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# The Clinical and Radiological Evaluation of Impacted Third Molar Position, Crown and Root Morphology

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**Abstract**

**Objective**. This study aimed to analyze the crown and root morphology of maxillary and mandibular third molars, and assess their position in relation to adjacent anatomical structures using clinical examination and radiographic images. **Materials and Methods**. A total of 176 extracted impacted or partially impacted third molars were included in this study. Orthopantomogram images (OPG) were used to evaluate the number of roots, position, depth of impaction relative to the occlusal plane of the second molar, and angulation of maxillary and mandibular third molars. The extracted teeth were examined to determine the actual number of roots. The root morphology was classified using the Alavi classification system for maxillary third molars and the Machado classification for mandibular third molars. Additionally, the number of cusps, crown dimensions, and morphology were analyzed using digital and dental calipers. **Results.** The extracted samples exhibited a significantly higher number of roots compared to the number assessed on OPG images ($P<0.001$). The majority of mandibular third molars had two fused roots (37.39%) and a five-cuspid crown (48.70%), while maxillary third molars had three fused roots (26.23%) and four cusps (42.62%). Both maxillary (60.66%) and mandibular third molars (61.74%) were predominantly vertically positioned. Regarding the depth of impaction, maxillary third molars were primarily classified as Class C (65.57%), while mandibular third molars were classified as Class B (47.83%). Differences in crown shape were observed, with maxillary crowns being mostly triangular (36.07%) and mandibular crowns being oval (38.26%). Maxillary third molars had shorter crowns compared to mandibular third molars ($P<0.05$). **Conclusion.** The root morphology of maxillary and mandibular third molars in the population of Bosnia and Herzegovina displays variability. Orthopantomogram imaging was found to be inadequate for accurate determination of the number of roots in third molars. The number of cusps on third molars cannot be relied upon as a predictor of the number of roots. The study's findings will have implications for dental practice, particularly for oral surgeons and restorative dentists.

**Key Words:** Wisdom Teeth ▪ Impacted Third Molar ▪ Root Morphology ▪ Crown Morphology ▪ Depth Of Impaction.

## Introduction

The impaction of third molars is considered a developmental feature of modern civilization that occurs due to a lack of space for their eruption, the presence of physical barriers that prevent them from reaching the occlusal plane, and malposition (1).

It is well known that third molars are characterized by morphological complexity and that their place within the dental arch affects almost all dental disciplines (2, 3). Their distal position and enhanced fissure system contribute to plaque retention and the development of caries, which consequently leads to the need for tooth restoration and endodontic treatment (4). From a dental prosthetic point of view, they can act as abutments for fixed prosthetic restorations (5). Difficulties

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with the eruption of third molars and their often irregular position in the oral cavity can affect the results of orthodontic treatment and lead to periodontal disease (6). In oral surgery, it is of great importance to be familiar with the morphological characteristics of third molars, as their operative extraction is one of the most common oral-surgical interventions (7). Both clinical and radiographic evaluation of the position of the third molars should be performed to reduce complications and achieve the best possible outcome. To the best of our knowledge, this is the first study that addresses the morphology of impacted and partially impacted third molars in the population of Bosnia and Herzegovina.

Therefore, the goals set for this study were to analyze the number and morphology of maxillary and mandibular third molar roots, the morphology and dimensions of their crowns, and their position regarding adjacent anatomic structures, using clinical examination and radiographic images.

## Materials and Methods

### *The Sample*

The patients were recruited from the Department of Oral Surgery, University of Sarajevo, Faculty of Dentistry with Dental Clinical Center, and they submitted signed informed consent forms after being introduced to the details of the study. With the exception of samples with crowns and roots damaged during operative extraction, fractured roots, and incomplete root and crown development, all intact, surgically extracted, impacted or partially impacted third molars were included in the study. Initially, 176 third molars (61 maxillary and 115 mandibular) were included in the study. The total sample size was drawn from 140 patients, with the youngest being 14 years old and the oldest being 59 years old (39 men and 101 women). The extracted teeth were stored in a 3% solution of sodium hypochlorite (NaOCl).

### *Analysis of the Orthopantomogram Images*

OPG images were used to determine the number of roots, the position of the third molars, the depth of their impaction measured in relation to the occlusal plane of the second molars, and the angulation of the maxillary and mandibular third molars (8-10). Orthopantomogram imaging was also used preoperatively to assess the number of roots of impacted and partially impacted third molars. The samples were divided into three categories: Group 1 had a single root, Group 2 had two roots, and Group 3 had three roots.

### *Analysis of the Number and Morphology of the Roots of Extracted Impacted or Partially Impacted Third Molars*

The extracted teeth were used to determine the real number of roots. On the basis of the data acquired, the sample was divided into 4 groups: Group 1 had a single root, Group 2 had two roots, Group 3 had three roots, and Group 4 had four roots.

In terms of morphology and the number of roots, maxillary third molars were classified using the Alavi classification system, while mandibular third molars were classified using the Machado classification (11, 12). In detail, the Alavi classification divides upper wisdom teeth into ten classes based on the number and shape of their roots (I- three roots: all separate, II- three roots: Buccal roots fused, III- three roots: Distobuccal and palatal fused, IV- three roots: all fused, V- two roots separate, VI- two roots fused, VII- one root conical, VIII- one root C shaped, IX-four roots fused, X- four roots other (11). According to root morphology, the Machado classifies mandibular third molars as convergent, parallel, fused, single, or divergent (12).

### *Analysis of the Crown Morphology of Impacted and Partially Impacted Third Molars*

The samples were used to analyze the number of cusps and the shape of the crown. The shape of the crown was classified according to the geometric figure it resembled: oval, cubic, rectangular, rhomboid, circular, triangular, and trapezoidal (13).

### *Metric Analyses of the Samples*

Metric analyses were performed using a stereomicroscope (Kern Opticus OZL 464) at 15x

magnification. The samples were photographed using a Kern Opticus ODC 824 camera, and digital images were stored in JPEG format. The digital caliper was calibrated and adjusted before each measurement on the basis of the calibration block, which is an integral part of the Kern Opticus OZL 464, in accordance with the manufacturer's instructions. In other words, the distance measured by the digital caliper must correspond to the distance measured by two points on the calibration block. JPEG images of the third molars were used to measure the length of the third molar roots, the mesiodistal (MD) diameter, and the buccolingual (BL) diameter of the crown, using a digital caliper. The "single line" option was used to measