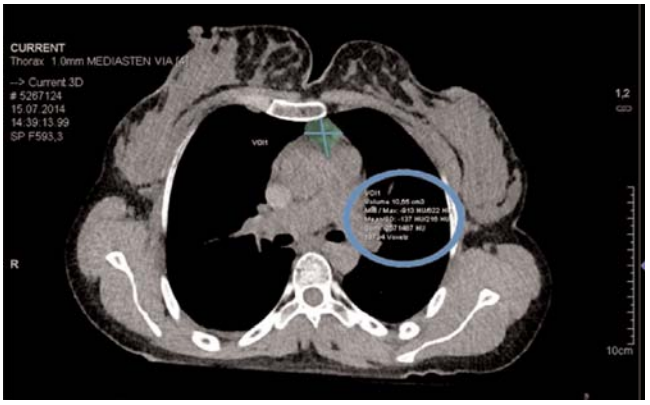

Figure 3. Measurements of volume (**blue circle**); transverse and vertical diameters (**horizontal and vertical lines**) on axial images.

The mean vertical diameter of the thymus was 2.509±0.865 cm in males and 2.326±0.846 cm in females. The vertical diameters showed no statistically significant difference among genders ($p>0.05$) (**Table 3**).

The widest transverse diameter of the thymus was 2.329±0.840 cm in males and 2.190±0.636 cm in females.

Table 2
Localization of thymus according to its relation with midsagittal plane.

	Midsagittal	Right	Left
Female	20 (11.05%)	5 (2.76%)	60 (33.15%)
Male	15 (8.29%)	7 (3.87%)	74 (40.88%)
Total	35 (19.34%)	12 (6.62%)	134 (74.03%)

Table 3
Distribution of the vertical diameter (cm), transverse diameter (cm) and volume (cm^3) of thymus according to gender.

Diameter		n	Mean	SD	p-value*
Vertical	Male	96	2.509	0.865	0.153
	Female	85	2.326	0.846	
Transverse	Male	96	2.329	0.840	0.217
	Female	85	2.190	0.636	
Volume	Male	96	14.921	9.920	**0.021**
	Female	85	12.003	6.386	

*$p<0.05$.

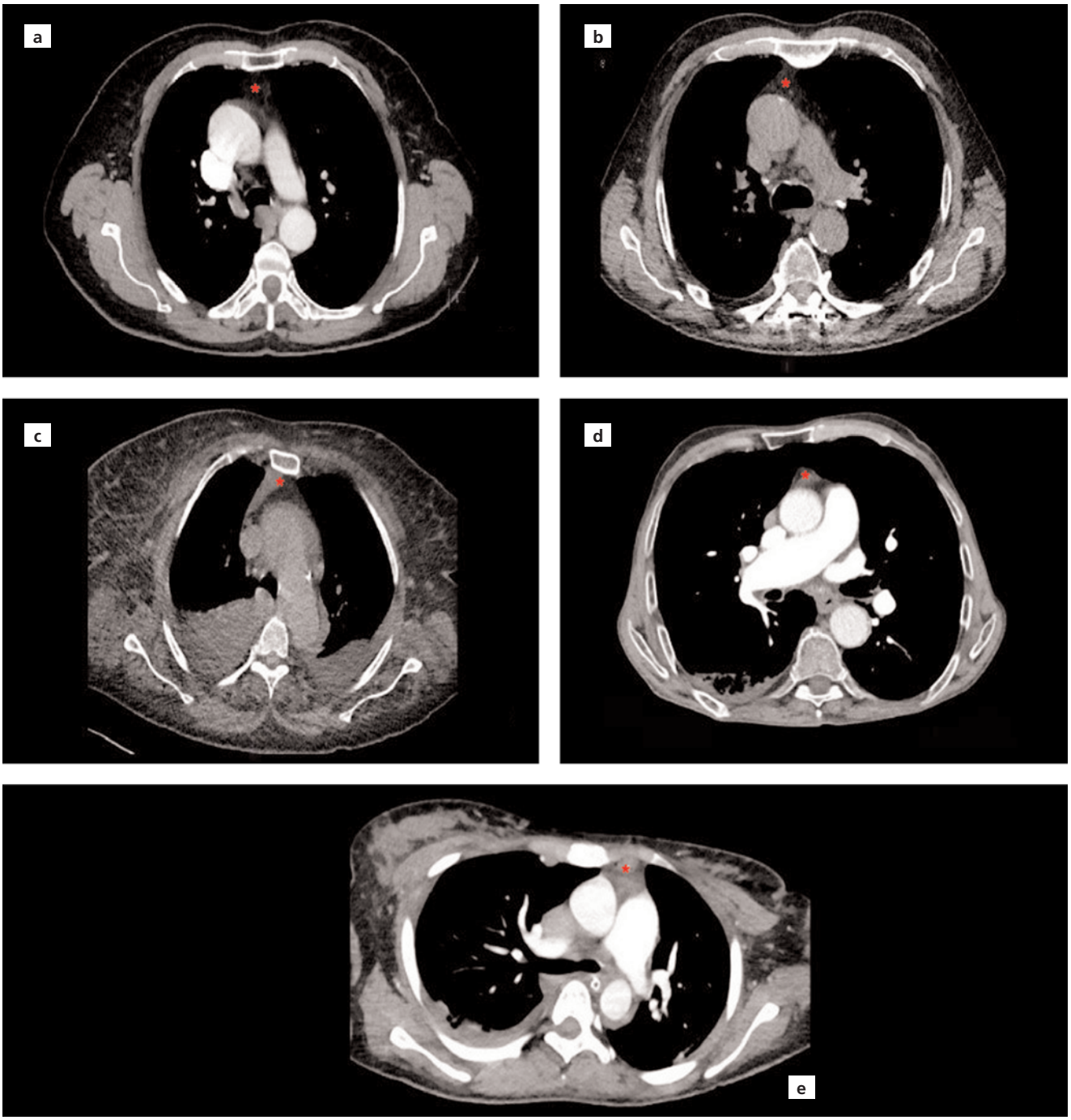

Figure 4. Classification of the density of the thymus under 5 types according to solid tissue component thymus. (**a**) Type 1 (solid tissue density: 0–25%); (**b**) Type 2 (solid tissue density: 25–50%); (**c**) Type 3 (solid tissue density: 50–75%); (**d**) Type 4 (solid tissue density: 75–100%); (**e**) Type 5 (solid tissue density: 100%).

Males had longer transverse diameters than females, however this difference was statistically significant ($p>0.05$) (**Table 3**).

The mean volume of the thymus was 14.921±9.920 cm^3 in males and 12.003±6.386 cm^3 in females. The average volume of the thymus in males was significantly higher than in females ($p<0.05$) (**Table 3**).

The vertical lengths showed no significant difference between males and females, but the difference was significant ($p<0.05$) between the age groups (**Tables 3** and **4**).

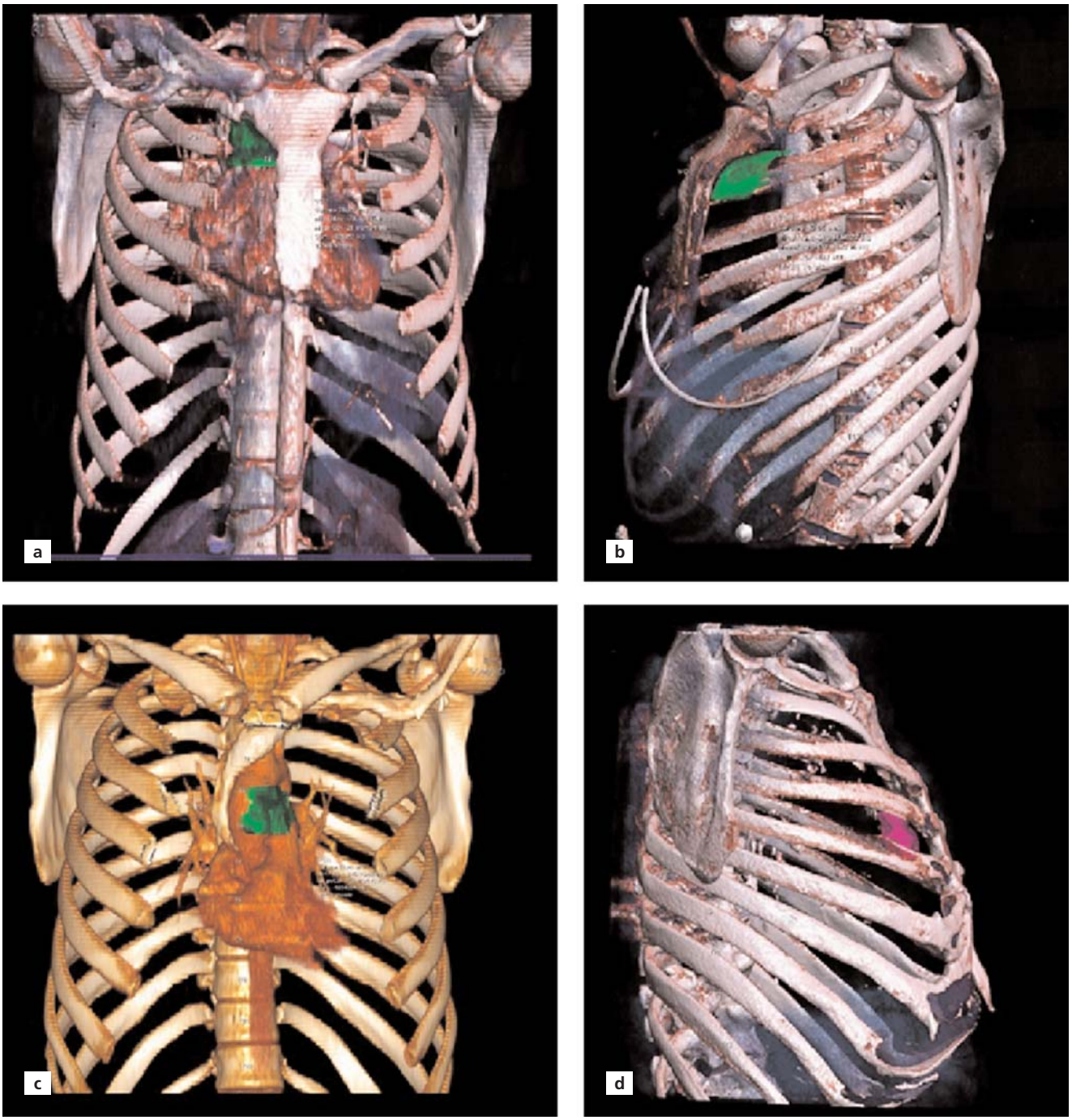

Figure 5. Determination of thymus position in relation to the vertebral level using VRT image. (**a**) T3–4 vertebral level; (**b**) T4–5 vertebral level; (**c**) T5–6 vertebral level; (**d**) T6–7 vertebral level.

The diameter and volume variables were seen to be significantly different according to age. According to the results of post-hoc comparisons there was a significant difference in the averages of vertical diameter between group 1 and groups 3, 4, 5 and 6 and between group 2 and group 4 ($p<0.05$) (**Table 4**).

As for volume, there was a significant difference ($p<0.05$) between group 4 and groups 1 and 5 (**Table 4**). In majority of the cases the density of the thymus was noted as Type 1 (40.33%) and in minority as Type 5 (4.42%) in all age groups. When the groups were evaluated separately, it was determined that in group 1; type 4

Table 4
Distribution of the vertical diameter (cm), transverse diameter (cm) and volume (cm^3) of thymus according to age groups.

	Group	Mean	SD	f	p-value*	Significant difference
Vertical diameter	1	1.875	0.589	6.019	0.000	1–3
	2	2.108	0.422			1–4
	3	2.767	0.986			1–5
	4	2.802	0.870			1–6
	5	2.411	0.970			2–4
	6	2.550	0.768			
Transverse diameter	1	2.105	0.661	2.224	0.054	
	2	2.166	0.693			
	3	2.105	0.703			
	4	2.587	0,865			
	5	2.155	0.686			
	6	2.346	0.774			
Volume	1	10.040	7.447	4.936	0.000	1–4
	2	12.480	6.675			4–5
	3	12.787	7.192			
	4	18.961	11.060			
	5	11.881	6.358			
	6	13.802	8.143			

*p<0.05.

(34.48%), in groups 2 and 3; type 2 (65.38% and 47.37%), in groups 4, 5 and 6; type 1 (52.63%, 53.66%, 67.89%) was most commonly found type (**Table 5**).

In all age groups, thymus was mostly located at T4–T5 vertebral level. When evaluating the vertebral level of thymus according to age groups, it was determined that the location of the thymus tends to be at T6–T7 vertebral level (**Table 6**).

Discussion

Computed tomography (CT) may be used for investigation of neck and mediastinal masses due to ease of acquisition and serves as an ideal tool for investigating the thymus. Contour of the orthotopic anterior mediastinal thymus on cross-sectional imaging varies with age. At its maximal volume during childhood, the thymus has a quadrilateral shape with convex borders. As it begins to involute and reduce in volume, it forms a triangular shape with convex or straight borders. By adolescence, thymus appears as a thin band of tissue anterior to mediastinal vascular structures. Similar to observations on other imaging modalities, the thymus typically moulds to the contours of the mediastinum and other surrounding structures without deforming or compressing them.[10]

A four-point classification system was suggested by different researchers depending on the ratio of fat and

Table 5
Distribution of the density type of thymus according to age groups.

Groups	Type 1	Type 2	Type 3	Type 4	Type 5	Total
1	6 (20.6%)	5 (17.24%)	6 (20.69%)	10 (34.48%)	2 (6.90%)	29 (100%)
2	0 (0.0%)	17 (65.38%)	7 (26.92%)	1 (3.85%)	1 (3.85%)	26 (100%)
3	6 (31.58%)	9 (47.37%)	3 (15.79%)	1 (5.26%)	0 (0.00%)	19 (100%)
4	20 (52.63%)	11 (28.95%)	2 (5.26%)	4 (10.53%)	1 (2.63%)	38 (100%)
5	22 (53.66%)	8 (19.51%)	3 (7.32%)	6 (14.63%)	2 (4.88%)	41 (100%)
6	19 (67.89%)	6 (21.43%)	0 (0.00%)	1 (3.57%)	2 (7.14%)	28 (100%)
Total	73 (40.33%)	56 (30.94%)	21 (11.60%)	23 (12.71%)	8 (4.42%)	181 (100%)

Table 6
The vertebral level of thymus according to age groups.

Group	T3–T	T4–T5	T5–T6	T6–T7	Total
1	6 (20.69%)	15 (51.72%)	7 (24.14%)	1 (3.45%)	29 (100%)
2	5 (19.23%)	12 (46.15%)	9 (34.62%)	0 (0.00%)	26 (100%)
3	4 (21.05%)	11 (57.89%)	4 (21.05%)	0 (0.00%)	19 (100%)
4	7 (18.42%)	17 (44.74%)	11 (28.95%)	3 (7.89%)	38 (100%)
5	6 (14.63%)	16 (39.02%)	12 (29.27%)	7 (17.07%)	41 (100%)
6	7 (25.00%)	9 (32.14%)	6 (21.43%)	6 (21.43%)	28 (100%)
Total	35 (19.34%)	80 (44.20%)	49 (27.07%)	17 (9.39%)	181 (100%)

soft tissue content of the thymus under CT guidance.[11,12] Accordingly, fatty degeneration of the thymus with age was noticed.[11,12] While, thymus dysfunction leads to serious disturbances in the body's defense mechanisms, its hyperactivity results in serious autoimmune diseases. In recent years, studies have been reported aiming to produce thymus tissue *in-vitro*, such as forming transplantable thymic organoids by biofabrication techniques.[13]

There are different views in the literature concerning the effects of thymus on fetal growth and development[15,16] and also the measurements of thymus.[17,18] Cho et al.[19] reported that the anterior-posterior diameter of thymus varied significantly according to its size and the location of the major blood vessels. They also reported that it would be difficult to determine the borders of thymus in every patient and measurements would take a long time. Özlü et al.[20] concluded that the transverse measurement of thymus was easier and more accurate when compared to the circumference of thymus. Luis et al.[21] evaluated the size of the thymus in pregnant women with prenatal ultrasonography and found out that the transverse diameter of thymus was bigger in male fetuses. Similarly Iscan et al.[22] reported that out of 65 newborns, males had a wider transverse diameter but the difference in between female and male fetuses was not statistically significant. Furthermore they also revealed that the transverse diameter and thymus index (transverse diameter × sagittal diameter) was directly proportional to the newborn's size and weight. The results of our study showed that the vertical and transverse diameters were bigger in males but the difference was not statistically significant.

Araki et al.[12] found out that apart from the transverse diameter of the thymus and the right lobe's length, there was a significant correlation between its size and age in women. The results of our study did not show any significant relationship between transverse diameter and age of the participants. The vertical lengths showed no significant difference between males and females, but the difference was significant ($p<0.05$) between the age groups (**Tables 3** and **4**). These differences were found especially between group 1 and groups 3, 4, 5 and 6 and between group 2 and group 4. These results suggest that it is important to evaluate the vertical diameter of the thymus in different age groups.

Three types of thymus have been described regarding the shape of thymus. Araki et al.[12] described arrowhead shape as the most commonly found shape as well as Yekeler et al.,[23] Tunaci[24] described mostly bilobal subtypes in late adolescence and early adulthood ages. Yekeler et al.[23] reported bilobal subtype (23.2%) as the least common type in their study. The results of our study suggests that the most common type is arrowhead (71.27 %) as reported by Araki et al.[12] and Yekeler et al.[23]

The location of thymus in fetuses and newborns was mostly reported as being in the middle by Hasini et al.[2] and Yekeler et al.,[23] Garly et al.[25] also revaled the location of the thymus in fetuses and suggested that the size of the thymus was related to mortalities after birth. All our participants were adults and the thymus was noted to be left to the midsagittal plane (74.03%) in most of our cases.

The size and weight of thymus has been shown to vary according to age. Roitt[7] reported that thymus continues to grow up to puberty whereas Hasselbalch et at.[8] reported that the size of thymus increases during the first month and then decreases after the 6th month. The results of our study showed that the volume of thymus is significantly bigger in males than in females ($p<0.05$). Significant differences between volume and age has been seen ($p<0.05$). This difference has been noted between group 4 and groups 1 and 5 (**Table 4**). According to these results we suggest that volume increases up to the ages 50–59 and then decreases after the age of 60.

The density of thymus was studied by different researchers.[22–26] These studies revealed that the quantity of solid tissue generally decreases with age. In our study, we used the classification system of Simanovsky et al.[14] Similar to what was revealed by Simanovsky et al.,[14] we found out that the quantity of solid tissue decreases with age and solid tissue density fits to Type 1 (10–25%) especially when age advances (>50 years).

There are very few reports on the level of thymus in the literature. In a study done on fetuses, the upper pole of thymus was shown to be at the level of the cervical vertebrae and the lower pole of thymus to reach the thoracoabdominal diaphragm.[2] The results of our study showed that the upper border of the thymus reaches to T3–T4 vertebrae and the lower border descends till the T6–T7 vertebrae. Thymus was most frequently located to be at T4–T5 vertebral level. Our results showed that the level of thymus does not show a major change according to different age groups but as age advances thymus tissue is frequently seen at level T6–T7.

Conclusion

MDCT images clearly defines the appearance of thymus and therefore it is important for surgeons and radiologists in terms of differentiating normal and variant structures and analysis of changes in thymus according to age.

Conflict of Interest

No conflict of interest was declared by the authors.

Author Contributions

The authors equally contributed to concept, design, data processing, literature reviewing, data analysis and interpretation, and writing manuscript.

Ethics Approval

The study was approved by Selçuk University Clinical Research Ethics Committee (Ethics No: 2015131). The study was also carried out in accordance with the Helsinki Declaration of Principles.

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Quantitative evaluation of the cerebellum in patients with depression and healthy adults by VolBrain method

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Abstract

Objectives: Besides the well-known sensorimotor control function, the cerebellum is also associated with cognitive functions and mood via the cerebral-cerebellar circuit. This study aimed to investigate possible cerebellar morphometric changes in untreated patients with depression.

Methods: Brain magnetic resonance (MR) images of 40 adults (age: 18–50 years), including 20 untreated depression patients and 20 healthy controls were analysed prospectively. Intracranial cavity and total cerebellar volumes were measured by using VolBrain. The cerebellum segmentation was performed with CERES to obtain the total gray matter volumes and cortical thickness of the lobules.

Results: Total cerebellar volume was 141.27±13.12 cm^3 in the depressed group and 142.63±8.01 cm^3 in the control group ($p>0.05$). The difference between males and females in the depressed group was not statistically significant ($p>0.05$). Total cerebellar volume was approximately 11% of total intracranial volume in both groups. The cortical thickness of lobule V (right-total), lobule VIIIB (right), and lobule IX (right) was smaller in the depressed group, independent of sex ($p<0.05$). Lobule V, VIIIB and IX volume was smaller and Crus-I cortical thickness was increased in depressed females ($p<0.05$).

Conclusion: The cerebellar volume and cortical thickness of cerebellar lobules in patients with depression show significant differences compared to healthy subjects.

Keywords: cerebellum; depression; neuroanatomy; neuroimaging

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Introduction

Cerebellum is a major structure of the hindbrain that is located near the brainstem. It contains more neurons than the rest of the brain, but take ups only 10% of the total brain volume. This part of the central nervous system is responsible for motor learning, balance and posture, as well as coordinating of voluntary movements.[1,2] There are studies suggesting and proving that the cerebellum is also associated with cognitive functions and mood.[3–5]

The cerebellum is divided into two cerebellar hemispheres and contains a narrow midline region (vermis). It is connected to the brainstem by three peduncles. Numerous sulci and fissures of varying depth subdivide the cerebellum into 10 lobules (lobules I–X). Primary fissure and posterolateral fissure, which are deeper than other fissures, divide the lobules into 3 main subdivisions as anterior lobe (lobules I–V), posterior lobe (lobules VI–IX), and flocculonodular lobe (lobule X). Three subdi-

visions of lobule VII (crus I, crus II, VIIB) and two subdivisions of lobule VIII (VIIIA, VIIIB) have been identified in cerebellar hemispheres.[2,5] Lobules I–V, a part of lobule VI and lobule VIII are the sensorimotor cerebellum. Lobules VI, crus I, crus II, lobule VIIB and lobule IX are the cognitive cerebellum. There are also definitions of "limbic cerebellum" or "emotional cerebellum" due to the relations of the sections in the cognitive cerebellum with the limbic system.[6,7]

Depression is a mood disorder which occurs with varying severity according to the number, type, and intensity of symptoms. Nowadays, worldwide accepted guideline (Diagnostic and Statistical Manual of Mental Disorders, DSM) is used to diagnose depression and determine the severity of the disease in individuals with depressive symptoms.[8] Furthermore, neuroimaging studies have also been conducted to detect volume changes in the brain and cerebellum in cases with depression.[9,10]

Manual measurements[11] and web-based fully automatic measurements were used in the studies investigating cerebellar volume changes.[6,12,13] Moreover, it has been emphasized that the recently developed fully automated multi-atlas applications that can be accessed remotely, such as VolBrain (MRI brain volumetric system) and CERES (A cerebellar segmentation tool) have the advantage of minimizing the manual volume measurement errors.[14–16]

This study aimed to evaluate the volume and cortical thickness changes in the segmental structures of the cerebellum by volumetric methods in patients with newly diagnosed depression and in healthy adults.

Materials and Methods

Depressed and control (non-depressed) groups were determined by a psychiatrist among individuals who applied to the psychiatry clinic of Selçuk University Medical Faculty Hospital. Brain magnetic resonance (MR) images of the participants were obtained in the radiology department of the same hospital. MR images have been processed and analysed by engineers and anatomists.

Twenty patients (14 females, 6 males) with depression between the ages of 19–47 and 20 healthy adults (9 females, 11 males) between the ages of 18–50 were included in the study. The depressed and control group was composed of individuals who applied to the psychiatry clinic. Beck Depression Test was applied to the individuals during a one-on-one interview by a psychiatrist. Scoring on the Beck depression scale can range from 0 to 63. An individual with a score of less than 10 is considered as healthy, while more than 10 is considered to have depression.[17] Accordingly, the depressed group composed of patients who got more 10 points on the Beck depression test and who were diagnosed with depression according to the DSM-4 diagnostic criteria. All the patients were more than 18 years of age and did not receive any medication before the diagnosis. The control group composed of individuals who scored less than 10 points in the Beck depression test and had sociodemographic characteristics similar to the group with depression. The individuals who had previously diagnosed as depression, who had received any medication because of depression, who had familial predisposition to depression, who had previously used any addictive drug or substance, who had brain surgery due to trauma or any kind of brain pathology, and who are younger than 18 years of age are not included to the study.

MR imaging in the depressed and control groups was performed by the same technician using a 1.5 T MAGNETOM Aera (Siemens, Germany). Brain MR images were acquired with a three-dimensional, T1-weighted rapid gradient echo (MPRAGE) array of high resolution 160 sections with DICOM format followed by a standardized MR protocol.: Structural T1 axial MPRAGE were acquired by the following sequences; TE: 3.54 ms, TR: 2400 ms, Fov= 192×192 matrix, flip angle= 90° and total scan time 5 min for 160 slices. T1-weighted MR images were downloaded from scanner and processed using different software. Images were saved in NIFTI format on a personal computer on a 64-bit Dell PC running Windows 10 operating system.

VolBrain (https://VolBrain.upv.es) is an online MRI brain volumetric system intended to help researchers automatically analyse volumetric brain data from MRI data without the need for any infrastructure. This system computation an anonymized MRI intracranial cavity volume (ICC; was defined as the sum of all white matter, grey matter and cerebrospinal fluid) NIFTI format and provides volume information of some macroscopic areas such as brain hemispheres, cerebellum and brainstem. The CERES (https://VolBrain.upv.es/members.php) pipeline on the VolBrain gets an anonymized MRI brain volume in NIFTI format and produces a pdf report containing volume and thickness of cerebellar lobules. It also provides cerebellar cortical thickness for each lobule.[14–16]

The NIFTI images of all subjects (20 depressed, 20 control) was uploaded separately to the VolBrain (https://VolBrain.upv.es) by using personal e-mail.

VolBrain pdf reports containing ICC and total cerebellar volume (TCV) and CERES pdf reports containing volume and cortical thickness of cerebellar lobules (I–II, III, IV, V, VI, Crus I, Crus II, VIIB, VIIIA, VIIIB, IX, X) have been send to the same e-mail address (**Figures 1–3**).

The percentage differences (PD) of volume (cm^3) and cortical thickness (mm) data between groups and gender were determined by using the following formulas. PD were calculated based on the mean and median values.[18]

PD between case and control =
[[depressed–non-depressed]/
[(depressed+non-depressed)/2]] × 100

PD between gender =
[[male- female]/[male+female]/2]] × 100

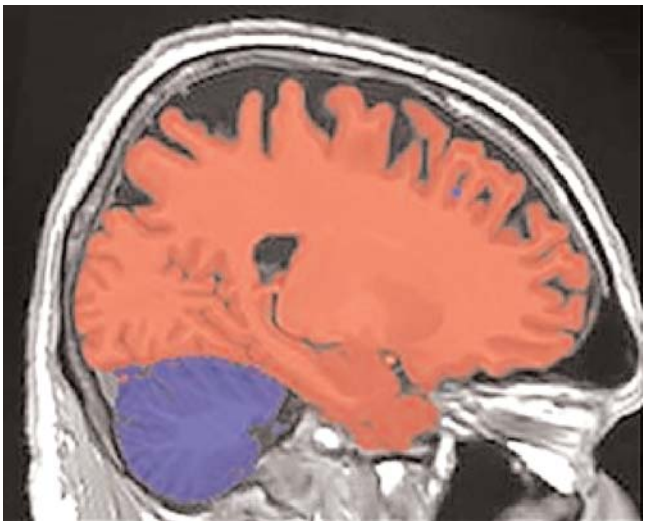

Figure 1. Demonstration of cerebellum with VolBrain.

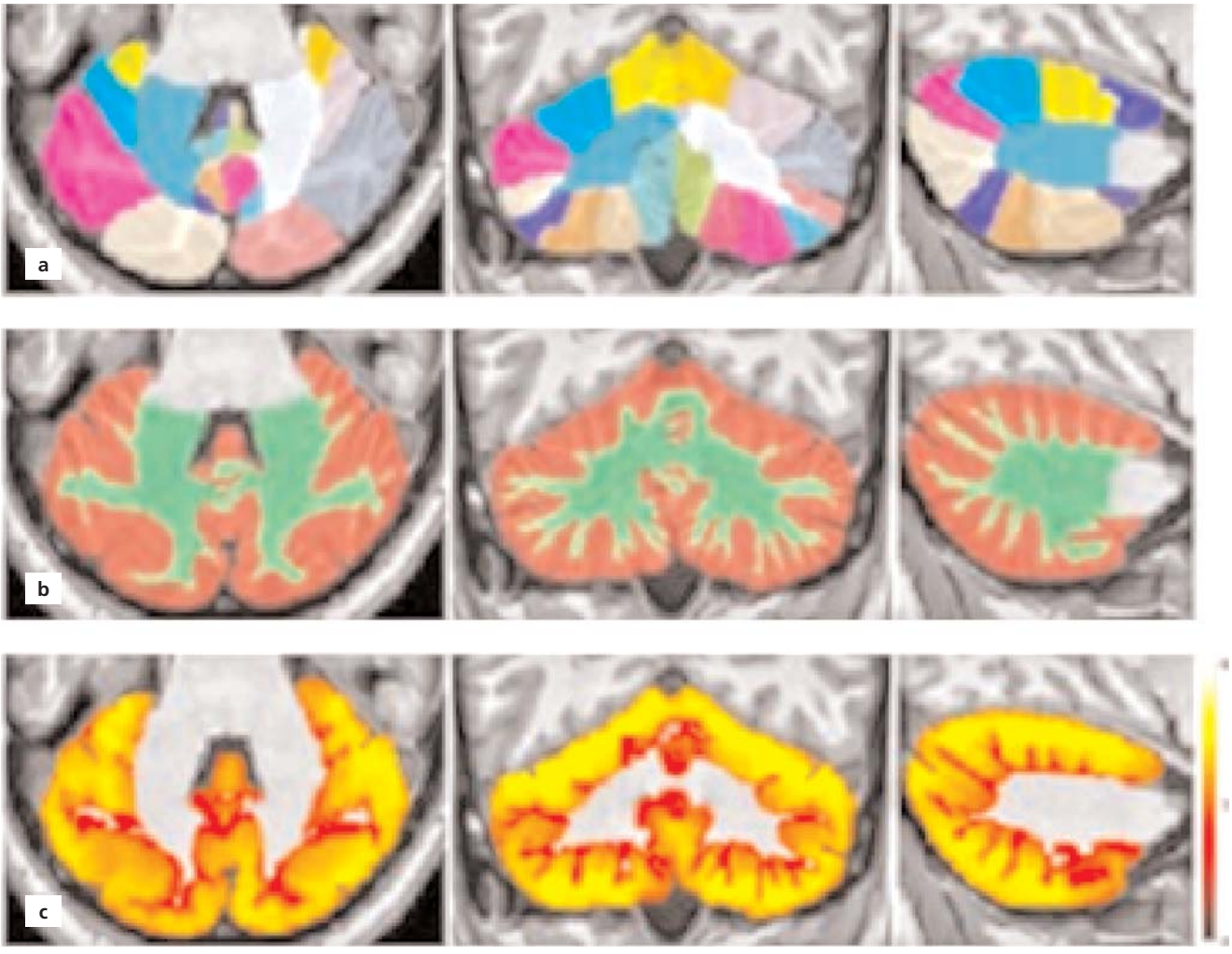

Figure 2. Segmentation of cerebellum. (**a**) lobules shown in different colours; (**b**) demonstration of white matter (**green**) and grey matter (red); (**c**) and demonstration of cerebellar cortex (**yellow**) obtained by CERES from the MR image of a 21-year-old depressed female patient.

CERES Volumetry Report version 1.0 release 03-10-2018

Patient ID	Sex	Age	Report Date
job270965	Female	21	24-Dec-2020

Image Information

Orientation	radiological
Scale factor	0.69
SNR	16.72
Total intracranial volume (cm^3)	1282.56

Volumes	Total (cm^3/%)	Right (cm^3/%)	Left (cm^3/%)	Asym.(%)
Cerebellum	112.31 (8.7564) [8.0672, 10.8352]	55.61 (4.3358) [4.0362, 5.4162]	56.70 (4.4206) [4.0178, 5.4322]	-1.9363 [-4.1753, 4.2355]
Lobule I-II	0.12 (0.0092) [0.0041, 0.0322]	0.06 (0.0049) [0.0019, 0.0148]	0.06 (0.0044) [0.0017, 0.0178]	10.5263 [-53.0108, 29.3219]
Lobule III	1.48 (0.1150) [0.0837, 0.1714]	0.70 (0.0543) [0.0419, 0.0864]	0.78 (0.0607) [0.0399, 0.0869]	-11.0590 [-21.1375, 23.4735]
Lobule IV	4.88 (0.3807) [0.2338, 0.4308]	2.36 (0.1838) [0.1073, 0.2199]	2.52 (0.1968) [0.1164, 0.2210]	-6.8243 [-32.1632, 24.5926]
Lobule V	6.67 (0.5204) [0.2338, 0.4308]	3.13 (0.2442) [0.1073, 0.2199]	3.54 (0.2762) [0.1164, 0.2210]	-12.2618 [-32.1632, 24.5926]
Lobule VI	13.93 (1.0860) [1.0124, 1.6499]	7.12 (0.5551) [0.4990, 0.8340]	6.81 (0.5309) [0.4970, 0.8324]	4.4564 [-16.2985, 16.5718]
Lobule Crus I	26.58 (2.0726) [1.4952, 2.4689]	13.25 (1.0329) [0.7353, 1.2382]	13.33 (1.0397) [0.7439, 1.2468]	-0.6501 [-14.4872, 12.2639]
Lobule Crus II	14.73 (1.1485) [0.8580, 1.5444]	7.48 (0.5834) [0.4240, 0.7954]	7.25 (0.5651) [0.4163, 0.7668]	3.1910 [-16.8116, 22.0961]
Lobule VIIB	7.78 (0.6066) [0.5120, 0.8921]	3.91 (0.3046) [0.2525, 0.4619]	3.87 (0.3020) [0.2441, 0.4456]	0.8529 [-19.5159, 26.5514]
Lobule VIIIA	8.83 (0.6882) [0.6589, 1.1006]	4.27 (0.3332) [0.3174, 0.5527]	4.55 (0.3550) [0.3198, 0.5697]	-6.3273 [-26.0779, 21.2538]
Lobule VIIIB	6.68 (0.5207) [0.4201, 0.7143]	3.06 (0.2388) [0.2030, 0.3679]	3.62 (0.2819) [0.2010, 0.3625]	-16.5821 [-24.1481, 26.1173]
Lobule IX	5.42 (0.4227) [0.3649, 0.7380]	2.69 (0.2099) [0.1845, 0.3687]	2.73 (0.2128) [0.1778, 0.3719]	-1.4025 [-12.6362, 13.5494]
Lobule X	1.17 (0.0915) [0.3649, 0.7380]	0.61 (0.0474) [0.1845, 0.3687]	0.56 (0.0440) [0.1778, 0.3719]	7.4249 [-12.6362, 13.5494]

Cortical thickness	Mean (*mm/norm.*)	Right (*mm/norm.*)	Left (*mm/norm.*)	Asym.(%)
Cerebellum	4.34 (3.998) [4.062, 4.659]	4.37 (4.018) [4.038, 4.676]	4.32 (3.979) [4.059, 4.668]	0.9586 [-0.0779, 0.0845]
Lobule I-II	1.57 (1.445) [0.530, 2.445]	1.44 (1.325) [0.482, 2.394]	1.68 (1.543) [0.534, 2.499]	15.0296 [-0.4798, 0.7235]
Lobule III	3.13 (2.885) [2.237, 3.833]	3.04 (2.796) [2.155, 3.821]	3.22 (2.960) [2.234, 3.916]	5.6609 [-0.3184, 0.4281]
Lobule IV	4.73 (4.352) [3.835, 4.944]	4.62 (4.250) [3.786, 4.963]	4.83 (4.446) [3.817, 4.983]	4.4883 [-0.1607, 0.1803]
Lobule V	4.55 (4.189) [3.835, 4.944]	4.52 (4.161) [3.786, 4.963]	4.58 (4.214) [3.817, 4.983]	1.2620 [-0.1607, 0.1803]
Lobule VI	4.77 (4.394) [4.122, 4.916]	4.82 (4.433) [4.089, 4.941]	4.73 (4.353) [4.109, 4.933]	-1.8191 [-0.1152, 0.1219]
Lobule Crus I	4.26 (3.924) [3.936, 4.750]	4.32 (3.976) [3.884, 4.786]	4.21 (3.872) [3.877, 4.816]	-2.6428 [-0.1913, 0.2013]
Lobule Crus II	4.01 (3.689) [4.098, 4.847]	4.11 (3.782) [4.082, 4.882]	3.91 (3.596) [4.041, 4.877]	-5.0451 [-0.1544, 0.1340]
Lobule VIIB	4.87 (4.481) [4.124, 4.929]	4.91 (4.522) [4.113, 4.962]	4.82 (4.438) [4.084, 4.941]	-1.8618 [-0.1316, 0.1085]
Lobule VIIIA	4.69 (4.315) [4.090, 4.914]	4.56 (4.196) [4.059, 4.952]	4.81 (4.424) [4.083, 4.916]	5.2870 [-0.1098, 0.1048]
Lobule VIIIB	4.13 (3.798) [4.057, 4.956]	4.00 (3.686) [3.962, 4.983]	4.23 (3.893) [4.093, 4.983]	5.4396 [-0.1161, 0.1754]
Lobule IX	3.57 (3.285) [2.657, 4.617]	3.75 (3.456) [2.662, 4.688]	3.38 (3.113) [2.599, 4.591]	-10.4202 [-0.3061, 0.1992]
Lobule X	2.04 (1.874) [2.657, 4.617]	1.73 (1.595) [2.662, 4.688]	2.34 (2.151) [2.599, 4.591]	29.6333 [-0.3061, 0.1992]

Grey matter vol.	Total (cm^3/%)	Right (cm^3/%)	Left (cm^3/%)	Asym.(%)
Cerebellum	83.98 (6.5479) [5.9956, 8.2106]	41.36 (3.2249) [2.9995, 4.1134]	42.62 (3.3230) [2.9857, 4.1076]	-2.9960 [-4.2532, 4.7521]
Lobule I-II	0.05 (0.0041) [0.0023, 0.0163]	0.02 (0.0019) [0.0009, 0.0076]	0.03 (0.0022) [0.0011, 0.0089]	-18.7883 [-97.3721, 52.2983]
Lobule III	1.05 (0.0819) [0.0442, 0.1055]	0.49 (0.0385) [0.0215, 0.0517]	0.56 (0.0434) [0.0213, 0.0551]	-17.5126 [-45.8571, 36.2282]
Lobule IV	4.22 (0.3288) [0.1958, 0.3617]	2.01 (0.1566) [0.0910, 0.1832]	2.21 (0.1722) [0.0957, 0.1877]	-13.7058 [-49.5257, 39.5528]
Lobule V	5.62 (0.4379) [0.1958, 0.3617]	2.65 (0.2068) [0.0910, 0.1832]	2.96 (0.2311) [0.0957, 0.1877]	-16.0230 [-49.5257, 39.5528]
Lobule VI	12.34 (0.9621) [0.8756, 1.4540]	6.28 (0.4898) [0.4290, 0.7329]	6.06 (0.4723) [0.4323, 0.7354]	5.2678 [-26.1337, 24.0047]
Lobule Crus I	22.62 (1.7633) [1.2212, 2.0699]	11.25 (0.8770) [0.5995, 1.0411]	11.37 (0.8863) [0.6053, 1.0452]	-1.5211 [-24.1779, 21.6198]
Lobule Crus II	12.64 (0.9858) [0.7376, 1.3581]	6.38 (0.4972) [0.3624, 0.6956]	6.27 (0.4887) [0.3592, 0.6785]	2.4992 [-27.7484, 33.1191]
Lobule VIIB	6.93 (0.5401) [0.4495, 0.7921]	3.51 (0.2734) [0.2249, 0.4148]	3.42 (0.2667) [0.2110, 0.3909]	3.5514 [-25.7706, 42.8813]
Lobule VIIIA	7.60 (0.5922) [0.5745, 0.9634]	3.63 (0.2827) [0.2776, 0.4855]	3.97 (0.3095) [0.2777, 0.4970]	-13.0608 [-38.3874, 33.3614]
Lobule VIIIB	5.43 (0.4231) [0.3495, 0.6123]	2.46 (0.1919) [0.1683, 0.3148]	2.97 (0.2313) [0.1667, 0.3121]	-26.9401 [-37.9655, 40.5584]
Lobule IX	4.14 (0.3225) [0.2635, 0.5786]	2.05 (0.1595) [0.1353, 0.2928]	2.09 (0.1630) [0.1252, 0.2888]	-3.0945 [-19.7674, 30.5306]
Lobule X	1.06 (0.0823) [0.2635, 0.5786]	0.53 (0.0414) [0.1353, 0.2928]	0.52 (0.0409) [0.1252, 0.2888]	1.7053 [-19.7674, 30.5306]

Figure 3. CERES Volumetry Report showing the cerebellar volume and cortical thickness of a 21-year-old depressed female patient.

All statistical analyses were performed using SPSS (Statistical Package for Social Sciences) for Windows (Version 21, Chicago, IL, USA). Histogram graphs and Kolmogorov-Smirnov test were used to determine the compliance of the variables to the normal distribution. It was determined that the data of the participants were distributed normally for the depressed and non-depressed groups, regardless of sex, but not distributed normally in the groups according to sex. Normally and non-normally distributed continuous variables were compared with Student's t-test and Mann-Whitney U test, respectively. For all analyses; $p<0.05$ was considered as statistically significant.

Results

The mean age of the participants was 29.85±11.50 (range: 19–47 years) in the depressed group and 29.90±8.55 (range: 18–50 years) in the non-depressed group. There was no statistically significant difference ($p>0.05$) between the mean ages of the two groups.

The mean ICC volume was 1423.19±131.27 cm^3 in the depressed group and 1426.8±91.44 cm^3 in the control group. The mean total cerebellar volume was 141.27±13.12 cm^3 in the depressed group and 142.63±8.01 cm^3 in the control group. Total cerebellar volume was approximately 11% of ICC volume in both depressed and control groups. The differences between ICC volume and total cerebellar volumes in the depressed and control groups were not statistically significant ($p>0.05$). In the depressed group, the ICC volume was statistically significantly bigger in males ($p<0.005$) (**Table 1**). PD between males and females was calculated as 13.68 for ICC volume and 8.30 for total cerebellar volume in the depressed group. It was remarkable that the PD determined by sex was lower in the non-depressed group.

In the second part of the volumetric analysis, the total and grey matter volumes and cortical thicknesses of the 10 lobules of the cerebellum were calculated with CERES (**Tables 2** and **3**). Comparison of lobular volume and cortical thickness between the depressed and control groups showed statistically significant differences in only a few lobular cortical thickness. The cortical thickness of lobule V (total and right), lobule VIIIB (right), and lobule IX (right) were statistically significantly smaller in the depressed group ($p<0.05$) (**Table 2**). Comparison between the groups according to sex showed no difference between the depressed and the control groups, while statistically significant differences were found regarding the volume and cortical thickness of cerebellar lobules between the males and females in

Table 1

Comparison of intracranial cavity volume (cm^3) and total cerebellar volume (cm^3) in depressed and control groups according to sex.

	Depressed						Control					
	Male (n=6)		Female (n=14)				Male (n=11)		Female (n=9)			
	Median	Perc.	Median	Perc.	p-value	PD	Median	Perc.	Median	Perc.	p-value	PD
ICCV*	1571.83	1495.99[a] 1631.83[b]	1370.53	1281.02[a] 1473.90[b]	.001†	13.68	1415.19	1376.05[a] 1513.26[b]	1395.94	1324.12[a] 1473.99[b]	.261	1.36
TCV*	150.52	133.86[a] 158.77[b]	138.52	132.31[a] 147.69[b]	.312	8.30	143.70	137.82[a] 148.11[b]	141.26	135.74[a] 144.61[b]	.289	1.71

*Mann-Whitney U test; †p<0.05; [a]25th percentile; [b]75th percentile. **ICCV:** intracranial cavity volume; **PD:** percentage difference according to sex; **Perc:** percentiles **TCV:** total cerebellar volume.

the depressed group. The volume and cortical thickness of lobule V (right, left, total), and the volume of lobule VIIIB (right) and lobule IX (left, total) were significantly smaller in depressed women (p<0.05). Crus I (right, left, total) cortical thickness of depressed women was significantly higher than depressed males (p<0.05). While the percentage of male-female PD in the volumes with statistically significant differences was between 17.94 and 30.39, the PD for cortical thickness was between 3.12 and 8.65 (**Table 3**).

Discussion

The location of the cerebellum in the posterior cranial fossa, makes it difficult to define its size, position and lobes. The morphology of the cerebellum and its morphological changes in pathological processes have been subject of previous studies. Cerebellar volumes of patients suffering from nervous system diseases (major depression, dementia, bipolar disorder, schizophrenia, monocular blindness, chronic tinnitus) were measured with different methods.[6,11,19–22] In some of these studies, VolBrain and similar volumetric methods were used, which provide automatic and accurate segmentation of the cerebellum on standard resolution T1-weighted brain MR images.[6,20–23]

The neurobiological processes that lead to depression have not been fully understood in extensive preclinical and clinical studies. Current studies have related depression with a reduction in the number and/or size of glia and neurons in different brain regions.[23,24] The role of the cerebellum in regulating emotions has been given more serious consideration over the past three decades. Complex connections between cortical areas such as the cerebellum and prefrontal cortex have been demonstrated with functional neuroimaging methods,[25] also studies based on clinical experience have been conducted in children and adults with cerebellar lesions who have emotional disorders.[26] There are also some volumetric studies on images of people diagnosed with affective disorders. Decrease in cerebellar volume has been reported in studies in cases of major depression and it is considered to be associated with the severity of the disease.[1,6,11,12] The present study aims to determine the differences in cerebellar volume and cortical thicknesses in patients who are diagnosed with depression regardless of its severity. The patients included in our study have not

Table 2

Statistically significant differences in the cerebellar volumes and cortical thickness between the depressed and control groups and the percentage differences.

	Depressed (n=20) Mean±SD	Control (n=20) Mean±SD	p-value	PD
Lobule V total cortical thickness (mm)*	4.67±1.38	4.75±0.10	.036†	1.69
Lobule V right cortical thickness (mm)*	4.56±1.15	4.68±0.15	.024†	2.59
Lobul VIIIB right cortical thickness (mm)*	4.26±0.23	4.42±0.25	.046†	3.68
Lobul IX right cortical thickness (mm)*	3.64±0.34	3.84±0.24	.042†	5.34

*Independent t-test; †p<0.05. **PD:** percentage difference (depressed vs control).

Table 3

The cerebellar volume and the percentage differences with statistically significant differences between males and females in the depressed group.

		Depressed					
		Male (n=6)		Female (n=14)			
		Median	Percentiles	Median	Percentiles	p-value	PD
Lobule V (right)*	TV	5.16	4.30† 6.05‡	3.95	3.51† 4.59‡	.033§	26.56
	GMV	4.34	3.63† 5.07‡	3.38	2.84† 3.76‡	.020§	24.87
	CT	4.72	4.61† 4.75‡	4.48	4.43† 4.59‡	.006§	5.21
Lobule V (left)*	TV	4.98	4.25† 5.70‡	4.16	3.51† 4.25‡	.003§	17.94
	GMV	4.40	3.73† 5.03‡	3.59	2.95† 3.74‡	.002§	20.27
	CT	4.88	4.84† 4.92‡	4.73	4.57† 7.87‡	.020§	3.12
Lobule V (total)*	TV	10.14	8.55† 11.75‡	8.09	7.09† 8.80‡	.015§	22.49
	GMV	8.75	7.37† 10.10‡	7.03	6.01† 7.42‡	.050§	21.79
	CT	4.79	4.77† 7.80‡	4.59	4.54† 4.76‡	.005§	4.26
Crus I (right)*	CT	4.04	3.88† 4.11‡	4.35	4.09† 4.44‡	.006§	7.38
Crus I (left)*	CT	3.87	3.74† 4.07‡	4.22	4.15† 4.30‡	.015§	8.65
Crus I (total)	CT	3.93	3.88† 4.08‡	4.28	4.16† 4.38‡	.006§	8.52
Lobule VIIIB (right)*	TV	4.54	4.17† 4.77‡	3.54	3.21† 4.28‡	.026§	24.75
	GMV	3.79	3.41† 4.03‡	2.79	2.52† 3.61‡	.015§	30.39
Lobule IX (Left)*	TV	3.94	3.59† 4.54‡	2.99	2.72† 3.72‡	.033§	27.41
	GMV	3.04	2.77† 3.54‡	2.35	2.09† 2.93‡	.033§	25.60
Lobule IX (Total)*	TV	7.90	7.20† 8.98‡	5.98	4.47† 7.61‡	.033§	27.66
	GMV	6.35	5.98† 7.57‡	5.14	4.51† 6.48‡	.041§	21.06

*Mann-Whitney U test; †25th percentile; ‡75th percentile; §p<0.05). **CT:** cortical thickness (mm); **GMV:** Gray matter volume (cm^3); **PD:** percentage difference (males vs females); **TV:** total volume (cm^3).

been treated with any medication, and the healthy volunteers had the same sociodemographic characteristics.

The studies in which the total cerebellar volume was calculated by manual methods on MR images of healthy individuals revealed significant differences according to sex (females, 115±11.29–134.6±6.8 cm^3; males, 126.01±10.38–152.2±10.5 cm^3).[27–29] In our automatic segmentation study, the total cerebellar volume in the healthy control group was 141.26 (135.74–144.61 cm^3) in women and 143.70 (137.82–148.11 cm^3) in men, but there was no statistically significant difference. The total cerebellar volume was approximately 11% of the ICC volume in both groups, consistent with the literature. Previous MRI studies showed shrinkage in some parts of the cerebellum with increasing age.[29,30] We did not include individuals elder than 50 years of age and we did not investigate the effect of age. However, it is understood from the literature that there is no consensus on the effects of age and sex on the size of the cerebellum.

Yılmaz et al.[16] calculated the total cerebellar volume as 152.12±20.40 cm^3 (95.45–183.72 cm^3) in 18 healthy males (22–30 years) using the VolBrain method. In our study, the total volume of the cerebellum was calculated as 150.52 cm^3 (133.86–158.77 cm^3) in depressed males and 143.40 cm^3 (137.82–148.11 cm^3) in non-depressed males with the same method. There was no statistically significant difference between the volumes of males in both groups. Differences in male total cerebellar volumes calculated by the same method may be due to number of the participants and individual differences.

Escalona et al.[11] investigated the effects of age, diagnosis of depression and sex on the total cerebellar volume in MR images using a manual method (Cavalier method). They emphasized that while age was not effective on cerebellar volume, depression and sex had a significant effect. The cerebellar volumes calculated by Escalona et al.[11] were 129.3±18 ml (females: 122.6±14 ml; males: 140.7±20 ml; PD: 13.74) in depressed patients and 143±5 ml (females: 136.6±12 ml; males: 149.8±15 ml; PD: 9.21) in the control group. Although they found the cerebellar volume smaller in the depressive group, they could not precisely mention whether the findings were present before the onset of symptoms, during the course, or secondary to the treatment received, since there were no pre-diagnosis MR images. In our study, the cerebellar volumes in the control group were similar to the results of Escolana et al.,[11] but not in the depressed group. While the difference between female and male cerebellar volumes was statistically significant ($p<0.005$) in the study of Escalona et al.,[11] no statistically significant difference was found in our study. Differences in cerebellar volume between the two studies may be due to differences in the severity of depression (major depression/newly diagnosed and untreated depression), measurement techniques (manual volume measurement/automatic multiple atlas applications), sample size and exclusion criteria (familial predisposition).

Previous studies used different automatic software to evaluate the relationship of depression with cerebellar (total, lobular) volumes and/or cortical thickness.[6,12,13,31] Depping et al.[6,12] analyzed post-treatment (medication and electroconvulsion) MR images of major depression cases with a voxel-based analysis method (Spatially Unbiased Infratentorial Toolbox -SUIT) and reported an increase in grey matter in some regions (IX, right VIIIa, left VIIb) compared to the control group. Bogoian et al.[13] showed a correlation between the volumes of lobule VI and lobule VIII and symptoms in 38 healthy adults (age: 51–80 years) who had depressive symptoms but were not diagnosed with depression. In these studies, data were not compared according to age and sex. Kim et al.[31] investigated the relationship between post-stroke depression and lesion site using MRIcron software on T1-weighted MR images in patients with isolated cerebellar stroke. They concluded that left cerebellum (especially crus II) damage was associated with the occurrence and severity of depression.

In our study, only the cortical thickness of lobule V, lobule VIIIB and lobule IX was significantly smaller in the depressed group regardless of sex. In addition, there were statistically significant differences between males and females in the volumes of lobule V, lobule VIIIB, and lobule IX in the depressed group, and in the cortical thickness of lobule V and crus I. In the depressed group, the percent difference between men and women was large regarding the volume (17.94–30.39) and small regarding the cortical thickness (3.12–8.65). In the control group, there was no significant difference between males and females in any of the 10 cerebellar lobules data.

The present study has some limitations. Firstly, the number of the samples were small and secondly; depression severity was not categorized and analysis by severity was not performed. Thirdly, the gender distribution in the groups was not equal. On the other hand, the unique aspect of the study is the inclusion of patients who had not received any medication before. Thus, the effect of the treatment can be the eliminated.

Conclusion

We evaluated the volume and cortical thickness of the anatomical subdivisions of the cerebellum in patients with depression at the time of diagnosis. The results of the study suggest that the changes in cortical thickness (particularly lobule V, VIII and IX) might be the initial morphological changes, which can be detected at the onset of depression. We believe that the determination of cerebellar volume and cortical thickness in people with depressive symptoms might help the early diagnosis and proper management of the patients with depression. Further studies with larger samples should be carried out to address these suggestions.

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Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contributions

OG: project development, data collection; GO: project development, data collection, data analysis, manuscript writing; SO: project development, data collection; YP: data collection; DAS: project development, data processing, statistical analysis, manuscript writing; İİU: project development, statistical evaluation, manuscript editing.

Ethics Approval

All procedures were approved by the Ethical Committee of Selçuk University (approval number 2016/310).

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Variations in the branching pattern of the popliteal artery: a CT angiography study

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Abstract

Objectives: The aim of this study was to reveal the different branching patterns of the popliteal artery by computed tomography angiography (CTA) in a large sample.

Methods: CTA images of 1500 lower extremities of 750 patients (603 males, 147 females) with a mean age of 56.4±19.6 were evaluated retrospectively. The variations in the branching pattern of the popliteal artery and the frequency of these variations were examined and classified under three main types.

Results: Type I–A was observed in 1422 extremities (94.8%) and noted as the most common branching pattern of the popliteal artery; Type I–B and Type I–C was observed in 39 extremities (2.6%); Type II in 37 extremities (2.4%) and Type III in 2 extremities (0.1%). The bilateral incidence of Type I–A was 90.8%. The incidence of bilateral variation was 0.4% for Type I–B and 0.1% for Type II–B. No statistically significant difference was found in terms of side and gender.

Conclusion: Evaluation of lower extremity arteriograms is important in the diagnosis and surgery of peripheral vascular diseases. For this reason, it is important to know the branching pattern of the popliteal artery. We believe that the classification system that we used will be useful in evaluating the different variations, particulary the branching levels of the branches of the popliteal artery.

Keywords: computed tomography angiography; fibular artery; popliteal artery; tibial artery; variation

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Introduction

The popliteal artery is the continuation of the femoral artery in the popliteal fossa and feeds the leg and foot. The popliteal artery extends to the lower border of the popliteus muscle in the popliteal fossa.[1,2] Here it divides into 2 branches, which are defined as the anterior tibial artery and the tibial-fibular trunk. The posterior tibial artery and its branch; the fibular artery, emerges from this trunk.[3] Anterior tibial artery passes to the anterior compartment of the leg by passing through an opening in the superior part of the interosseus membrane. Continuing distally, it extends on the dorsal side of the foot, and here it is named as dorsalis pedis artery.[4] The posterior tibial artery starts from the lower border of the popliteus muscle as the terminal branch of the popliteal artery and approaches to the tibia while continuing distally as lateral and medial plantar arteries underneath the abductor hallucis muscle.[5] The fibular artery is deeply located on the back of the leg, close to the fibular area. Developmental distress of embryological structures contributes to variations in the branching pattern of the arteries.[6] The variations regarding the branching of the popliteal artery are common.[7] Knowing the normal anatomical course and variations of the popliteal artery in the diagnosis of clinical applications such as arteriosclerosis, vascular graft surgeries, direct surgical repair, transluminal angiography, embolectomy or arterial injuries is important for a successful evaluation and management of peripheral vascular diseases.[7–11] Although the branching pattern of the popliteal artery is subject to wide range of variations, there are limited studies done on large

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number of samples. Therefore; the aim of this study was to reveal the possible different branching patterns of popliteal artery belonging to different genders by computed tomography angiography (CTA) in a large number of samples.

Materials and Methods

CTA images of 1550 lower extremities of 775 patients were evaluated retrospectively. However, 50 of 1550 extremities were excluded from the study due to reasons such as atherosclerosis, artifacts and vascular occlusion. Thus, branching pattern and variations of the popliteal artery in 1500 extremities of 750 patients (603 males, 147 females) with a mean age of 56.4±19.6 were examined. The scans were performed using a 256-slice dual-source scanner (SOMATOM Definition Flash, Siemens Healthcare, Forchheim, Germany) with a collimation of 128 mm × 0.6 mm, a pitch of 1.2. The standard scanning parameters were set to 120 kVp and 80 mAs. The main data sets were reconstructed in to axial slices of 1 mm thickness. Images of popliteal artery and its branches were analyzed via post-processing software (Snygo Via, Siemens, Germany).

The classification method suggested by Kim et al.[10] was used to evaluate the popliteal artery. The characteristic of this branching pattern is as follows:

- **Type I:** The popliteal artery divides into braches at the lower border of the popliteus muscle. In Type I–A; the popliteal artery branches into 2 as anterior tibial artery and tibiofibular trunk. In this pattern the tibiofibular trunk gives rise to posterior tibial artery and fibular artery. This pattern is regarded as the regular type. If tibiofibular trunk is absent and if anterior tibial artery, posterior tibial artery and fibular artery form a root together, it is defined as trifurcation or Type I–B. If the first branch of the popliteal artery is the posterior tibial artery, it is considered as Type I–C. In this subtype, the tibiofibular trunk branches into anterior tibial artery and fibular artery[10] (**Figure 1**).

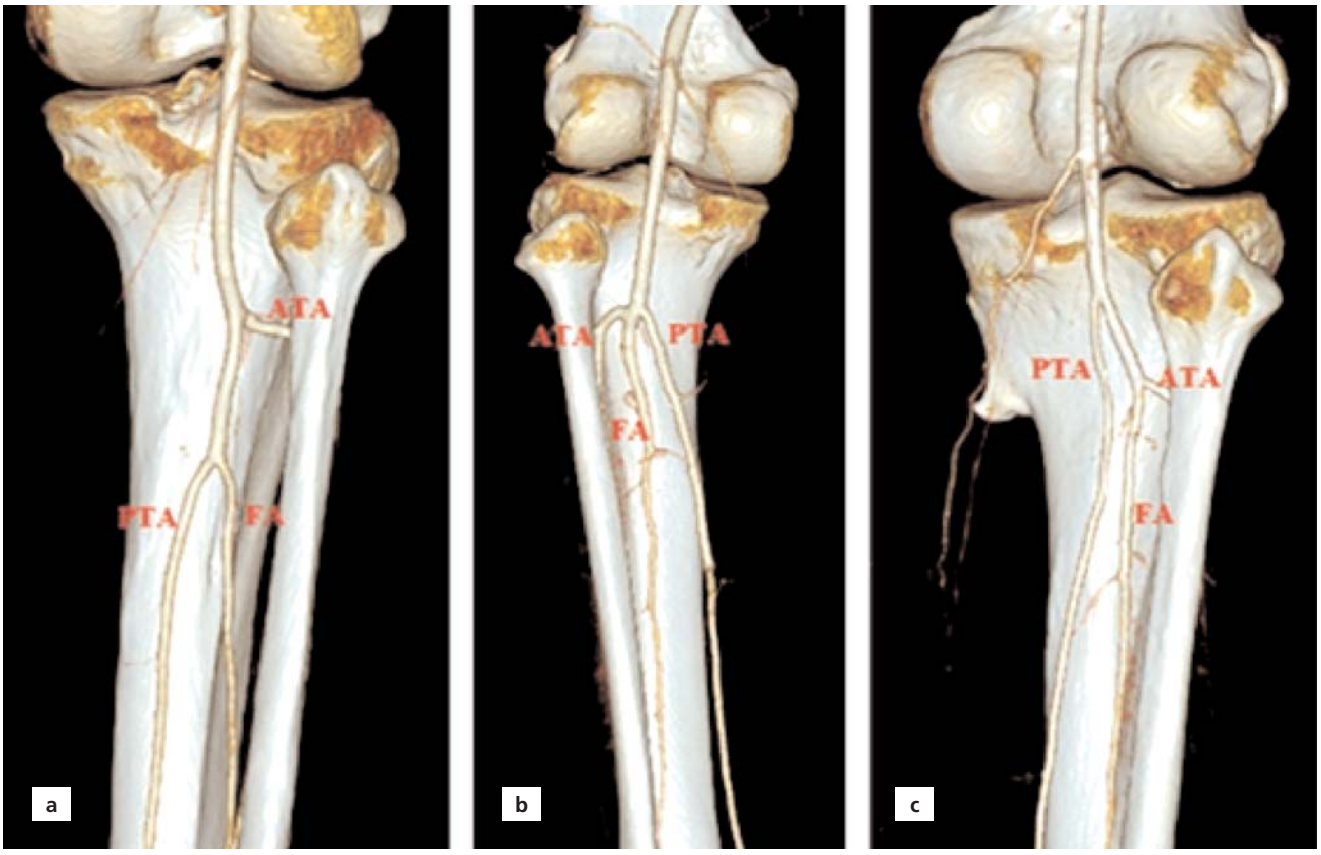

Figure 1. Type I subgroups in CTA images. (**a**) Type I-A branching pattern in a 69-year-old male. Note that anterior tibial artery (**ATA**) is the first branch, and posterior tibial artery (**PTA**) and fibular artery (**FA**) are arising from a common root; (**b**) Type I-B branching pattern in a 60-year-old male. **ATA**, **PTA** and **FA** diverge directly from the popliteal artery; (**c**) Type I-C branching pattern in a 67-year-old male. **PTA** is the first branch of the popliteal artery. **ATA** and **FA** are arising from a common root.

- **Type II:** Popliteal artery branches above the popliteus muscle. In Type II–A1; the anterior tibial artery branches superior to the knee joint; In Type II–A2, the anterior tibial artery branches from the popliteal artery at the knee level and its proximal part makes an arc. In Type II–B, the first branch of the popliteal artery is the posterior tibial artery. Anterior tibial artery and fibular artery originate from the common root. Finally, in Type II–C, the fibular artery, branches out superior or at the level of the knee joint. Anterior tibial artery and posterior tibial artery also originate from a common trunk[10] (**Figure 2**).
- **Type III:** The popliteal artery has a hypoplastic or aplastic branching as a result of the change in distal blood supply. Type III–A is defined as the hypoplastic-aplastic posterior tibial artery, where there is only distal part of the posterior tibial artery which originates from the fibular artery (**Figure 3**). Type III–B is defined as the hypoplastic-aplastic anterior tibial artery, where the dorsalis pedis artery originates from the fibular artery. Type III–C is defined as hypoplastic-aplastic anterior tibial artery and posterior tibial artery, where the distal part of the anterior tibial artery and the posterior tibial artery originate from the fibular artery.[10]

The data were evaluated using IBM SPSS (Statistical Package for Social Sciences) for Windows (Version 21, Chicago, IL, USA). Descriptive statistics were given as number of units (n), percentage (%). Age distribution was given as mean±standard deviation and median values. Comparisons of gender according to variation types were evaluated with Fisher's exact test in 2×2 and r × c tables.[12] A p-value <0.05 was considered as statistically significant.

Results

The study included CTA images of 603 males (80.4%) and 147 females (19.6%). The ages of the patients ranged from 7–91 years, with an average age of 56.4±19.6 (median: 59.0

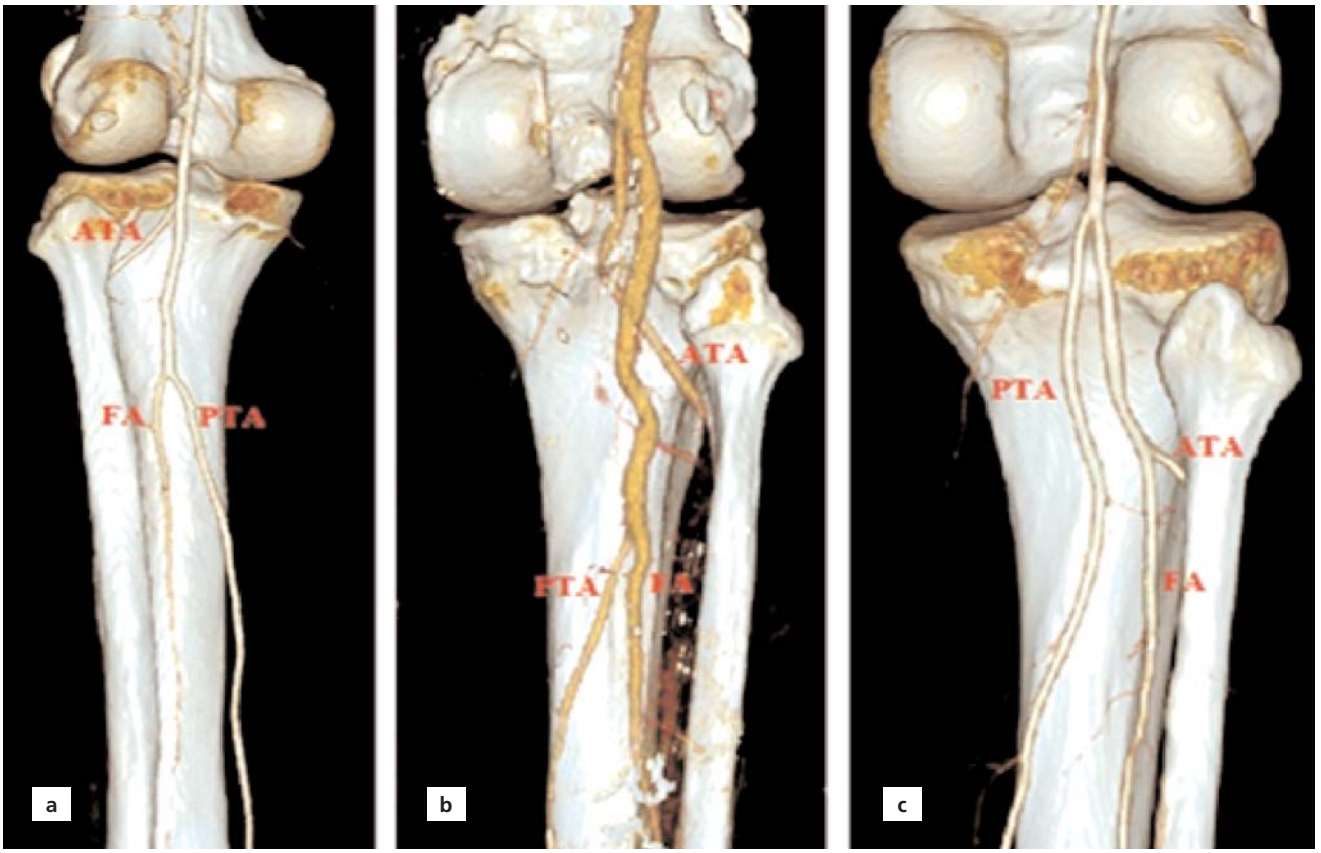

Figure 2. Type II subgroups in CTA images. (**a**) Type II-A1 branching pattern in a 71-year-old male where anterior tibial artery (**ATA**) branched at a high (proximal) level; (**b**) Type II-A2 branching pattern in an 83-year-old male with high branching of **ATA** making a medial curve initially and then turning laterally; (**c**) Type II-B branching pattern in a 67-year-old male where posterior tibial artery (**PTA**) branched at a high (proximal) level. **FA:** fibular artery.

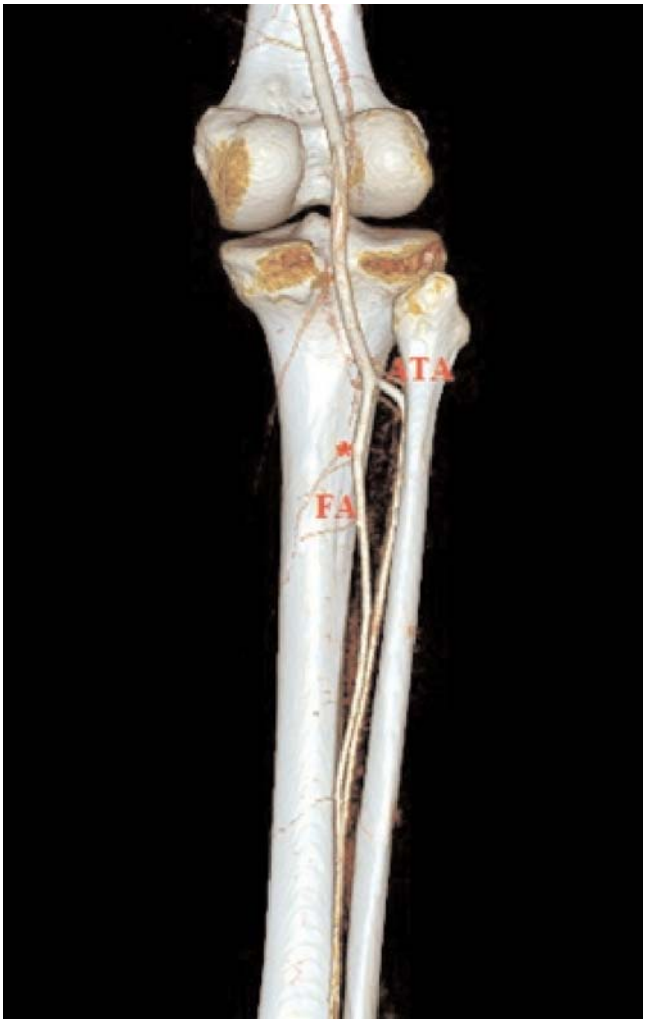

Figure 3. Type III-A branching pattern in CTA image of a 54-year-old woman. *Hypoplastic posterior tibial artery. **ATA:** anterior tibial artery; **FA:** fibular artery.

years). Out of 750 patients 709 (94.5%) had Type I–A, 19 (2.5%) had Type I–B and 11 (1.5%) had Type II–A1 branching pattern on the left side. And 713 (95.1%) had Type I–A, 12 (1.6%) had Type II–B and 11 (1.5%) had Type I–B branching pattern on the right side. Bilateral evaluation revealed that 681 (90.8%) had Type I–A, 3 (0.4%) had Type I–B and 1 (0.1%) had Type II–B branching pattern. The total number of patients with bilateral variation was 4 (0.5%), and the total number of extremities was 8 (0.5%). The total number of patients with unilateral variation was 65 (8.7%), and the total number of extremities was 130 (8.7%) (**Table 1**).

Statistical analysis revaled no difference in branching pattern in terms of sides of the extremities (p=0.701) (**Table 2**) and in terms of the gender (p=0.165) (**Table 3**). However the branching pattern in different sides showed a statistically different distribution in terms of gender (p=0.032). The frequency of bilateral branching pattern in females was significantly higher than in males. The frequency of unilateral branching pattern in males was statistically higher than in females (**Table 4**).

Discussion

Vascular development in the embryonic period determines anatomical diversity. Most of the variations are expressed by some combinations such as persistent primitive arterial segment, abnormal fusion, segmental hypoplasia or segmental aplasia.[9] Knowing the anatomy of these variations is very essential for radiological planning and surgical interventions.[13,14] While the vascular system of the lower extremity was investigated on limited number of cadavers in some of the previous studies,[15,16]

Table 1
Branching pattern in left and right legs of 750 patients.

	Right Leg															
	Type I-A		Type I-B		Type I-C		Type II-A1		Type II-A2		Type II-B		Type III-A		Total	
Left Leg	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Type I-A	**681**	**90.8**	6	0.8	2	0.3	8	1.1	1	0.1	10	1.3	1	0.1	709	94.5
Type I-B	15	2.0	**3**	**0.4**	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	19	2.5
Type I-C	4	0.5	1	0.1	**0**	**0.0**	1	0.1	0	0.0	0	0.0	0	0.0	6	0.8
Type II-A1	10	1.3	0	0.0	0	0.0	**0**	**0.0**	0	0.0	1	0.1	0	0.0	11	1.5
Type II-A2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Type II-B	2	0.3	1	0.1	0	0.0	0	0.0	0	0.0	**1**	**0.1**	0	0.0	4	0.5
Type III-A	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	**0**	**0.0**	1	0.1
Total	713	95.1	11	1.5	3	0.4	9	1.2	1	0.1	12	1.6	1	0.1	750	100

n: Number. Bilateral (right and left) values are shown in bold font.

Table 2
Comparison of branching pattern in left legs in terms of gender.

	Males (n=603)		Females (n=147)		Test statistics	
Subtype	n	%	n	%	X^2	p
Type I-A	567	94.0	142	96.6	2.953	0.701
Type I-B	16	2.6	3	2.0		
Type I-C	6	1.0	0	0.0		
Type II-A1	9	1.5	2	1.4		
Type II-B	4	0.7	0	0.0		
Type III-A	1	0.2	0	0.0		

Table 3
Comparison of branching pattern in right legs in terms of gender.

	Males (n=603)		Females (n=147)		Test statistics	
Subtype	n	%	n	%	X^2	p
Type I-A	569	94.3	144	97.9	9.170	0.165
Type I-B	10	1.7	1	0.7		
Type I-C	3	0.5	0	0.0		
Type II-A1	9	1.5	0	0.0		
Type II-A2	1	0.2	0	0.0		
Type II-B	11	1.8	1	0.7		
Type III-A	0	0.0	1	0.7		

the studies done on radiological images made it possible to observe the arterial anatomy on larger samples.[11,13,17–19] CTA is a preferred method in the detection of visceral injuries and fractures in trauma patients as well as extraluminal pathologies, including aneurysms, because of its short imaging time and thin sections.[17–19]

Considering the current CTA studies in the literature, the incidence of variational branching patterns in the lower extremity and the number of extremities are reported as; 16.4% in 126 extremities by Yanık et al.,[20] 13% in 636 extremities by Çalışır et al.,[21] 11.3% in 1261 extremities by Demirtaş et al.[11] and 10.8% in 1242 extremities by Kil and Jung.[22] In our study, 1500 extremities were examined, and the incidence of the variations in the right leg was found as 5.5% and in the left leg as 4.9%.

Regarding the variations in the branching patterns of the popliteal artery, Kim et al.[10] modified the Lippert system[23] and presented a new classification in branching pattern of the popliteal artery. This classification has 3 main branching pattern categories and three subgroups for each.[10,22] The incidence of the Type I pattern (94.8%) in our study was the most common branching pattern as similar to the current studies in the literature.[8,11,24] Type I–A, which is one of the subgroups of Type I, was observed to

Table 4
Comparison of laterality of the variations in terms of gender.

	Males (n=603)		Females (n=147)		Test statistics	
Subtype	n	%	n	%	X^2	p
Bilateral	544	90.2	141	95.9	4.856	0.032
Unilateral	59	9.8	6	4.1		

be the most common branching pattern and defined as the regular pattern. Type I–C was the least common Type I pattern compared to the others.[8,10,22,25] The results of our study showed that the incidence of Type I–A was 94.2%; Type I–B, 2%; and Type I–C, 0.6%.

High level (proximal) branching of the popliteal artery was noted as Type II. Previous studies report the incidence of the Type II as 1.6%–7.8%.[3,10,20,21,22,26] The results of our study is consistent with the literature and the incidence of the Type II pattern was 2.4%. While Type II–A and Type II–B patterns were reported to be relatively more common, Type II–C was reported less frequently.[8,14,21] The incidence of Type II–C was determined as 0.2% by Day and Orme[8] and Kim et al.,[10] but this pattern was not encountered in our study. Type II–A1 (2.2%) was reported to be the most common branching pattern in its category.[24] In our study, Type II–A1 was the most common pattern which was present in 1.3% of our cases.

The studies done by using different methods report the incidence of Type III branching pattern in a range of 1% to 11.4%.[8,10,14,22,27] Previous CTA studies by Oner and Oner[28] revealed this incidence as 4.1%, Çalışır et al.[21] as 3.6% (Type III–C pattern was not reported) and Yanık et al.[20] as 3.4% (Type II–B and Type III–C pattern was not reported). According to our results, the incidence of Type III branching pattern was 0.13% which actually is the incidence of Type III–A; since Type III–B and Type III–C variation patterns were not encountered.

Yanık et al.[20] revealed the bilateral incidence of Type I–A as 83%. In our study, the bilateral incidence of Type I–A was 90.8%. Oner and Oner[28] reported the rate of bilateral variation in the popliteal artery branching pattern as 5.9% and the rate of unilateral variation as 9.4%. In our study, the rate of bilateral variation was 0.5%, while its distribution was 0.4% for Type I–B and 0.1% for Type II–B; the unilateral variation rate was found to be 8.7%.

In the comparison of the variations in the branching of the popliteal artery among genders, variations in females were reported more than in males.[28] But some other studies suggested that there was no statistically significant difference in terms of genders.[26] The variations in the right leg (p=0.165) and left leg (p=0.701) in terms of gender showed statistically similar distribution in our study as well.

Conclusion

In this study, the branching patterns of the popliteal artery were determined in a large sample. The diversity of branching patterns can be associated with the number of the samples in the studies. We suggest that the detailed anatomical knowledge of the variations in the branching pattern of the popliteal artery (in terms of level and localization of the branching) is crucial for the interventional radiologists and vascular surgeons in evaluation of the vascular supply of the leg to decrease any kind of complications during the vascular interventions.

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Conflict of Interest

The authors declared that they had no conflict of interest.

Author Contributions

NGÇ: project development, data collection, data processing, writing the article; ZF: project development, data collection, editing the article and significant contributions to concept of the study; AKK: data processing, interpretation, editing the article; AN: data collection and interpretation.

Ethics Approval

This study was approved by the Selçuk University School of Medicine Non-Interventional Clinical Research Ethics Committee (approval date and number: 2018/284).

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Mandibular condyle and ramus angles in healthy individuals: a multidedector computed tomography study

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Abstract

Objectives: The aim of this study was to determine the distribution of the mandibular condyle horizontal inclination angle and condyle-ramus angle among different age and gender groups in asymptomatic healthy individuals.

Methods: This study was conducted including computerized tomography (CT) images of 100 patients aged between 18–90 years.

Results: The mean horizontal angle was 22.37° on the right side, 23.32° on the left; the condyle-ramus angle was 97.40° on the right side, 98.39° on the left.

Conclusion: Knowing mandibular condyle horizontal inclination angle and condyle-ramus angle would be useful for radiologist during CT evaluation of mandible after a surgery or trauma and for surgeons to plan their approaches properly during surgical interventions.

Keywords: mandibular angles; mandibular condyle; mandibular ramus; temporomandibular joint

Anatomy 2021;15(3):223–229

Introduction

The mandible is the largest bone of the face. It is formed by a ramus and a body.[1] Ramus is the part that includes the condylar process. The condylar process has a neck and a head, also called the condyle, which makes the temporomandibular joint. The condyle lies in the glenoid fossa of the temporal bone. The mediolateral length of the glenoid fossa is more than its anteroposterior length, which makes it fit to the condyle. The condyle is approximately 15–20 mm in width, and 8–10 mm in anteroposterior length.[2]

After birth, the condyle grows in a superior-lateral-posterior direction while the height of the ramus increases and the mandibular fossa deepens.[3] Most of the growth of the body and the ramus happens at 5–6 years of age.[4] The mandibular shape and size finalize 2 to 3 years after menstruation in females, and 4 years after sexual maturity in males.[4] Therefore, the normalized angle and size measurements should be done after approximately 18 years of age.

Developmental malformations of the temporomandibular joint can be attributed to 7 to 11 weeks of gestation, which is the time that the neural crest cells migrate and form the first draft of the bone and cartilage.[5] Any disruption at this point in life may result in distinct morphological differences such as hypoplastic/aplastic, hyperplastic or bifid condyle.[6] Other than the developmental malformations, some acquired morphological disturbances may be seen with the condyle and the ramus secondary to trauma, or some systemic diseases such as rheumatoid or juvenile idiopathic arthritis.[7] This type of injury may result in function loss, malocclusion, ankylosis of joint, and deviation of the mandible.[8]

Since the morphology of the condyle is subject to changes due to various disturbances, it is important to know its normal position and its angles, as well the position and the angles related with the mandibular ramus. In this study, we aimed to evaluate the normal horizon-

tal inclination angle of the condyle, the angle between the longitudinal planes of the condyle and ramus using multidetector computerized tomography (CT) for to evaluate any pathologies or malformations related with the temporomandibular joint. We also aimed to compare our results between genders and different age groups.

Materials and Methods

This study was conducted on CT images of 100 patients (49 females, 51 males) between 18–90 years of age. Patients younger than 18 years were not included because the bony growth finalize at around that age for both sexes.[4] The images were collected between 1st of January and 1st of May, 2022. The patients were undergone CT evaluation for any other reason than complaint or pathology related to temporal or mandibular area.

A multidetector CT (GE Healthcare, USA) was used to obtain the images. The parameters were used as; 120 kV, effective mAs= 150 mAs, slice thickness= 1 mm, matrix= 512×512, collimation= 128×0.6 slice increment=0.7 pitch= 0.8 field of view. Images were analyzed after obtaining from hospital's PACS system. All images were analyzed on the same 24-inch medical monitor with an ideal screen display.

Inclusion and exclusion criteria were decided upon the patients' CT images and health records on our hospital system. One of our main inclusion criteria was that both condyles could be seen symmetrical and simultaneously on the axial slices. If this was not the case, the image was replaced with another since the angles could not be measured correctly. Any patients with structural abnormalities seen during the evaluation were excluded as well. According to information gathered from patients' health records, any patient who had trauma, surgery or any kind of lesion related to our area of interest were not included in our research. Other inclusion criteria were the age of the patients and optimal quality of the CT scan without any artifacts (**Figure 1**).

The condylar horizontal inclination angle was measured as the angle between the longitudinal planes of the condyle and ramus on the ipsilateral side on the axial CT images. First, the midsagittal plane which separated the head into two symmetrical halves was determined. Then a perpendicular line to midsagittal plane was drawn, and defined as the coronal plane. After this, the maximum mediolateral length of the condyle seen on the appropriate axial images was determined. This can also be defined as the longest line connecting two sides of the condylar poles.[9] The angle between this line and the coronal plane was determined as the horizontal inclination angle

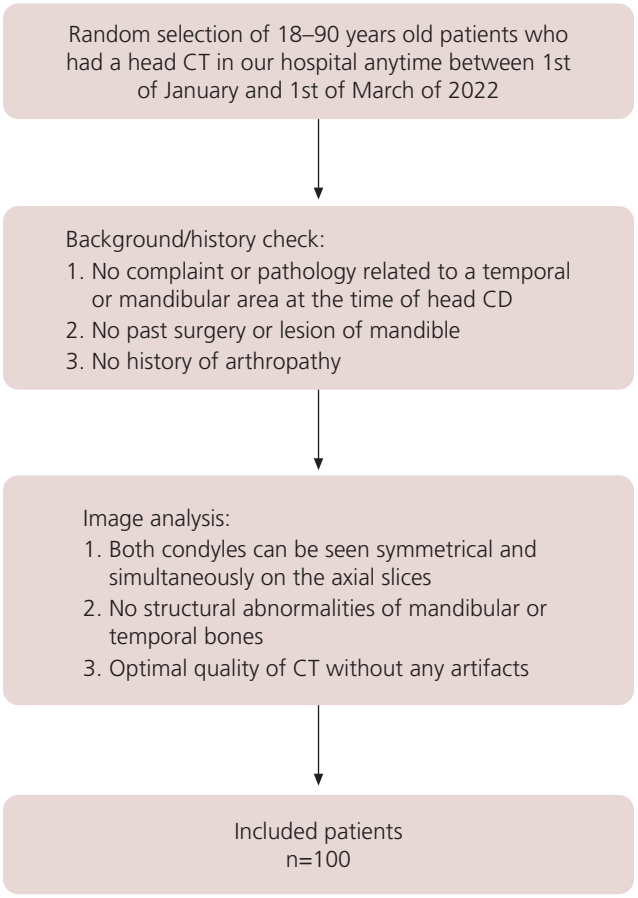

Figure 1. Flow-chart used in inclusion and exclusion criteria of patient selection.

(**Figure 2**). And the angle between this line and the longitudinal plane of the ramus was defined as the ramus angle (**Figure 3**). The axial slice that enables visualization of most of the ramus of mandible was determined and the longitudinal plane of the ramus was drawn through the midline of the ramus.

Two radiologists (5 and 15 years of experience) made the measurements twice at different times. The mean, standard deviation and range were calculated for descriptive statistics. Variables with normal distribution were expressed as mean±standard deviation. For comparison of angles on each side between gender and age groups, independent sample t-test was conducted for normally distributed parameters, and the Mann-Whitney U test was used for non-normally distributed. The intraclass correlation coefficient was used to evaluate the interobserver reliability for measurements. A significant difference was concluded if $p<0.05$. Statistical analyzes were

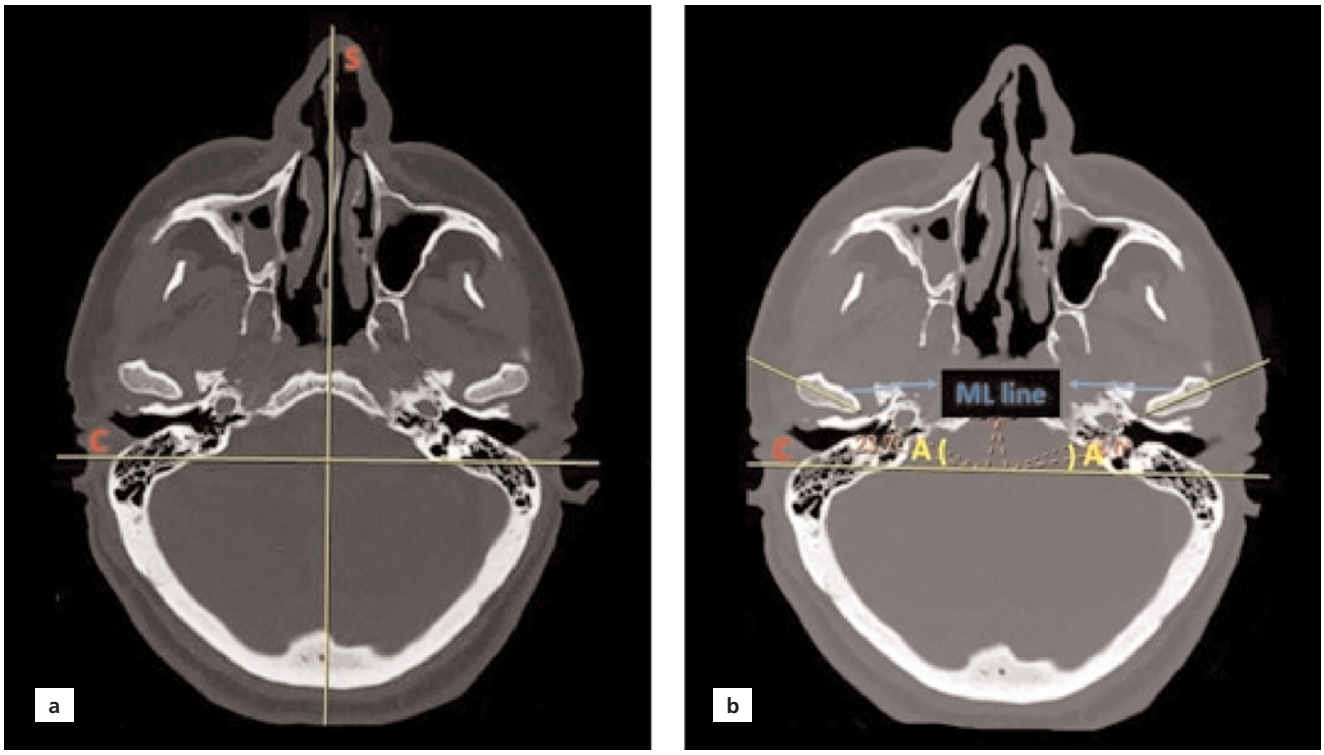

Figure 2. Axial CT images of the condylar horizontal inclination angle. (**a**) midsagittal (**S**) plane and coronal plane (**C**) are drawn perpendicular to each other; (**b**) mediolateral line (**ML line**) is determined for each condyle as the maximum length of the condylar poles. The horizontal angle of inclination (**A**) is measured on the coronal plane.

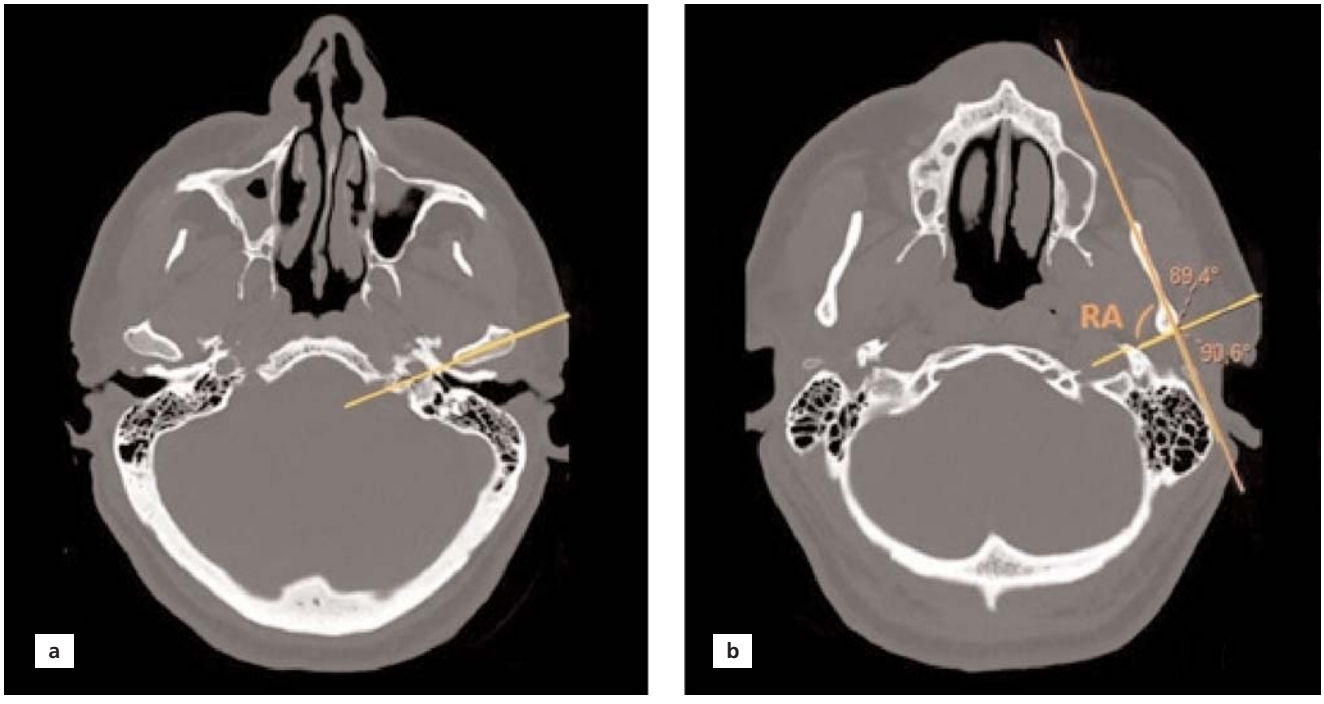

Figure 3. Axial CT images of the ramus angle. Mediolateral line of the condyle (**yellow line**) is drawn and (**a**) its projection is followed onto the consequent image until most of the ramus is visualized; (**b**) ramus angle (**RA**) is measured as the angle between the condylar line and the longitudinal plane of ramus (**orange line**) that goes through its midline.

Table 1
Mean and min-max values of the measurements.

	Mean (°)	Min–max (°)	Intraclass correlation coefficient	%95 confidence interval
Right horizontal inclination angle (n=100)	22.37	11.0–36.5	0.980	0.97–0.99
Left horizontal inclination angle (n=100)	23.32	5.5–38.0	0.968	0.95–0.96
Right ramus angle (n=100)	97.40	85.5–114.5	0.919	0.88–0.95
Left ramus angle (n=100)	98.39	81.75–116.5	0.901	0.85–0.93

performed with Statistical Package for Social Sciences (SPSS Version 23, Armonk, NY, USA).

Results

The mean age of patients in our research study was 48.5 years (range: 18–89 years) and the mean age was 48 for females (n=49) and 49 for males (n=51) (**Figure 4**).

Results of the measurements on each side were given in **Table 1**. The intraclass correlation coefficients were measured according to both researchers' results. The coefficient was found to be more than 0.9 for all measurements, which indicates excellent reliability. Therefore, statistical measurements were made by taking the average of both researchers' results.

The mean horizontal inclination angle was 22.37°± 5.85° for right condyle and 23.32°±6.17° for left. The ramus-condylar angle was 97.40°±5.58° on the right side and 98.39°±6.69° on the left. The angle between the condyles ("Co-Co angle") was measured by subtracting the sum of inclination angles of each side from 180°. So, the mean Co-Co angle was approximately 104.31°.

The statistical analyses showed no significant difference between right and left sides for both horizontal inclination and ramus condylar angles (p>0.05). The difference between females and males was also not statistically significant for both angles (p>0.05) (**Table 2**).

When the patients are divided into three age groups according to equated arrangement in a descending order, three groups were formed as in **Table 3**. There was no significant difference between age groups for both horizontal inclination and ramus condylar angles (p>0.05).

Discussion

In this study, we measured the mandibular condyle angles and ramus angles on axial CT images of 100 patients without a history of temporomandibular disease. The purpose of this study was to determine a mean value for these angles for clinical purposes, and to conclude whether there was any difference between gender and age groups or not.

Numerous factors can cause condylar angle discrepancies,[9,10] so it is important to distinguish the normal and abnormal condylar anatomy in order to recognize its diseases and disorders. In our study, we excluded any patients with disease that could alter the normal anatomy; such as systemic diseases,[11] bone diseases,[12] trauma[13] and any metabolic diseases.[14]

In a study done by Pamukcu et al.,[9] temporomandibular joints of 3 groups of people were investigated on healthy controls and patients unilateral and bilateral temporomandibular joint disease. The horizontal inclination angle of condyle was revealed as 19.5°±6.4° for the control group, which is less than our overall average (22.2°±5.5°). The mean inclination angle found in unilateral osteoarthritis group was 20.5°±6.5° and in

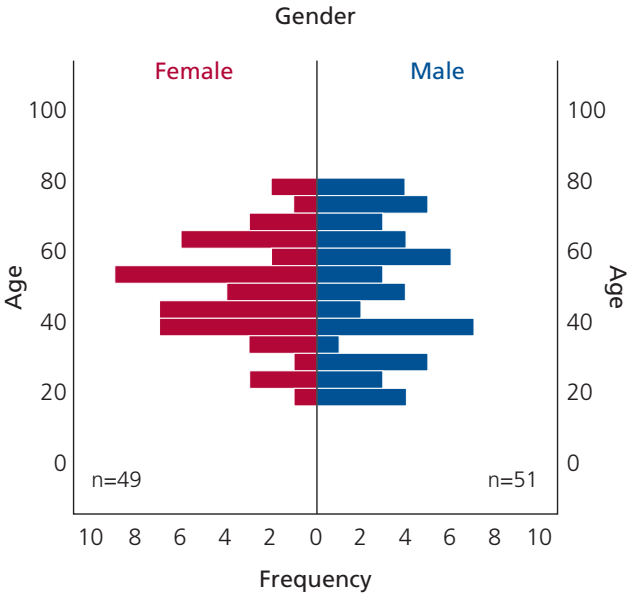

Figure 4. Distribution of patients according to their age and gender.

bilateral osteoarthritis group was 22.7°±7.6°. The results of the control group and the group of unilateral osteoarthritis was significantly different from our results. However, the overall average of horizontal angles revaled by Pamukcu et al.[9] was close to our results.

In a study by Wangan et al.,[15] the horizontal inclination angle was found as 22.55° on the right side, and 20.01° on the left. The difference on each side was found as statistically significant. Our results are alike on the right side, but differ on the left with no significant difference. This difference can be attributed to the population difference. Also, a difference as such can arise from the fact that we conducted our measurements on the axial images of CT scans, but Wangan et al.[15] conducted measurements on dry mandibles. This may lead to a discrepancy between the coronal planes drawn on CT image vs imaginary plane in reference to dry bones.

Sertel Meyvacı et al.[16] measured the angle between the mediolateral axis of condyles to give so-called a "co-co angle" of a control group and a group of patients who had temporomandibular joint disorders. They found the "co-co angle" of the control group to be 137.09°±12.23°. The co-co angle for our research was calculated as 134.26°; which is similar to value reported by Sertel Meyvacı et al.[16] They suggested that the horizontal angle of the condyle is not significantly changed related to temporomandibular joint disorders.

In a study done on to compare the difference of measurements on 2D vs 3D-CT images,[17] the horizontal angles on the right and left sides was found to be significantly different on 2D-CT images, however the significance was disappeared when measurements transferred to 3D models. All of our measurements were done on axial CT images, and no significant difference was found between right and left side. Nevertheless, we suggest that 3D reconstructed models can be combined with 2D images to get a better result and to provide a better spatial anatomy of the temporomandibular joint.

Lee et al.[18] investigated horizontal condylar angle between healthy adults and the patients with unilaterally affected joints. They compared the mean angles of the control groups (23.83°±7.69°), unaffected side of osteoarthritis patients (22.51°±7.72°) and the osteoarthritis side (29.54°±10.54°). No significant difference between the angles of the control patients and the unaffected joints was shown, but the contralateral affected joints had a significantly greater condylar angle. Their mean results of the control and unaffected joint angles were in concordance with our findings. In addition, the fact that they measured the horizontal angles of each side individually met with our design of the research. We suggest that this fact can affect the results since angles between two sides can differ.[19]

Table 2

Results of the measurements according to gender.

	Gender	Mean±SD (°)
Right horizontal (n=100)	M (n=51)	23.32±5.55
	F (n=49)	21.53±5.53
Left horizontal (n=100)	M (n=51)	24.60±6.06
	F (n=49)	22.02±5.52
Right ramus (n=100)	M (n=51)	97.19±6.72
	F (n=49)	97.98±5.68
Left ramus (n=100)	M (n=51)	98.84±7.09
	F (n=49)	98.19±6.87

Table 3

Mean condylar horizontal inclination and condylar ramus angles in different age groups regardless of gender and side.

Age groups	n	Horizontal angle mean±SD (°)	Ramus angle mean±SD (°)
18–40	35	22.74±5.87	99.11±6.16
41–58	33	22.47±5.56	98.19±4.69
59–80	32	23.36±4.98	96.27±5.02

Previous studies compared the condylar morphology and temporomandibular disc abnormalities with the horizontal angle. A statistically significant correlation was shown between disc displacement and larger or smaller horizontal angles.[20] Moreover, the horizontal angle was significantly associated with internal derangement; being increased in patient group.[21,22]

The ramus angle measurement is less widely investigated than the horizontal inclination angle. Ocak et al.[23] measured the angle between the long axis of mandibular condyle and long axis of ramus of mandible on the coronal images. However, we made this measurement on the axial images. We suggest that it would be more appropriate to compare the difference between measurements made on coronal vs axial images of the same individuals.

Knowledge of the condylar angles can help in making more accurate condyle prosthesis and reconstruction models. Temporomandibular joint diseases are mostly preferred to be treated by reconstruction; use of alloplastic prosthesis to replace the condyle is rare and limited to specific cases such as tumor or advanced trauma.[24] Reconstruction is achieved by grafts in which a

"neocondyle" is created.[25] Neocondyle positioning is a meticulous process because lack of it may lead to joint disorders. Understanding the condylar angles can help with appropriate positioning of the condylar grafts.

One of the limitations of our study is that the number of participants in our study was limited. Contributing of other hospitals would be useful to draw an average result of mandibular angles for the Turkish population.

Conclusion

We suggest that our results would be useful for condylar reconstructions, protheses, and for to have better understanding in terms interpretations of images after a temporomandibular joint disease or trauma.

Conflict of Interest

The authors declare no conflict of interest regarding the methods and results in this study.

Author Contributions

BEC: Project development, data collection and analysis, editing; CA: Data collection and analysis, manuscript writing.

Ethics Approval

The study was approved by the University of Health Sciences Ankara City Hospital Clinical Research Ethics Committee (No: E2-22-1822) and carried out in accordance with the Helsinki declaration of principles.

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Effect of motivational behaviors and race/ethnicity on academic success in physical therapy students: a preliminary study

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Abstract

Objectives: Doctor of Physical Therapy (DPT) program admissions criteria and markers indicative of academic success appear to be mismatched. Acceptance into a DPT program implies that students have developed self-regulated learning strategies however, motivation behaviors are not typically assessed during the admissions process. The aim of this study was to determine direct effects of motivational behaviors and race/ethnicity on academic success and the moderating effect of race/ethnicity on motivational behaviors.

Methods: Thirty-three first-year DPT students participated during their first foundational course, clinical anatomy. Motivation subscales from the motivated strategies for learning questionnaire (MSLQ) were used to assess student motivation behaviors which were then compared to course grades.

Results: Self-efficacy for learning and performance was significantly correlated with course grade [$r(31)=0.44$, $p< 0.05$]. Course grade differed at a statistically significant level by race/ethnicity [$t(31)=2.93$, $p<0.01$]. Race/ethnicity ($B=0.05$, $SE=0.01$, $\beta=0.42$, $p<0.008$) and self-efficacy for learning and performance ($B=0.02$, $SE=0.01$, $\beta=0.39$, $p<0.01$), remained significantly related to course grade.

Conclusion: Self-efficacy for learning and performance and ethnicity are factors that determine academic success and could be utilized in DPT programs to aid in the development of teaching strategies to support students.

Keywords: academic success, anatomy, ethnicity, motivation, physical therapy, race

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Introduction

Currently, physical therapy education is faced with two interlinked concerns, that of a persistent failure rate in Doctor of Physical Therapy (DPT) programs and lack of student diversity in DPT programs.[1–4] First, the attrition rate in DPT programs has been reported at approximately 6%.[5–7] Secondly, diversity in DPT programs in the United States of America are not representative of the projected patient population of 76.3% Caucasian, 18.5% Latino/Hispanic, 13.4% African Americans, with the exception of the Asian population which is projected at 5.9%.[1,8,9]

Admission into a DPT program is typically based upon cognitive markers such as, college GPA and GRE test scores that indicate a student's academic ability.[3] However, even using these markers, there are DPT students who are not successful at maintaining the academic standards of a program.[5–7]

Attrition rates from DPT programs has been shown to be greater for students of groups that are underrepresented in the profession, especially when the program is not in an Historically Black Colleges and Universities (HBCUs) or Hispanic serving Universities.[9,10] Some studies have indicated that underrepresented students may have increased difficulty with standardized testing,

or reduced confidence associated with entering a predominantly Caucasian profession.[1,11,12] Other studies have indicated that students of color, enrolled in programs that are rich in diversity, for example HBCUs, have not displayed academic or testing difficulties.[2–4,10]

There has been an increasing emphasis to improve diversity in DPT education on the National level as well as through the Mission and Vision goals within The Philadelphia College of Osteopathic Medicine Georgia (PCOM) and PCOM Department of Physical Therapy.[12,13] Some of the initiatives in the PCOM Department of Physical Therapy involve reaching out to students in undergraduate and secondary education in order to promote a clearer understanding of education and careers in physical therapy among underserved populations. Further, improved program and career visibility can be gained by providing admissions counseling and educational sessions to showcase physical therapy and other healthcare careers at local HBCUs as well as by recruiting and hiring a diverse faculty to be more representative of the community.[13,14]

The DPT program at PCOM has adopted, from its inception, a holistic admissions review process where applicants are considered for admissions based upon markers that are broader than GRE scores and undergraduate GPA. The admissions review process involves an interview, conducted by faculty and current students, to assess components of emotional intelligence, familiarity with the physical therapy profession, the applicant's life experiences, and to assess the prospective applicant's desire and reason for wanting to become a physical therapist.[14]

Ultimately, there appears to be a mismatch between the markers designed to predict success and actual success in DPT education.[2,7,8,10] Progressing from undergraduate school to the rigors of graduate level DPT education has been described as a formidable venture for students.[15] Cognitive markers alone may not provide a clear prediction of a student's ability to succeed. With attrition rates and diversity initiatives in mind, an examination of components of motivation, may provide insight into the make-up of a successful student entering DPT education. Students who are accepted into DPT programs may possess the cognitive components of self-regulated learning (SRL) required for academic success, but they may be lacking motivational behaviors required to continue driving SRL.[3] Self-regulated learning has been described by a set of cognitive strategies and processes that combined with motivational beliefs and abilities, allows learners to execute performance.[16–18] However, motivation may be the key guiding force because motivation initiates behavior and helps guide that behavior to successful goal attainment.[16,19,20]

Motivation is comprised of a set of behaviors that include goal orientation, self-efficacy for learning and performance, perceptions of the task including difficulty and task value, and affective reactions.[16,17] Motivation may be the pivotal factor in determining success because learners may possess strategies in the cognitive, behavioral, and context areas, but without properly aligned goals, positive self-efficacy, interest and drive, success will likely be unattainable.[17,21]

A review of the literature suggests that academic success is comprised of relationships between self-regulated learning strategies, such as deep learning and resource management, and motivational beliefs, self-efficacy for learning and performance and task value.[16–20] Measuring motivational behavioral factors related to academic success would appear to be beneficial in understanding how some students excel while others have difficulty maintaining academic success.[16,22–24]

However, there is a dearth of information regarding motivation behavioral traits for first-year DPT students. Previous studies utilizing the Motivated Strategies for Learning Questionnaire (MSLQ) to study motivation in physical therapy education have not examined graduate level physical therapy education programs or did not assess the impact of race/ethnicity on motivation or academic success or did not compare motivation scores to academic success.[24–27] Therefore, the purposes of this study were to determine: 1) the correlation between motivational behaviors and academic success, 2) the moderating effect of race/ethnicity on motivation behaviors and academic success in a foundational clinical anatomy course, 3) the predictive nature of motivation behaviors and race/ethnicity on academic success.

Materials and Methods

Newly admitted DPT students enrolled in PT 601G Clinical Anatomy course were eligible to participate in the study. The study was presented in an information session to the cohort of 40 students by a department administrator. Thirty-three students consented to enroll in the study (response rate 33/40, 82%). Ethics approval for this study was granted by the College Institutional Review Board (IRB) (protocol number H19-033E).

This study was a postpositive relational quantitative study which used the motivation section of the MSLQ to assess student motivational behaviors. The motivation section consists of seven subscales with questions designed to assess intrinsic and extrinsic goal orientation, task value, control of learning beliefs, self-efficacy for learning and

performance, and test anxiety.[28] Each question describes a behavior that is ranked by the subject using a seven-point Likert scale ranging from one (not at all true of me) to seven (very true of me) (**Appendix 1**).[28,29] The MSLQ motivation subscales have been shown to have good reliability and to be predictive of performance for college students at the course level[28,30] and medical students.[31]

A pair of research questions was developed for each motivational behavior examined. The first research question of each pair asked if there was a direct relationship (correlation) between self-assessment values on the MSLQ for that motivation subscale and clinical anatomy course grade. The second research question of the pair introduced race/ethnicity as an interaction term and asked if there was a moderating effect of a student's race/ethnicity on the motivation behaviors.

The students were given information on where to obtain a summary of the study and consent forms if they wished to participate. Student participation was hidden from the primary investigator, who was the course director, until after course grades had been assigned. At no point did the primary investigator speak about the project to the students.

During the third week of the Clinical Anatomy course (PT601G), each student received an email with a Survey Monkey® (San Mateo, CA) link which contained questions about participant demographics and the motivation subscales of the MSLQ (**Appendix 1**). Once PT 601G had been completed and the final grades submitted, the students who participated in the study were linked by computer to their student course grades, without revealing their names to the course director.

The clinical anatomy course (PT601G), used for the current investigation, was a seven-credit course offered during the summer term (10 weeks) which was the first term of year one for newly admitted DPT students. The course was comprised of 156 contact hours at a ratio of two hours of lecture to 10 hours of laboratory. The lecture component of the course consisted of a variety of face-to-face teaching and learning techniques which included traditional lecture, clinical case examination, interleaving, elaborative interrogation, drawing, and flipped classroom. The laboratory portion of the course consisted of instructor and self-guided full-body cadaver dissection with five students working as a team to dissect each specimen. Evaluation in the course was comprised of two multiple-choice written examinations (each 10% of the grade), a combination of weekly written and laboratory quizzes (17% of the grade), a multiple-choice final examination (17% of the grade), participation and professionalism (3% of the grade), palpation practical examination (17% of the grade) and two oral laboratory examinations (each 13% of the grade) the format of which has been previously described.[32]

The demographic information, course grades, and motivation subscale scores were tabulated using Microsoft Excel for Mac (Version 16.36, Microsoft Corp., Redmond, WA, USA). The data was analyzed using Statistical Package for Social Sciences (SPSS Version 25, Armonk; NY, USA). Subject age, gender identification, race/ethnicity, motivation subscales (independent variable), and course grade (dependent variable), were analyzed using descriptive statistics.

Normality of the distribution of the data for each independent and dependent variable was assessed. Bivariate level direct effects between the explanatory variables and dependent variable (course grade) were examined using Pearson r correlations, independent t-test, and one-way ANOVA. Independent t-test was used to determine which demographic characteristics were significantly related to the dependent variable. All study variables related to the dependent variable at a statistically significant level ($p<0.05$) in bivariate analysis were included as covariate variables in the regression models incorporated in the multivariate analysis.

Multiple linear regression was used to test the direct effects of the independent variables, as well as the indirect moderating effect of race/ethnicity on the independent variables and their effect on the dependent variable of academic success. Specifically, a separate multiple linear regression model was created that modeled the dependent variable as a function of each independent variable, as well as the study variables significantly related to the dependent variable in bivariate testing. If the independent variable was significantly related to the dependent variable at this step, the direct effect was supported.

Next, an interaction term was added to the multiple linear regression model (the independent variable by the moderating variable) and the analysis was repeated. If the interaction term was statistically significant within this analysis, then the indirect effect examining moderating effects of race/ethnicity was supported.

All test assumptions associated with the parametric analysis were checked, including normality, linearity, homoscedasticity, and no undue influence of outlier scores, to assure the validity of the inferential analysis.

In terms of statistical power regarding the multiple linear regression model, the G*power software indicated that a medium/large size effect ($f=0.25$) using a model

with three predictors with power set at 0.80 and alpha set at 0.05, would require a sample size of 34 study participants.[33] The current study's sample size of 33 study participants provided approximately sufficient statistical power for the current analysis given the variability noted in available software, such as G*power to determine sample size.[34] Further, given that the impetus for examining the problem was inspired by experiences within a specific group of students at a specific time in DPT education then subject selection became constrained to those conditions.

Results

Data indicated that the sample was about half female (n=17; 45.5%), predominantly of a Caucasian racial/ethnic identity (n=23; 67.0%) and had an average undergraduate GPA of 3.47 (**Table 1**).

The means, standard, deviations, skewness, and kurtosis of the data for each independent variable or motivational behavior and for the dependent variable of academic success, described by course grade, were analyzed. The data for each MSLQ subscale had a normal distribution as evidenced by the skewness and kurtosis being less than three times their respective standard deviations (**Table 2**).

Analysis indicated that course grade differed at a statistically significant level by race/ethnicity, [t(31)=2.93, p<0.01]. Specifically, those subjects who identified as Caucasian evidenced a higher course grade (0.93±0.03) relative to those subjects identifying as non-Caucasian (0.90±0.02). Analysis also indicated that course grade did not differ at a statistically significant level by gender, [t(30)=0.58, p=0.57] (**Table 3**).

Pearson r correlations indicated that academic success was not significantly related to intrinsic goal orientation [r(31)=0.12, p=0.50], extrinsic goal orientation [r(31)=-0.10, p=0.58], task value [r(31)=0.01, p=0.94], control of learning beliefs [r(31)=0.20, p=0.26], or test anxiety [r(31)=0.28, p=0.12] (**Table 4**).

However, analysis did indicate that course grade was significantly related to self-efficacy for learning and performance [r(31)=0.44, p<0.05]. Where higher self-efficacy for learning and performance scores were associated with a higher course grade (**Table 4**).

One-way ANOVA indicated that the overall model examining the moderating effect of race/ethnicity on the relationship between self-efficacy for learning and performance (SEL) and course grade was statistically significant [F(32)=6.51, p<0.002] and explained 40% of the variance in the dependent variable (R^2=0.40, adjusted R^2=0.34).

Table 1
Descriptive analysis of demographics of study participants (n=33).

Mean age (years)	**Range**
24.7±3.0	21–36
Gender	**n (%)**
Male	15/33 (45.45)
Female	17/33 (51.52)
Unreported	1/33 (3.03)
Race/ethnicity	**n (%)**
Caucasian	23/33 (67.0)
Non-Caucasian	10/33 (33.0)
Non-Caucasian Breakdown	**n (%)**
African American	2 (0.06)
Asian	6 (0.18)
Hispanic	1 (0.03)
Middle Eastern	1 (0.03)
Undergraduate GPA	**Mean (range)**
n=31	3.47±0.30 (3.0–4.2)

Table 2
Descriptive analysis: motivation subscale scores and course grade.

Variable	Mean±SD	Min-max	Scale range	Skewness (SE)	Kurtosis (SE)
Intrinsic goal orientation	5.48±0.83	3–7	1–7	-0.99 (0.41)	2.04 (0.80)
Extrinsic goal orientation	5.30±1.03	3–7	1–7	-0.48 (0.41)	-0.37 (0.80)
Task value	6.75±0.36	6–7	1–7	-1.61 (0.41)	1.77 (0.80)
Control of learning beliefs	6.14±0.67	5–7	1–7	-0.43 (0.41)	-1.15 (0.80)
Self-efficacy for learning and performance	5.61±0.67	4–7	1–7	0.10 (0.41)	0.04 (0.80)
Test anxiety	4.26±1.36	2–7	1–7	0.11 (0.41)	-0.78 (0.80)
Course grade	0.92±0.03	0.87–0.96	0–1.0	0.10 (0.41)	-0.93 (0.80)

Linear regression indicated that the interaction term between self-efficacy for learning and performance and race/ethnicity was not statistically significant (B=0.01, SE=0.01, β=1.66, p=0.18) (**Table 5**).

One-way ANOVA testing of grade for the course as a function of self-efficacy for learning and performance (SEL) and race/ethnicity, indicated that the overall model was statistically significant (F(32)=8.57, p<0.001) and explained 36% of the variance in the dependent variable (R^2=0.36, adjusted R^2=0.32). Furthermore, within the full multivariate model race/ethnicity remained significantly related to course grade, (B=0.05, SE=0.01, β=0.42, p<0.008), where a Caucasian racial identity was related to higher course score (**Table 6**).

Additionally, self-efficacy for learning and performance remained significantly related to course grade (B=0.02, SE=0.01, β=0.39, p<0.01), where higher self-efficacy for learning and performance scores explained higher course grades (higher academic success).

Table 3

T-test of academic success (course grade) and categorical variables.

Variable	n	Mean±SD	t/F(df)	p-value
Gender			0.58 (30)	0.57
Male	15	0.92±0.03		
Female	17			
Race/ethnicity			2.93 (31)	0.006
Caucasian	23	0.93±0.03		
Non-caucasian	10	0.90±0.02		

Discussion

This is the first study to examine the roles that motivation and ethnicity may have played in determining course grade in a DPT anatomy course. There was a positive correlation between the motivation subscale of self-efficacy for learning and performance and course grade and a positive correlation between race/ethnicity and course grade. Multivariate analysis demonstrated that course grade was a function of self-efficacy for learning and performance and race/ethnicity.

The current findings are consistent with previous literature demonstrating that self-efficacy was positively related with academic performance.[26,35,36] Notably, the motivation subscale of self-efficacy for learning and performance stood out as being independent of learning strategies with a positive contribution to academic performance directly and was deemed a valuable indicator of students who may be at risk for failing.[35] A positive correlation has also previously been demonstrated between academic performance and self-efficacy; however, the predictive value of self-efficacy for learning and performance was not previously examined.[26] The current study demonstrated the predictive value of self-efficacy for learning and performance on course grade.

The current study demonstrated significant correlations between race/ethnicity and course grade. However, did not demonstrate a moderating effect of race/ethnicity on academic success for any of the motivation behaviors. Race/ethnicity remained significantly related to course grade where a Caucasian racial identity was related to higher course scores. Some previous studies have indicated that students from underrepresented groups may have increased difficulty with standardized testing, possibly due to academic and non-academic issues.[1,10–12,14] Low self-efficacy combined with perceived difficulty of trying to enter a profession that historically has been predominantly Caucasian, can create a barrier to success for students from underrepresented groups.

The current findings highlight the importance of self-efficacy for learning and performance in determining aca-

Table 4

Pearson r correlations: academic success (course grade) & MSLQ subscales.

Variable	1	2	3	4	5	6	7
1. Academic success	–	0.12	-0.01	0.01	0.20	0.44*	-0.28
2. Intrinsic goal orientation		–	-0.03	0.37*	0.38*	0.60†	-0.07
3. Extrinsic goal orientation			–	0.07	0.12	0.13	0.29
4. Task value				–	0.54†	0.41*	0.01
5. Control of learning beliefs					–	0.65†	-0.13
6. Self-efficacy for learning and performance						–	-0.24
7. Test anxiety							–

*p<0.05; †p<0.01.

Table 5

A linear regression model examining the moderating effect of race/ethnicity (RE) on the relationship between self-efficacy for learning and performance (SEL) and course grade (n=33).

Variable	B	SE	β	p-value
Race/ethnicity	-0.07	0.07	-1.17	0.32
SEL	0.005	0.01	0.12	0.61
SEL by RE	0.02	0.01	1.66	0.18

Model: $F(32)=6.51$; $p<0.002$; $R^2=0.40$; adjusted $R^2=0.34$.

Table 6

Final multivariate model for testing grade for course as a function of self-efficacy for learning and performance (SEL) and race/ethnicity (RE).

Variable	B	SE	β	p-value
RE	0.02	0.01	0.42	0.008
SEL	0.02	0.01	0.39	0.01

Model: $F(32)= 8.57$; $p<0.001$; $R^2=0.36$; adjusted $R^2=0.32$.

demic success. In the case of creating a successful learning environment for students from underrepresented groups, strategies to improve self-efficacy may need to begin in undergraduate school, prior to applying to a DPT program. A variety of non-school related factors, such as family obligations and support, socioeconomic status, and cultural experiences can shape how students see their abilities to attain success.[37]

However, the perceived racial barriers that may limit success in DPT education are also present in those processes leading up to and including admissions review. A lack of representation of students from underrepresented groups in DPT education may stem from a lack of adequate exposure and advisement of physical therapy as a graduate degree and career option.[14,38] Black and Latinx students have noted that their undergraduate experiences were limited in providing guidance, resources, and support for entering a DPT program.[14]

The perceived racial barriers toward success, or toward continuing on to DPT education, reduce self-efficacy thereby reducing the likelihood for success when applying to DPT school and consequently may hinder success after the student enrolls in a DPT program.[14,37] Strategies to combat these barriers, such as positive reinforcement, mentoring by physical therapists, and career counseling, need to be implemented early in a student's education to combat the challenges faced by students from underrepresented groups who may be considering a career in physical therapy.[14]

Once a student has been accepted into a DPT program, their ability to succeed hinges on self-efficacy for learning and performance. The current findings support the idea that efforts aimed to improve self-efficacy in learners where it may be limited may be beneficial to academic success. Since self-efficacy is rooted in self-perception, teaching strategies must focus on reducing the ambiguity between a student's perceived ability and their actual ability, by providing precise and timely feedback.[39] Other strategies that aid the development of self-efficacy include providing clear instructions and expectation of outcomes, and through teachers enabling modeling and guided skill perfection.[39] Students can also be given a stepwise progression of increasingly difficult tasks that promote mastery, with each step being a small goal that when combined lead to a larger goal. Small incremental steps along with goal setting, allows students to succeed in a way that can bolster self-efficacy and lead to improved confidence.[39–41] In the broader sense, students may need to reflect on the meaning of self-efficacy as it pertains to their specific situation and their perception of the ability to attain success.[40] However, teachers can help by properly coaching, being timely and precise with feedback, and by focusing on those aspects of performance that may have been correct as opposed to concentrating on those that were negative.[39–41]

On a program level, organizational policies that promote and support academic integration and linking of subject material can improve student engagement and thereby improve self-efficacy.[2] Methods of improving self-efficacy such as using collaborative and team-based learning approaches, improved teacher to student communication, and improved assessment techniques have been shown to improve students' academic success rates in one DPT program.[2]

The design of the study, to use one cohort in one class, limited the sample size and therefore limited the generalizability of the results. The diversity of cohort, due to the small sample size, may not have accurately represented diversity in a typical DPT program. Students from the clinical anatomy course volunteered for the study which may have introduced selection bias as those students volunteering may have had stronger self-confidence, self-efficacy, by their choice to participate.

Further, a determination of students who may be the first in their family to obtain a graduate degree or who may have recently immigrated to the United States and for whom English was a second language was not made. The lack of this determination may have affected study participation. For example, students who may not have felt confident with the English language may have failed to participate in the study or during participation may have misun-

derstood some of the questions. Such a determination would also better align the study with the definition of students from underrepresented groups thereby being consistent with American Council of Academic Physical Therapy definition.[42]

It is recommended that the current study be repeated with additional cohorts to determine the utility of using the motivational behaviors of the MSLQ as a preadmission screen to shed light on an applicant's ability to succeed in a DPT program. A qualitative questionnaire to determine each student's diversity background (first-time graduate degree, English comprehension, socioeconomic status, etc…) may improve our understanding of underrepresented group status. Research examining the role of motivation and race/ethnicity in more clinical coursework is recommended. Additionally, an examination of the roles that motivation and race/ethnicity may play in academic success as students' progress through the DPT program school is also recommended.

Conclusion

Behaviors and academic success were examined in light of race/ethnicity. The results suggested that the motivational behavior of self-efficacy for learning and performance and race/ethnicity were significantly related to academic success. Where increased self-efficacy for learning and performance resulted in, and predicted, a higher course grade. Similarly, Caucasian racial identity was also associated with, and predictive of, a higher course grade.

Further, it has been shown that certain components related to self-efficacy can limit motivation in students from underrepresented groups, such as fear of success and fear of failure, or fear of the feeling of not belonging.[37,40] Therefore, the current study provides a rationale for implementing the strategies that bolster self-efficacy and indicates that those strategies may be more closely applied to and benefit students from underrepresented groups.

Conflict of Interest

The authors have no conflict of interest in this work.

Author Contributions

PAF: Protocol/project development, data collection and analysis, manuscript writing/editing; SLG: Project development, manuscript writing/editing; AMRA: Manuscript writing/editing.

Ethics Approval

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Appendix 1

Participant demographics and the motivation subscales.

Demographic information

1. Student PCOM email: .....@.....
2. What is your age in years?
   - ☐ Please specify: _____
   - ☐ I prefer not to answer.
3. How do you currently describe your gender identity?
   - ☐ Please specify: _____
   - ☐ I prefer not to answer.
4. Undergraduate GPA: _____
5. Grade you expect to get in this class (PT601G) _____
6. Which categories describe you? Select all that apply to you:
   - ☐ American Indian or Alaska Native—For example, Navajo Nation, Blackfeet Tribe, Mayan, Aztec, Native Village of Barrow Inupiat Traditional Government, Nome Eskimo Community
   - ☐ Asian—For example, Chinese, Filipino, Asian Indian, Vietnamese, Korean, Japanese
   - ☐ Black or African American—For example, Jamaican, Haitian, Nigerian, Ethiopian, Somalian
   - ☐ Hispanic, Latino or Spanish Origin—For example, Mexican or Mexican American, Puerto Rican, Cuban, Salvadoran, Dominican, Columbian
   - ☐ Middle Eastern or North African—For example, Lebanese, Iranian, Egyptian, Syrian, Moroccan, Algerian
   - ☐ Native Hawaiian or other Pacific Islander—For example, Native Hawaiian, Samoan, Chamorro, Tongan, Fijian, Marshallese
   - ☐ White—For example, German, Irish, English, Italian, Polish, French
   - ☐ Some other race, ethnicity, or origin, please specify: _____
   - ☐ I prefer not to answer.

Please continue to the Questionnaire

The Motivated Strategies for Learning Questionnaire (MSLQ)[28]

The following 31 questions ask about your motivation for and attitudes about this class. Remember there are no right or wrong answers, just answer as accurately as possible. Use the scale below each question to answer the questions.

- If you think the statement is very true of you, circle 7; if a statement is not at all true of you, circle 1.
- If the statement is more or less true of you, find the number between 1 and 7 that best describes you.

	1 not true of me	2	3	4	5	6	7 very true of me
1. In a class like this, I prefer course material that really challenges me so I can learn new things.	☐	☐	☐	☐	☐	☐	☐
2. If I study in appropriate ways, then I will be able to learn the material in this course.	☐	☐	☐	☐	☐	☐	☐
3. When I take a test, I think about how poorly I am doing compared with other students.	☐	☐	☐	☐	☐	☐	☐
4. I think I will be able to use what I learn in this course in other courses.	☐	☐	☐	☐	☐	☐	☐
5. I believe I will receive an excellent grade in this class.	☐	☐	☐	☐	☐	☐	☐
6. I'm certain I can understand the most difficult material presented in the readings for this course.	☐	☐	☐	☐	☐	☐	☐
7. Getting a good grade in this class is the most satisfying thing for me right now.	☐	☐	☐	☐	☐	☐	☐
8. When I take a test, I think about items on other parts of the test I can't answer.	☐	☐	☐	☐	☐	☐	☐
9. It is my own fault if I don't learn the material in this course.	☐	☐	☐	☐	☐	☐	☐
10. It is important for me to learn the course material in this class.	☐	☐	☐	☐	☐	☐	☐
11. The most important thing for me right now is improving my overall grade point average, so my main concern in this class is getting a good grade.	☐	☐	☐	☐	☐	☐	☐
12. I'm confident I can understand the basic concepts taught in this course.	☐	☐	☐	☐	☐	☐	☐
13. If I can, I want to get better grades in this class than most of the other students.	☐	☐	☐	☐	☐	☐	☐

Appendix 1 ***[Continued]***

Demographic Information.

	1 not true of me	2	3	4	5	6	7 very true of me
14. When I take tests, I think of the consequences of failing.	☐	☐	☐	☐	☐	☐	☐
15. I'm confident I can understand the most complex material presented by the instructor in this course.	☐	☐	☐	☐	☐	☐	☐
16. In a class like this, I prefer course material that arouses my curiosity, even if it is difficult to learn.	☐	☐	☐	☐	☐	☐	☐
17. I am very interested in the content area of this course.	☐	☐	☐	☐	☐	☐	☐
18. If I try hard enough, then I will understand the course material.	☐	☐	☐	☐	☐	☐	☐
19. I have an uneasy, upset feeling when I take an exam.	☐	☐	☐	☐	☐	☐	☐
20. I'm confident I can do an excellent job on the assignments and tests in this course.	☐	☐	☐	☐	☐	☐	☐
21. I expect to do well in this class.	☐	☐	☐	☐	☐	☐	☐
22. The most satisfying thing for me in this course is trying to understand the content as thoroughly as possible.	☐	☐	☐	☐	☐	☐	☐
23. I think the course material in this class is useful for me to learn.	☐	☐	☐	☐	☐	☐	☐
24. When I have the opportunity in this class, I choose course assignments that I can learn from even if they don't guarantee a good grade.	☐	☐	☐	☐	☐	☐	☐
25. If I don't understand the course material, it is because I didn't try hard enough.	☐	☐	☐	☐	☐	☐	☐
26. I like the subject matter of this course.	☐	☐	☐	☐	☐	☐	☐
27. Understanding the subject matter of this course is very important to me.	☐	☐	☐	☐	☐	☐	☐
28. I feel my heart beating fast when I take an exam.	☐	☐	☐	☐	☐	☐	☐
29. I'm certain I can master the skills being taught in this class.							
30. I want to do well in this class because it is important to show my ability to my family, friends, employer, or others.	☐	☐	☐	☐	☐	☐	☐
31. Considering the difficulty of this course, the teacher, and my skills, I think I will do well in this class.	☐	☐	☐	☐	☐	☐	☐

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Frontloading gross anatomy: impacts on medical student performance

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Abstract

Objectives: The human gross anatomy course offered at the University of California, Davis, School of Medicine, is part of a partially integrated foundational block in the first year of the medical curriculum. The block organization was implemented in 2006 in part to foster the horizontal integration of four basic science courses. However, simultaneous instruction in multiple courses presented a challenging workload to students, especially considering the large amount of information covered in anatomy. In an attempt to improve student outcomes, the gross anatomy course was compressed and frontloaded to the first 13 weeks of the foundational block while instructions of other courses were shifted later to make room for the frontloaded gross anatomy course. To assess the effect of frontloading of anatomy on students' performance, we retrospectively compared the anatomy examination scores between before and after frontloading of the anatomy content.

Methods: Student performance in the gross anatomy course was compared between the pre-frontloading (2013–2015) and post-frontloading (2016–2018) cohorts. Average scores of each examination category (quizzes, midterms, practical and written finals, and overall grades) were calculated and compared between the two cohorts.

Results: Scores on the written final and practical final examinations and the overall grade in gross anatomy improved significantly ($p<0.05$) in the post-frontloading cohort (n=323) compare to the pre-frontloading cohort (n=343).

Conclusion: Moving gross anatomy forward and offering a compressed course may be an option for educators looking to improve student performance without increasing student contact hours, concomitantly allowing focused learning and mastery of anatomy content.

Keywords: anatomical education; assessment; curriculum reorganization; gross anatomy; student performance

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Introduction

The University of California, Davis, School of Medicine offers the four-year Doctor of Medicine (MD) program for students with a bachelor's degree. The program discussed in this report consists of 2 years of preclinical curriculum and 2 years of clinical curriculum. In 2006 the preclinical curriculum was revised from a traditional discipline-based organization with free-standing, department-based courses taught for the length of a quarter (10 weeks) to a more integrated, block-based organization with multiple courses taught in parallel for the length of a block created by the fusion of two quarters (18 weeks). Blocks of differing lengths allowed multiple courses to be taught simultaneously, improving opportunities for horizontal integration. The first 18-week Foundation Block concentrated on providing foundational knowledge in the basic sciences and included courses in gross anatomy, physiology, histology and biochemistry. These courses were offered in parallel with a course entitled Doctoring, which emphasized the physical examination, doctor-patient communication and biostatistics.[1] After the two introductory blocks, which filled most of the first academic year, the curriculum shifted to a pathophysiology and organ systems-based curriculum. This curriculum reorganization permitted us to coordinate content delivery between multiple basic science courses and integrate basic sciences with clinical experiences taught in Doctoring. Its organization was aligned with the nationwide movement towards integrated medical curriculum[2] and was favorably reviewed by the accredit-

ing authority, Liaison Committee on Medical Education (LCME) in 2014.

The perceived benefits of the integrated curriculum for medical student's performance are improved knowledge retention and clinical reasoning skills enhanced by conceptual integration.[2] This is likely the product of deep learning stimulated by applying principles of basic science in the context of clinical problem solving.[3] It has been shown that problem-based learning (PBL) is an effective pedagogy to enhance the integration of basic and clinical sciences.[4] When the effectiveness of PBL was investigated in anatomy education, however, it was indicated that the main determinant of students' performance outcome was not necessarily the format of instruction, but rather the context in which students learned anatomical knowledge. In one study, levels of anatomical knowledge gain were compared between two groups of students, one taught in PBL-based curricula and the other taught in traditional medical curricula, and no significant differences were found between the two groups.[5] The authors suggest that the crucial element for successful anatomy education is teaching anatomy in a clinical context, and as long as this condition is fulfilled, a traditional curriculum was capable of achieving high student performance. The importance of teaching anatomy linked to clinical contexts was reiterated by another report by Doomernik et al.[6] In this study, long-term (~1.5 years) anatomy knowledge retention was assessed in the student body attending an integrated, problem-based medical curriculum. The authors showed that traditional knowledge recall based on radiology imaging declined more rapidly than knowledge gained through clinical cases.[6] More recently, the positive effect of learning anatomy in clinical contexts in compressed instructions was reported.[7] To compensate for a reduced instructional duration, the authors emphasized correlating the functions with the anatomical structures. Although the instructional content was abbreviated, using clinical symptoms as an instructional focal point maintained students' performance.[7] Together, these reports highlight that the context in which anatomy knowledge is learned by students is the principal determinant of students' learning outcome.

When the horizontally integrated curricular reorganization was implemented at our school in 2006, we encountered an unintended consequence; the new curriculum required incoming students, many of whom had been away from the classroom for many years, to rapidly develop study skills at the very beginning of medical school to be successful in five large courses taught in parallel. From the cognitive learning theory standpoint, this circumstance could place these students who likely possess less pre-existing knowledge bases into a disadvantageous position, because a high volume of unfamiliar materials taught simultaneously would easily overwhelm those individuals' working memory capacity.[8] This situation could lead to a highly stressful, uncongenial learning condition.[9] A logical solution to this unintended consequence was to decrease the volume and complexity of materials taught concurrently, thereby reducing the cognitive load the first-year students have to confront at the very beginning of the curriculum.[10] Accordingly, the instructors of the basic science courses agreed in 2016 to move much of the content of the gross anatomy course into the first 13 weeks of the block and to reduce the content of other courses while the gross anatomy course was running. Much of this displaced content was moved to the final 6 weeks of the block, after the completion of gross anatomy. As the result of frontloading of the anatomy content, on the one hand, horizontal integration with the rest of basic science courses and Doctoring was reduced. On the other hand, intra-disciplinary integration[11] within the anatomy course was enhanced because of more focused integration of regionally taught gross anatomy content with embryology, ultrasound, and radiology.

In this report, to address the effect of frontloading of anatomy on students' performance, we retrospectively examined the scores of multiple-choice written examinations and laboratory practical examinations recorded in 2013–2015 (pre-frontloading) and in 2016–2018 (post-frontloading) in the gross anatomy course at the University of California, Davis, School of Medicine.

Materials and Methods

Human subjects research exemption was granted by the Internal Review Board (IRB) at the University of California, Davis (IRB ID: 1613920-1). The compliance with the Family Educational Rights and Privacy Act (FERPA) was approved by the Office of Medical Education (OME) at the University of California, Davis. All student data in this study were analyzed independently from any student identifiers using spreadsheets provided by the OME. Medical College Admission Test (MCAT) scores and undergraduate grade point averages (GPAs) were found on the School of Medicine's publicly available current and cached web pages. The student cohorts analyzed in this report were not subdivided based on gender or age, based on our previous observation that these characteristics did not affect students' examination scores in gross anatomy at UC Davis.[12]

The courses described here as gross anatomy and histology are officially titled Developmental, Gross and Radiographic Anatomy (CHA400, 7.5 units) and Cell and

Tissue Biology (CHA402, 4.5 units). The course of gross anatomy integrates clinically relevant anatomy, human embryology, surface anatomy, radiographic anatomy, and ultrasound anatomy. The latter three components are taught by physicians with appointments in the departments of Pediatrics, Radiology, and Emergency Medicine, respectively. The course consists of 55 lecture hours (35 in gross anatomy, 10 in embryology, 9 in radiographic anatomy, and one in ultrasound anatomy) and 81 laboratory hours during which students dissect a human cadaver in teams of 4 or 5, learn surface anatomy, and apply ultrasound anatomy in group sessions. Student's performance assessed in this report consists of the following four components: (1) quizzes - multiple choice questions offered approximately biweekly based on learning objectives from gross anatomy, embryology and radiographic anatomy lectures, (2) midterms - three midterm laboratory practical examinations that include questions on anatomical structures and functions based on dissected cadavers, animated ultrasound images and surface anatomy questions with a standardized patient, and one oral presentation given to an instructor and the student's dissection partners, (3) practical finals - a comprehensive laboratory practical examination with the same components as midterm practical, and (4) written finals - a comprehensive written multiple choice examination. The weight of each component in the overall course grade is as follows: the 70 total quiz questions are worth 20%, the midterms each 10% (total of 30%), the oral presentation 10%, and the final examination 40% (practical final 20%, written final 20%). All preclinical courses at UC Davis School of Medicine are pass-fail with no letter grades, and a grade of 75% or higher is used as a passing grade for the gross anatomy course. This cutoff score was selected empirically based on the past student performance as it corresponded to the letter grade C before the transition to the pass-fail grading occurred.

In the years of 2013 to 2015 the gross anatomy course was instructed over 18 weeks, with lectures and laboratory sessions primarily offered on Tuesdays and Thursdays, and in the years of 2016 to 2018 when the course was frontloaded the course was instructed in 13 weeks on Tuesdays, Thursdays and Friday. The content of the gross anatomy course remained nearly the same (a new embryology lecture on the development of the palate and face replaced a formal embryology review session starting in 2017), and the total number of student contact hours remained the same after frontloading. The other basic science courses in the foundational block accommodated the frontloading of gross anatomy by reducing their content while gross anatomy was in progress and increasing their student contact hours after the gross anatomy course was complete. For comparison, the monthly contact hours for the 2015 (pre-frontloading) and 2016 (post-frontloading) are presented in **Table 1**.

To evaluate the effect of the frontloading on the outcome of students' course performance, the past examination scores in the gross anatomy and histology courses were retrospectively collected and compared between pre- and post-frontloading student cohorts. The first-year medical students who took the gross anatomy course in 2013–2015 were grouped into the pre-frontloading cohort

Table 1

Number of student contact hours the year before (2015) and the year after (2016) frontloading gross anatomy.

	Month*	Anatomy	Physiology	Histology	Biochemistry
2015	August	31	21	19	14
	September	31	23	12	6
	October	29	16	15	10
	November	29	20	13	10
	December	16	4	8	4
	Total	136	84	67	44
2016	August	47	12	7	6
	September	44	20	13	10
	October	40	13	16	10
	November	5	20	15	17
	December	0	15	16	4
	Total	136	80	67	47

*Since the first day of classes varies from year to year, months are defined here as 4-week periods, with the first 4 weeks being August, the second 4 weeks being September, etc.

(n=323) and those in 2016–2018 (n=343) were grouped into the post-frontloading cohort. Examination scores of quizzes, midterms, practical finals, and written finals were calculated and analyzed as separate categories using Excel spreadsheet. To examine the unpaired data sets of the pre-frontloading and the post-frontloading cohorts, averages and standard deviations of scores of the cohorts in each examination category were calculated and statistical differences were determined using a Student's t test assuming equal variance and a two-tailed distribution. Significance was set at $p<0.05$. We chose to focus on the student data of these 6 years to keep potential effects of variables such as significant class-size expansion and the replacement of an instructor which occurred in 2019.

Results

The results of the curriculum changes showed to provide a more supportive learning environment for students by: (1) reducing the overall complexity and quantity of learning materials introduced during the first few months, (2) allowing concentration on learning activities in anatomy laboratories, radiology and ultrasound sessions, and (3) giving an opportunity to redevelop study skills while concentrating on anatomy. Likely reflecting these positive aspects, the mean scores of the practical finals, the written finals, and the overall course grades of the post-frontloading cohort (2016–2018) were statistically higher than those of the pre-frontloading cohort (2013–2015), and the mean scores of quizzes and midterms maintained the equivalent levels between the two cohorts (**Table 2**). Effect size (Cohen's d)[13] for each of practical finals, written finals, and the overall course grade was 0.33, 0.17, 0.17, respectively. Albeit the effect size was relatively small, statistically significant improvement in students' performance indicates that the frontloaded schedule helped to improve students' learning of gross anatomy without detrimental effect.

Discussion

Frontloading of the gross anatomy course reported here allowed us to achieve the focused integration within the anatomy related content and reduce hours of non-anatomy courses in the first half of the block. In a previous study, we found that only one in three first year students at the University of California, Davis, School of Medicine had taken an undergraduate course in human anatomy prior to matriculation.[12] Most students, therefore, are unfamiliar with human anatomy when they begin classes. Combined with the sheer volume of information they need to master in the course, gross anatomy is perceived as challenging, or even daunting as previously reported.[14] That frontloading of gross anatomy improved student performance on the anatomy practical final and written final examinations shows that designating focused time for mastering anatomy content had positive effect. The gross anatomy course described in this report experienced a 25% reduction in lecture hours in 2001. When the effect of this hour-reduction was investigated, it was shown that characteristics including age, gender, MCAT, GPA, and undergraduate coursework in anatomy did not correlate with the course performance.[12] Corroborating this report, the prematriculation academic records of the pre- and post-frontloading cohorts of this study are also comparable - the MCAT scores (averaging the 81st percentile in both 2013–2015 and 2016–2018) and the undergraduate grade point averages (3.69 in 2013–2015 and 3.64 in 2016–2018), indicating it is unlikely that the test score improvement was due to the academic or innate characteristics specific to the cohorts. Although the class size has increased steadily between 2013 and 2018 (the average class size of the pre-frontloading, 110 students; that of the post-frontloading, 115 students), the larger class size of the post-frontloading cohort did not appear to have negative effect on the performance in gross anatomy. Together, we consider the improved student performance in the post-

Table 2

Class performance in gross anatomy prior to frontloading (2013–2015) and after frontloading (2016–2018) in the medical curriculum.

Assessment	n	p-value	2013–2015 grade (percentage mean+SD)	n	2016–2018 grade (percentage mean+SD)
Quizzes	343	n.s.	85.7±8.4	343	86.6±7.4
Midterms	343	n.s.	90.0±7.0	343	90.2±5.6
Practical finals	343	<0.001	86.0±8.5	343	88.5±6.8
Written finals	343	<0.05	88.1±8.0	343	89.4±7.0
Overall grade	343	<0.05	88.8±5.7	343	89.6±4.8

n.s.: not significant (p>0.05); **SD:** standart deviation.

frontloading cohort in general was likely the result of students having more study time at the beginning of the block dedicated to gross anatomy and not having other final examinations competing with their study for the gross anatomy final examinations.

Improvements may also have come from students having an opportunity to develop good study habits earlier on during a less impacted curriculum. Though not measured empirically, the collaborative learning environment fostered in the gross anatomy dissection laboratory appeared to cultivate a strong sense of camaraderie among students in the early part of the foundational block. This may contribute to students developing the habit of studying in groups and helping each other's learning.[15] The collaborative atmosphere of the class nurtured by the frontloaded gross anatomy course may also help students reduce stress, which has been shown to negatively affect academic performance of medical students and aid them in navigating through the heavy academic demands.[16,17]

Removing the gross anatomy examinations from the final examination week may have also contributed to improved student performance in other courses. In this study we chose to analyze the final examination grades for the histology course, since this course was relatively unchanged during the six-year period analyzed in this report. The format of the physiology final examination changed significantly in 2017 (from an examination prepared by course instructors to that selected from the National Board of Medical Examiners Question Bank). The manner in which the biochemistry course grade was calculated also changed significantly during the study period by increasing the weight of attendance at journal clubs in final grades. These changes led us to preclude these two courses from our analysis. In histology, the post-frontloading cohort performed significantly better than the pre-frontloading cohort on their histology final examination - overall course grade: 2013–2015, 87.2±8.2, n=325; 2016–2018, 88.6±7.4, n=345 ($p<0.05$). This improvement on the histology final examination associated with frontloading gross anatomy may be the result of more time being available to study histology content during the final examination week. Since study time dedicated to the anatomy final examination in December was no longer needed in the frontloaded curriculum, the other courses gained a week to provide additional instructions and review sessions prior to their final examinations.

Studies by others have shown that the best way of improving gross anatomy knowledge is to spend more time teaching anatomy, and to revisit anatomy during the clinical years.[18] However, turning back the clock to increase time spent teaching anatomy is unlikely to be a viable option as schools consider ways of improving student performance.[19] McBride and Drake[20] reported that students spend on average 129 contact hours in gross anatomy classroom activities and dissection laboratories at North American medical schools. Our course has a total of 116 gross anatomy contact hours (35 lecture and 81 laboratory hours), and the contact hours available to teach this discipline have been capped. Others seeking to improve student performance in gross anatomy without increasing contact hours should consider the potential benefits of frontloading their content within an otherwise integrated foundational block, since as reported previously, the score on a gross anatomy comprehensive examination is positively correlated with scores on the USMLE Step 1 and passing the examination.[21] It is also possible that offering gross anatomy as a compressed, stand-alone course would result in similar improvements in student outcomes, as suggested by numerous studies in other disciplines.[22]

Where to place gross anatomy in the medical school curriculum has been a topic of heated debate for generations. In a thoughtful and entertaining review of the subject, Sinclair[23] argues that integrating anatomy with other foundational courses is probably irrelevant to student learning, as only basic anatomical concepts are needed for successful learning of physiology and biochemistry. Nevertheless, integrating gross anatomy with other foundational courses is a popular curricular approach,[20] though upon closer examination it is unclear if courses attempting integration are not merely being taught at the same time. Muller et al.[24] discussed how the integrated "foundations of human care" block offered at the start of the University of California, San Francisco's medical curriculum served as an example. Student evaluations of the block noted that histology and gross anatomy were, in fact, only well integrated with other foundational courses when they were studying cardiovascular systems, and for the bulk of the block the anatomical sciences were taught independently.[24] In addition, integrated curricula often present challenges to providing adequate levels of anatomical knowledge to medical students due to the general trend of reducing contact hours of basic science disciplines including anatomy.[2,25,26] One attractive solution for this challenge could be vertical integration of basic sciences into the clinical curricula;[3] however, this approach often faces the practical challenge of how to blend basic sciences into tightly scheduled clerkship schedules.[27]

Alternatively, one might argue that gross anatomy can be better integrated with certain applied clinical coursework than other foundational courses, as this would per-

mit lessons in the clinical relevance of the subject matter and earlier experiences with clinical problem solving. The recent study investigating preferred timing of cadaveric dissection in the curriculum by medical students (enrolled and graduated) reports the preclinical years as above all the most preferred time.[28] The main reasoning behind this preference was students' view of cadaveric dissection as a fundamental exercise to develop anatomical knowledge before transitioning to the clinical curriculum. The fact that the gross anatomy course at the University of California, Davis is fully integrated with surface, radiographic and ultrasound anatomy, taught by clinicians, may help it succeed as a quasi "stand-alone" course near the beginning of the curriculum to provide comprehensive anatomical knowledge foundation. This organization exemplifies the "intra-disciplinary integration of content" that delivers learning materials in an ordered, cohesive manner within a discipline.[11] The authors argue that curriculum design employing an inter-disciplinary integration model would likely present a challenge to gross anatomy because of the regional approach it takes for instruction. In this sense, the success of our current frontloaded gross anatomy course relies upon well-integrated intra-disciplinary instruction and the streamlined sequence of anatomical material presentation made possible by all-inclusive cadaver dissection laboratory sessions. An alternative way of maintaining the regional approach ideal for instruction of gross anatomy was achieved by the Morehouse School of Medicine integrated curriculum employing gross anatomy as the backbone of the curricular design.[29,30] Others have found that the benefits of an integrated curriculum became most evident at the later phase of the curriculum and led to improved mastery of knowledge in both basic and clinical sciences.[31]

Our report has limitations. First, the effect of frontloading on long-term retention of anatomical knowledge was not assessed. Evaluating anatomical knowledge of third year students rotating in relevant clerkships such as surgical rotation would be ideal to gain direct correlation between the frontloading curriculum and knowledge retention. In addition, because of the curriculum structure at our institution, we do not have the opportunity to compare the frontloaded format and the fully integrated curriculum within the context of our student body.

Conclusion

We have shown that frontloading a gross anatomy course in a compressed foundational curriculum can improve student outcomes both in the anatomy course as well as in the histology course being taught in the same block. This approach would be especially applicable to a gross anatomy course in which intra-disciplinary integration of content is well-established. Beginning of summer 2021, the University of California, Davis, School of Medicine rolled out a new integrated and learner-oriented curriculum. In this curriculum design we retained the frontloading format; the gross anatomy discipline is housed with histology and clinical skills disciplines as a single course to allow cohesive integration of the fundamentals in gross anatomy, micro anatomy and physical examination. This well-woven structure provides an excellent knowledge building block for the first-year students, functioning as the "pre-integration" foundational knowledge base[11] that prepares students for the subsequent courses revolving around integrated problem based and case-based learning sessions.

Conflict of Interest

No conflicts declared.

Author Contributions

RPT: project development, data collection/analysis, manuscript writing/editing; HA: data analysis, manuscript writing/editing; KAB: data collection/analysis, manuscript editing.

Ethics Approval

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Vertical integration of anatomy curriculum in the undergraduate clinical education period: medical students' perspectives

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Abstract

Objectives: The adaptation of the knowledge and skills acquired in preclinical medical education to the clinics by vertical integration would be more permanent when combined with clinical skills. The aim of the study was to determine the needs of the students in clinical internship education on anatomy and to plan the relevant anatomy subjects before clinical internships by rearranging the curriculum as needed.

Methods: The study was carried out on a questionnaire form applied to 4th, 5th, and 6th-grade students of Bursa Uludağ University Faculty of Medicine. In addition to demographic information, 16 multiple-choice and open-ended evaluation questions were asked in the questionnaire.

Results: 335 students participated in the study. 84.4% of the participants reported that they had needed basic anatomy knowledge and they had to study again before the clinical internship. 69.59% of the participants stated that among the courses taken in the basic sciences education period, anatomy should be integrated into the clinical internships. 88.24% of the participants stated that anatomy education should be integrated before starting clinical internships in the surgical departments.

Conclusion: As a result of the feedback received from the students with the current study, it was seen that some of the anatomy information obtained during the preclinical basic sciences period was forgotten until the clinical internship period and they should be remembered again. We support that integrated clinical anatomy lessons should be taken into the clinical education period.

Keywords: anatomy education; clinical anatomy, medical education; vertical integration

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Introduction

Anatomy, which has been the cornerstone of medical education for hundreds of years, is an important resource for the examination of a patient, putting diagnosis, and informing the pathological findings to the patient and other healthcare professionals. The role of anatomy in the process of raising physician candidates and supporting modern medical practices is very well known. Since the beginning of medical education, anatomy has been included in the curriculum in all medical faculties.[1] The knowledge of anatomy is significant not only for medical education but also for the use of the obtained information in medical practice.[2] For medical students to minimize the medical errors, anatomy taught with both theoretical and practical applications should be supported with a clinical approach. Knowing the importance of anatomy and experiencing the anatomical knowledge in clinical practice will also contribute to the development of medical skills of students.[3]

Reducing time in anatomy education, which is the indispensable touchstone of the medical curriculum, leads to the suffocation of anatomy knowledge.[4] In recent years, there have been debates in the community of surgical professionals regarding the decline in anatomy education at the undergraduate level. In these discussions, issues related to the decrease in the time allocated to anatomy

lesson, the teaching staff and the dissections performed draw attention. Although it is difficult to evaluate this decrease in anatomy education objectively, some studies show that the knowledge level of physicians who should be qualified is below the acceptable level.[1,5,6]

Integration has been established between the disciplines taught at the same stage in traditional medical education such as anatomy, physiology, biochemistry. Integration in medical education can be horizontal, vertical and spiral. By definition, horizontal integration is the simultaneous delivery of similar subjects in basic sciences by different disciplines within the scope of a committee or block. Vertical integration is the simultaneous basic and clinical sciences education. Spiral integration is a combination of horizontal and vertical integration.[7]

In Turkey, basic medicine is taught particularly in the first three years. However, it is well known that, the knowledge and skills acquired especially in the early periods needs to be repeated to combine the basic knowledge with clinical experience.[8] For this reason, horizontal and vertical integration of the education program in Turkey is one of the national accreditation requirements of pregraduate medical education.[9]

The aim of the study was to determine the needs of anatomy knowledge in clinical practice, considering the views of students in clinical practice and raise awareness of the inclusion of clinical anatomy education in the medical education curriculum with vertical integration.

Materials and Methods

Students (4th and 5th grades and intern doctors) of Bursa Uludağ University Faculty of Medicine were included in the study. Due to the Covid-19 pandemic, questionnaire forms were applied online. The link addresses of the questionnaire are shared in student contact groups. Only volunteer students participated in the study. Filling out the questionnaire forms for the study was finalized in January 2021. Each student had the right to participate the survey once. A total of 335 volunteers (129 from fourth grade, 111 from fifth grade and 95 from intern doctors) participated in the study. In the questionnaire form, sixteen questions prepared with the five-point Likert scale (1=Strongly Disagree, 2=Disagree, 3=Undecided, 4=Agree, 5=Strongly Agree) for their opinions on the vertical integration of clinical anatomy education in addition to open-ended questions. SPSS (Statistical Package for Social Sciences) for Windows (Version 22, Chicago, IL, USA) was used for descriptive statistical analysis including the frequency distributions, mean score and standard deviation.

Results

The questionnaire form was answered by 335 volunteers (129 fourth-grade students, 111 fifth-grade students, and 95 intern doctors). Of these volunteers, 150 were males (44.8%) and 185 were females (55.2%).

The questionnaire and the rate of answers given in Likert scale were shown in **Table 1**.

The highest rate of the answers given to the direct question of "In which clinical training did you need to have your anatomy knowledge repeated?" was as "surgical trainings" at a rate of 82.98%. Among the surgical educations, the most common answer was general surgery with a rate of 42.38% and gynecology with a rate of 19.41%.

The highest rate of the answers given to the direct question of "How did you complete your forgotten information and lack of anatomy information?" was as "anatomy books and atlases" at a rate of 37.31%. This answer was followed by "anatomy lecture notes" (21.01%) and online sources (9.85%).

Another direct question was: "What do you think should be the difference between clinical anatomy education and basic topographic and systematic anatomy education?" To this question; 51.34% of the participants stated that the clinical anatomy should be taught with examples of the cases related to diseases, 32.53% stated that more usable information should be taught without unnecessary details.

The direct question "Which of the courses taken during the basic medical education period should be integrated into clinical education?" was answered as "anatomy" by 60.59% of the participants. Additionally, 37.91% declared that physiology and pharmacology should be integrated in clinical education.

Another direct question was: "In which internship did you most need to have your anatomy knowledge repeated?" To answer this question, 88.24% of the participants stated that anatomy education should be integrated before starting the clinical internships in the surgical departments and 31.37% of the participants stated that anatomy education should be integrated before the general surgery internship. In addition to this, %14.32 of the participants declared that the anatomy education should be integrated to clinical education of the orthopedics and traumatology internship.

The final direct question was: "Which of the courses given during the basic medical education period should be integrated into the clinical training education?". The results showed that 69.59% of the participants suggested anatomy to be integrated to the clinical internships. In addition to anatomy, the other answers were physiology and pharmacology.

Discussion

There have been debates about the place of anatomy in the medical curriculum.[5,10–12] There has been little consensus among medical education models on issues such as how much time should be devoted to anatomy education, how much content should be included, and how anatomy education should be given.[13]

Considering the history of medical education, it is seen that anatomy education is generally given in the first year of the undergraduate period. Although the specialists in clinical training re-evaluate the anatomy during the examinations, the physician candidates are exposed to very limited anatomy teaching in the following periods. It may be a solution to integrate anatomy education with vertical integration into the medical curriculum so that students can be exposed to anatomy education both in pre-clinical and clinical practice and in later professional life. By adapting this method, the amount of unnecessary theoretical anatomy knowledge given as a basis for clinical training and practice at the beginning of medical education will be reduced.[1]

In the report titled "Tomorrow's doctors: recommendations for undergraduate medical education" published by the General Medical Council in 1993, it was stated that the discontinuation of discipline-based education and the application of integrated (integrated) medicine formed by the combination of basic medicine and clinical medicine disciplines would be more effective.[14] Tomorrow's doctors (1993) stipulated that basic education in the first years of undergraduate education should be revised in later years.

The clinical importance and application of the anatomy, which is acquired in the first years of basic education is forgotten in the following years. Clinical educators reported that basic knowledge of clinical education should be reconstructed before moving into clinical practice.[2,15–17] The needs for the integration of the subjects in the curriculum have been clearly discussed in medical education meetings and published in the literature.[3] It was emphasized that the contents of the curriculum applied in medical schools should be oriented to the application by integration.[15]

In our study, 82.98% of the volunteers who participated in the survey answered that they needed to repeat anatomy knowledge in surgical trainings. Although anatomy education seems necessary mostly for surgical sciences, it is also important for any healthcare provider who will apply invasive procedures to the patients. Anatomy is necessary for performing emergency procedures, evaluating radiological images, performing a physical examination of a patient, and referring the patient to another doctor. This requirement is common to all branches of medicine.[1]

In the study of Waterson and Steward[12] in which 362 specialist doctors from Aberdeen University hospitals consulted, 64% of the participants stated that the current students did not have sufficient anatomy knowledge and 22% stated that the knowledge base was sufficient. In our study, totally 61.5% of the participants (18.8 strongly disagree, 42.7 disagree) declared that at the beginning of the clinical education, they didn't remember most of the anatomy knowledge they received during the basic medical education (Survey question 1, **Table 1**).

In the study by Waterson and Steward,[12] 68% of the participants stated that extending anatomy education to the medical curriculum would be valuable, while 17% stated that it would not be. In our study, in total, 53.1% of participants (39.1% agree, 14.0 strongly agree) stated that topographic anatomy should be integrated into clinical education (Survey question 7) and totally 82.3% of the participants (51.6 agree, 30.7 strongly agree) declared that systematic anatomy should be integrated into clinical education (Survey question 9, **Table 1**).

In current study, 51.34% of the participants stated that the clinical anatomy should be taught with examples of the cases related to diseases and 32.53% stated that more usable information should be taught without unnecessary details. In the study of Waterson and Steward,[12] the participants have come to a general consensus that the clinical significance of the anatomical structures should be taught rather than morphological details in the first years of undergraduate education.

Medical education is an interactive transformation process that results in students learning to care for patients by actively interacting with people. Much of this process can take place in clinical skill laboratories where basic and clinical sciences can be integrated.[18] Educators who organize medical education curriculum should adjust the most appropriate balance between basic and clinical sciences. In innovative educational approaches such as problem-based learning it is aimed to integrate clinical sciences with basic sciences.[6]

In a study of Khan et al.[19] majority of the 200 participants agreed that "Applying anatomy knowledge to clinical practice is a skill that should be reinforced early in medical education". And nearly all of them agreed "With anatomy, it is first necessary to learn as many facts as possible and then learn to apply them in the clinical skills".

As a result of the study conducted by Dawson et al.;[2] 48% of the students who were at the beginning of the clinical education stated that the basic anatomy education received in the first years should be given in the form of teaching packages in the following years. Most of the students who are at the beginning of their clinical practice

Table 1

The descriptive statistical analysis including the frequency distributions (%), mean score and standard deviation values of the answers given to the questions. .

Questions	Strongly disagree	Disagree	Undecided	Agree	Strongly agree	Mean±SD
At the beginning of the clinical education (Period 4-5), I remembered most of the anatomy knowledge I received during the basic medical education.	18.8%	42.7%	21.5%	15.8%	1.2%	2.37±0.54
In the clinical education process, I used and benefited most of the anatomy knowledge I received during basic medical education.	9.0%	32.8%	27.5%	28.1%	2.7%	2.83±0.56
During the clinical education process, I needed the anatomy knowledge I received during the basic medical education period, but I needed to study this information again.	0.3%	6.6%	8.7%	54.3%	30.1%	4.07±0.45
In my clinical education, I used my resources in basic medical education in terms of anatomy knowledge.	9.0%	30.1%	11.6%	37.9%	11.3%	3.12±0.66
In the clinical training, deeper and advanced information was given in terms of anatomy.	18.5%	45.4%	18.2%	13.4%	4.5%	2.40±0.6
Education of topographic anatomy (introduction to anatomy, basic information about anatomy, muscle, bone and joint anatomy) is sufficient to be given in basic medical sciences.	8.1%	36.4%	17.3%	31.6%	6.6%	2.92±0.61
Topographic anatomy training should also be given within clinical sciences.	5.4%	23.0%	18.5%	39.1%	14.0%	3.33±0.62
Systematic anatomy (circulatory, respiratory, urogenital, digestive and nervous system anatomy) education is sufficient during the basic medical education period.	15.8%	45.1%	19.7%	15.2%	4.2%	2.46±0.57
Systematic anatomy training should also be given at the beginning of the relevant clinical education within the clinical sciences.	5.0%	6.3%	9.9%	51.6%	30.7%	4.03±0.48
Anatomy education in the clinical sciences period should be given by the specialist of the relevant clinical education.	3.0%	11.9%	28.4%	45.7%	11.0%	3.50±0.52
Anatomy education should be given by anatomists during the clinical education period.	7.2%	27.5%	31.6%	25.7%	8.1%	3.00±0.58
Anatomy education in the clinical education period should only be repeated as a seminar.	7.5%	7.5%	21.5%	43.9%	4.2%	3.14±0.57
Anatomy training during the clinical training period should be repeated on the cadaver.	15.5%	31.9%	18.5%	25.7%	8.4%	2.79± 0.66
Anatomy training during the clinical training period should be repeated both as a seminar and on the cadaver.	9.3%	29.9%	20.0%	28.1%	12.8%	3.05±0.66
Anatomy education in the clinical education period should be interactive and student-centered.	1.2%	6.6%	10.7%	52.2%	29.3%	4.01±0.48
Anatomy training should also be in the 3rd year	13.4%	27.5%	23.9%	26.3%	9.0%	2.89±0.65

agreed that anatomy lectures should be given in general surgery, cardiology and orthopedics departments. 69.6% of those who completed their clinical practice stated that anatomy lectures should be given in general surgery and orthopedics departments.

In our study, 31.37% of the participants stated that anatomy education should be integrated before starting the general surgery internship and %14.32 of the participants suggested that the anatomy education should be integrated to clinical education of the orthopedics and traumatology internship. Finally we would like to emphasize once more that anatomy education is an important part of clinical education, and that education should be based on practical training with cadavers.[20]

As conclusion, the results of the feedback received from the students indicated that some of the anatomy knowledge obtained in the period of pre-clinical period was forgotten until the clinical internship education and they had to be remembered again. In this context, we believe that integrating anatomy courses into clinical internship education and applying the vertical integration model by reviewing the curriculum will increase the quality of medical education.

Conflict of Interest

There are no conflicts of interest.

Author Contributions

All the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version. All authors have read the content of the article and accept their responsibility. SB: project development, data collection, data analysis, manuscript writing, editing manuscript; NTC: project development, manuscript writing; IMK: project development, data analysis, manuscript editing; MOA: data analysis, manuscript editing.

Ethics Approval

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A rare anastomosis between basilic and brachial veins

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Abstract

Variations in the veins of upper extremity are common. Knowing these variations is important for interventions to be carried out in this region. In this case report, a rare anastomosis between basilic vein and brachial vein is presented. During a routine cadaver dissection, a short and thick branch of the basilic vein was noticed to provide anastomosis between the basilic vein and the brachial vein in the right upper extremity of a 54-year-old male cadaver. The diameter of the basilic vein was quite narrow at the proximal part above the anastomosis. In addition, the axillary vein was noticed to be formed as a continuation of brachial vein, not basilic vein. The variation presented in this case report may cause serious complications, such as the rupture of the vessel in venous interventions related with the basilic vein.

Keywords: basilic vein, brachial vein, venous anastomosis, venous catheterization

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Introduction

Basilic vein (BV) is one of the major superficial veins of the upper limb. The BV starts from the medial side of the dorsal venous network of the hand and goes up the ulnar side of the dorsal aspect of the forearm. The BV, which runs superficially along the medial edge of the biceps brachii, gets deeper by piercing the deep fascia slightly below the middle part of the arm and continues as the axillary vein (AV) in the axillary fossa. Brachial vein (BrV) is one of the deep veins of the upper extremity and it is usually a paired vein as lateral and medial BrV. BrV, which is formed by the combination of radial and ulnar veins, drains into the AV in the axillary fossa.[1]

Variations in the veins of the upper extremity are common.[2] Anatomical variations in these veins are important for procedures such as blood sampling, blood transfusion, hemodialysis and venous catheterization.[3,4] It has been reported that the variations of these veins may cause complications such as hematoma.[5]

The aim of this study was to report a rare anastomosis between BV and lateral BrV, which may be significant during venous interventions.

Case Report

During a routine cadaver dissection performed in the laboratory of Gaziantep University Faculty of Medicine, Department of Anatomy, a short and thick branch of BV was noticed to provide an anastomosis between the BV and BrV, at the proximal 1/3 of the right arm of a 54-year-old male cadaver. This branch emerged from the BV after it pierced the deep fascia. This anastomotic branch separated from the BV run proximally and drained to the lateral BrV at an angle of 140 degrees (**Figure 1**). It was observed that the diameter of the BV in the proximal part above the anastomosis (1.5 mm) was narrower when compared to the diameter at the distal part below the anastomosis (4 mm). The diameter of the lateral BrV at the proximal part above the anastomosis (5.5 mm) was larger than the diameter at the distal part below the anastomosis (5 mm). Approximately 2 cm above the anastomosis, the medial BrV and lateral BrV united to each other and drained into the AV. Contrary to the normal configuration, AV was seen to be a continuation of BrV, not BV. The variation was unilateral and the left arm of the cadaver showed a regular pattern in terms of venous drainage.

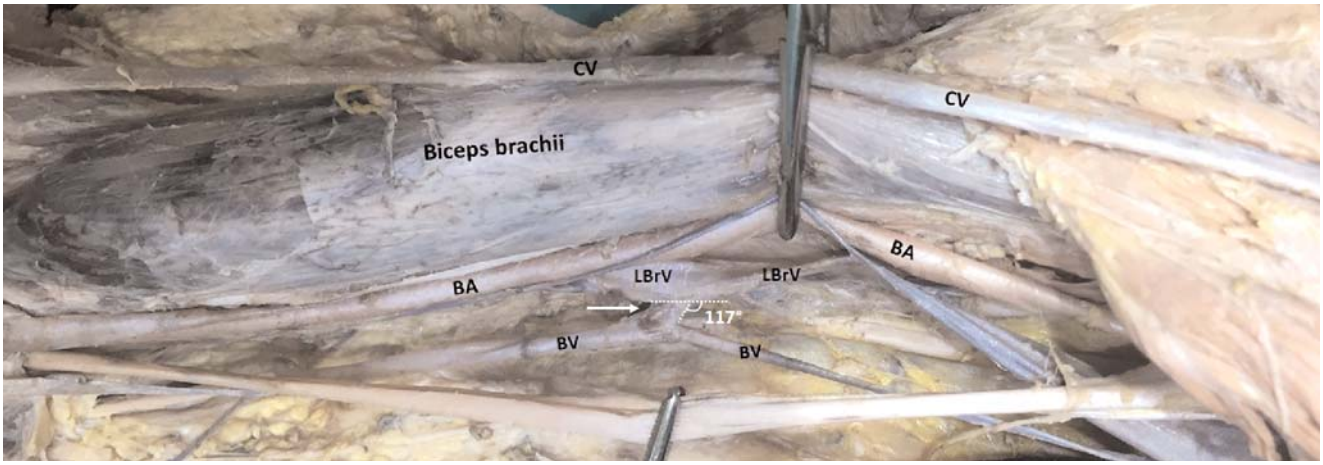

Figure 1. Anterior view of the arm. Anastomotic branch (**white arrow**) that provides anastomosis between the **BV** (basilic vein) and **LBrV** (lateral brachial vein). **BA:** brachial artery; **CV:** cephalic vein.

Discussion

In addition being a suitable vein for venipuncture, the BV can be used as a graft in arteriovenous graft or fistula procedures applied for vascular access in patients with chronic renal failure and in bypass operations when the great saphenous vein is not suitable as a graft.[3,6] BV can also be preferred for peripheral venous catheterization.[4] For this reason, a through information regarding the anatomical course and variations of BV is important in terms of reducing the risk of complications in clinical interventions.

In this case report, BV was observed to make anastomosis with lateral BrV in the proximal arm through a thick and short branch. In a detailed literature review, it was found that there was only one case with an anastomotic connection similar to this case between BV and BrV in the upper arm.[7] In the case reported by Kumar et al.,[7] unlike the present study, it was reported that a single BrV in the middle of the arm combined with the BV without an anastomotic branch, providing an anastomosis in the form of a chiasma. Moreover, BV and BrV were separated from each other after a short course.

Although there are quite a limited number of studies reporting BV agenesis in the upper extremity,[8] there are studies reporting a BV thinner than normal.[2,9] Okamoto[9] reported the presence of two very thin BV in the 200 arms they examined. According to what has been reported in classical anatomy books; BV, which is thicker than cephalic vein (CV), increases in diameter from the arm to the axillary fossa and continues as AV in the axillary fossa.[1] In this case report, it was determined that BV is getting thinner at the proximal part of the anastomosis in the arm. Due to the narrower diameter of BV at the proximal part above the anastomosis and the presence of a thick anastomotic branch, it is predicted that a significant part of the blood in the BV drains into the lateral BrV through this anastomosis.

In this case, there are two ways the catheter can proceed; in the first condition, the catheter may move above the anastomosis through the BV, whose diameter is much narrower than normal. In the second condition, the catheter may enter the anastomotic branch, and then the lateral BrV. Since the vein is narrow in the first, and in the second, there is an angulation between the two veins (BV and lateral BrV), which may cause difficulty in advancing the catheter, furthermore, the vein may rupture.

Conclusion

In this study, a rare anastomosis between BV and lateral BrV via a short and thick branch is reported. Such a variation can create a barrier to the catheter that travels through the vessel during the venous catheterization process using BV. During such a procedure, if the practitioner encounters resistance in the arm area, it should be taken into consideration of the possibility of such a variation. For invasive procedures to be applied in this region, especially venous catheterization, it is important to know the normal anatomy and variations of the vessels of this region.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

Author Contributions

SSA: data collection, data analysis, manuscript writing and editing; MO: data collection, data analysis, manuscript writing and editing.

Ethics Approval

The study was conducted in accordance with the ethical rules of the Declaration of Helsinki and its later amendments. Scientific studies on cadaver in our institution do not require ethical approval.

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Radio-anatomical aspects of a rare case: interpeduncular lipoma

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Abstract

Intracranial lipomas can be associated with other congenital abnormalities, but they are commonly found incidentally on imaging studies. Although the location of intracranial lipomas can be quite variable, they are extremely rare in interpeduncular fossa. We report a case of interpeduncular lipoma with its radio-anatomical features in terms of distinction with pathologies that can appear similarly, as the unexpected location of rare cases can be challenging for radiologists. The MR images of a 55-year-old male patient suffering from episodic dizziness attacks and impaired walking showed two different lipoma masses in interpeduncular fossa and chiasmatic cistern which are isointense with adipose tissue in T1, T2-weighted and FLAIR sequences. Intracranial lipomas can be located in the corpus callosum and almost in all cisterns, however they are extremely rare in interpeduncular fossa. Due to the mass effect, the structures located in close proximity of the lipomas should be evaluated.

Keywords: anatomy; interpeduncular lipoma; MRI

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Introduction

Lipomas, which are benign masses, are seen rarely in the central nervous system. They account for less than 0.1% of all intracranial tumors.[1] Although intracranial lipomas (ICL) can be associated with other congenital abnormalities, they are commonly found incidentally on imaging studies. The patients present rarely with neurological symptoms that differ according to the location of the lesions. Therefore, ICL can cause persistent headaches, convulsions, mental retardation, and cranial nerve defects.[1–3]

The location of ICL can be quite variable. However, most of them are located in the pericallosal cistern with the incidence of 0.011%.[4] It is less common for ICL to be on the surface of cerebral hemispheres and in the interpeduncular fossa. It could be estimated that interpedicular lipomas account for approximately 2% of all ICL.[5] We report a case of interpeduncular lipoma with its radio-anatomical features in terms of distinction with pathologies that can appear similarly, as the unexpected location of rare cases can be challenging for radiologists.

Case Report

A 55-year-old male patient suffering from episodic dizziness attacks for 23 years applied to the neurology department when his headache was increased over the last two weeks. His past medical history revealed that he used olmesartan and acetylsalicylic acid with the diagnosis of hypertension. The patient's presyncope and dizziness attacks lasted 7–8 seconds in transition to the erect posture. He said that his walking balance was impaired during attacks, regardless of the direction of the motion. Neurological examination showed ataxia without lateralization in the straight line and persistent horizontal nystagmus with a rapid phase in the direction of gaze. The patient had no nausea and objective vertigo tests were negative. There was no signs of diplopia, dysphagia, dysarthria, or facial deficits but there was low frequency tinnitus in the right ear.

Upon these physical examination findings, brain MRI was requested with suspicion of posterior fossa pathology and the patient was scanned with GE™ Signa Explorer device (General Electric Healthcare, Boston,

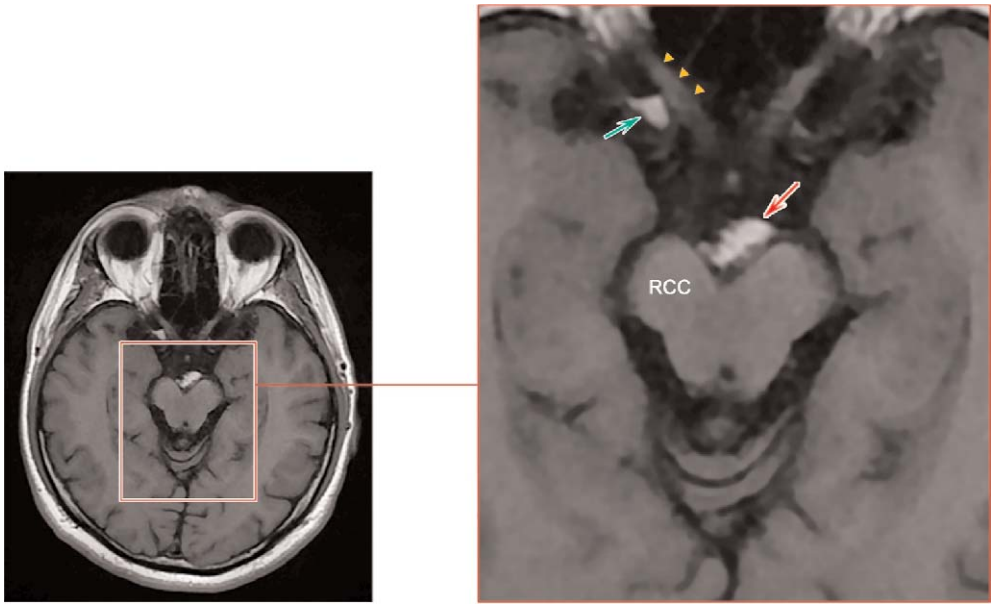

Figure 1. T1-weighted axial image. Hyperintense lesions in interpeduncular fossa (**red arrow**) and chiasmatic cistern (**green arrow**) in close proximity of the optic nerve (**orange triangles**) were defined as lipomas. **RCC:** right cerebral crus.

MA, USA). Images were taken in sagittal T1-weighted (T1W) (TR: 2534, TE: 10.8), coronal T2-weighted (T2W) (TR: 4133, TE: 96.5), axial T1W (TR: 2115, TE: 9.3), T2W (TR: 7885, TE: 108) and fluid attenuated inversion recovery (FLAIR) (TR: 9000, TE: 94.6) sequences with a slice thickness of 5 mm. There was no pathology in the posterior fossa on imaging.

In all sequences, two lipoma masses which are isointense with adipose tissue were detected. First one, which was extended more prominently to the left of the midline, was approximately 12.2×8.5 mm in size and localized in the interpeduncular cistern (**Figures 1** and **2**). Second one was approximately 6.2×5.1 mm in size and located at the lateral side of right carotid artery and optic nerve in the anterolateral of the chiasmatic (suprasellar) cistern (**Figures 1**, **3** and **4**). Lesions were suppressed in the FLAIR images (**Figure 5**). There were no signs of restricted diffusion but mild chronic ischemic-gliotic changes were observed in the cerebral parenchyma.

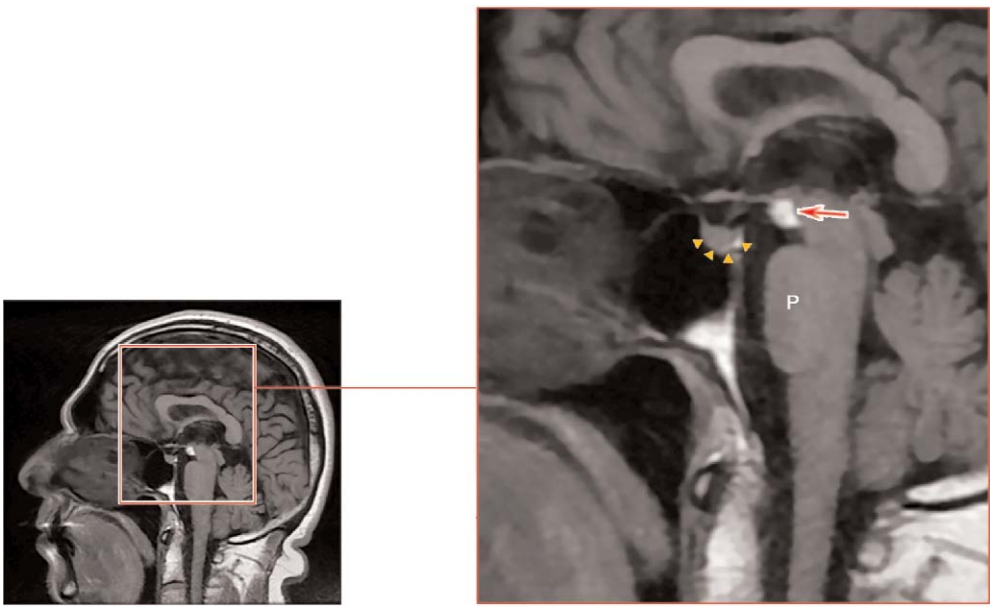

Figure 2. T1-weighted sagittal image. Interpeduncular lipoma (**red arrow**), sella (**orange triangles**) and pons (**P**) were demonstrated.

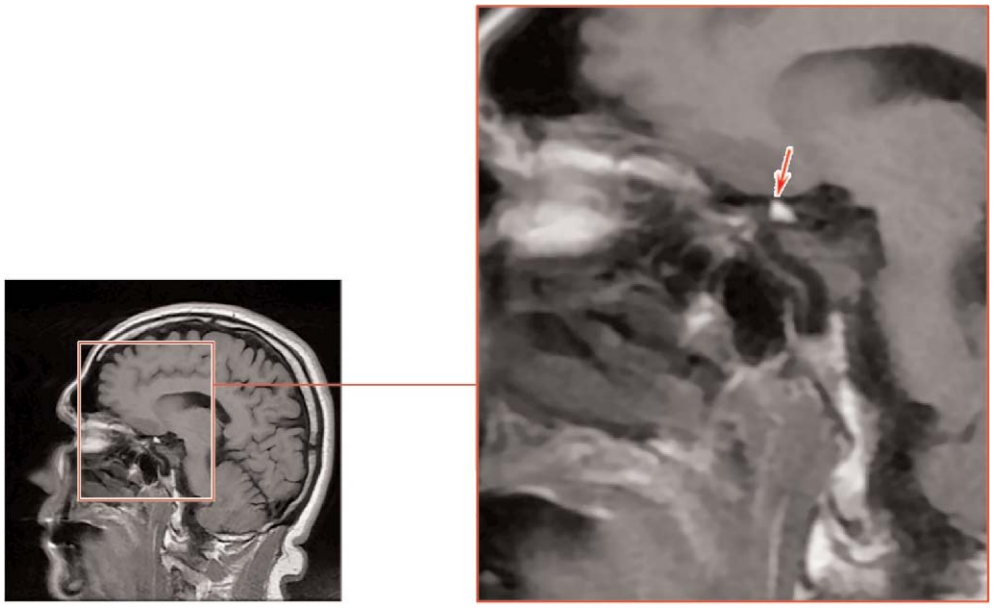

Figure 3. T1-weighted sagittal image of the lipoma in chiasmatic cistern (**red arrow**).

Significant inflammatory mucosal changes in the right frontoethmoidal sinus and chronic mucosal retention cyst in the lateral wall of the left maxillary sinus were present in the sinonasal cavities on imaging.

Discussion

ICL can be located in the corpus callosum and in almost all cisterns, however they are extremely rare in interpeduncular fossa.[5] It can be said that the incidence of ICL are not related to age or gender. These lesions are considered as congenital midline malformations. Although there are several explanations for development of the ICL in the central nervous system, it is widely accepted that abnormal persistence and differentiation issues of the primitive meninges lead to expand adipose tissue in the subarachnoid space and ultimately cause lipomas which might be supported by the cisternal localization of the most ICL.[6]

Neurological symptoms are rare due to the fact that ICL grows very slowly. Therefore, these cases are often detected incidentally. Headaches, epilepsy and rarely hydrocephalus might be associated with ICL.[7] They may need to be surgically removed to relieve pressure or open blockages. Due to the mass effect, the immediate neighborhoods of the lesion should be described in detail. The absence of any vision problems or strabismus in our case is due to the fact that the tumor did not exert any pressure on the optic nerve or other motor nerves of the eye, as seen in the scans. However, it can be thought that ataxia, nystag-

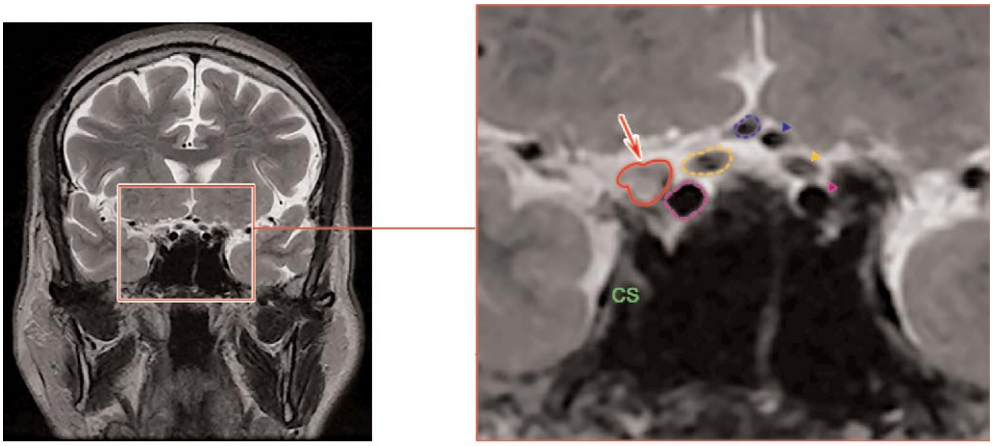

Figure 4. T2- weighted coronal image. Lipoma in chiasmatic cistern (**red arrow and circle**), right and left optic nerves (**orange dashed circle-orange triangle**), right and left anterior cerebral arteries (**blue dashed circle-blue triangle**), right and left internal carotid artery (**purple dashed circle-purple triangle**), right cavernous sinus (**CS**).

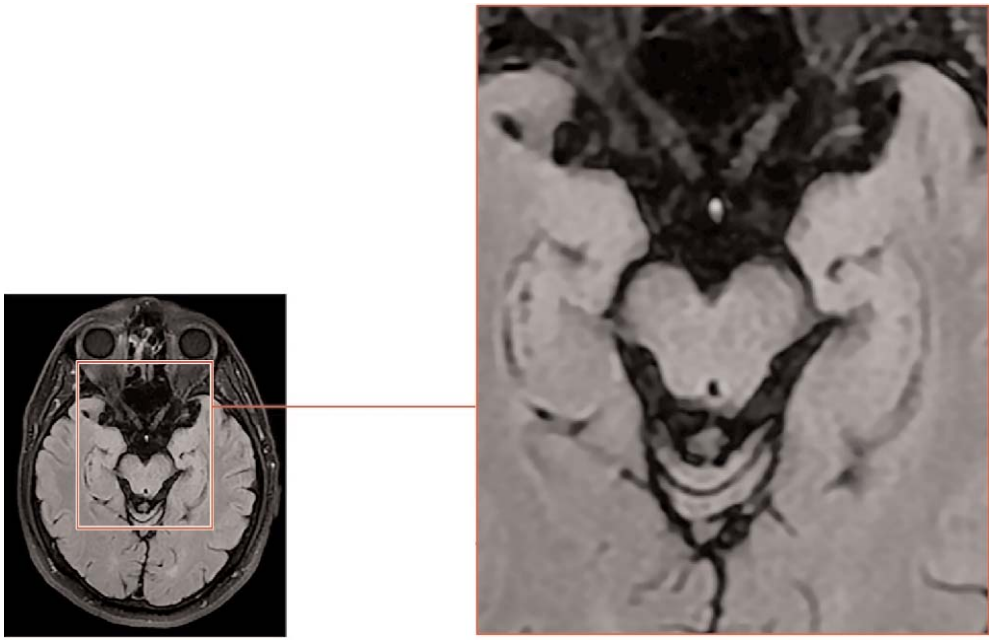

Figure 5. FLAIR axial image taken from the same level as the **Figure 1**. Lipomas are suppressed in this sequence.

mus, tinnitus and presyncope attacks may occur due to increased intracranial pressure or instant pressure peaks in the associated vascular network.

Lipomas appear as homogeneous and hyperintense masses on T1W and T2W images, while they are hypointense on fat suppressed T1W and T2*W. The reason why they are hypointense in T2*W is magnetic susceptibility and chemical shift effect. The visibility of lipomas is not enhanced with contrast material. Computerized tomography (CT) scans may help in diagnosis. Lipomas usually have density of between -50 UH and -100 UH on CT.[8]

It can be said that it is not difficult to make a diagnosis on MR images, since the lesion is in adipose tissue intensity in all sequences. However, fat suppressed sequences should not be ignored for more reliable diagnosis. Additionally, in some cases, calcification may accompany these lesions.[9] If fat suppressed sequences or diffusion weighted images are not taken into consideration, ICL may be confused with pathologies such as dermoid cyst, white epidermoid cyst, hemorrhagic intracranial metastasis, metastatic melanoma or subacute hematoma, which may give a similar appearance on other sequences.[5,10] Moreover, a confusing appearance may occur due to lipomatous transformation of neuroectodermal tumors which notably is rare. Dermoid cysts are high intensity on T1W images and more heterogeneous than lipomas.[11] Consequently, radio-anatomic features of these lesions could be essential for management of the cases.

Conflict of Interest

The authors have no conflicts of interest to disclose.

Author Contributions

FÇ: scanning and clinical follow-up, critical revision of manuscript; MAG: manuscript writing and editing.

Ethics Approval

This report has been prepared in accordance with the Helsinki Declaration and does not require any kind of approval of the Ethical committee. However, informed consent obtained from the patient for the report to be published.

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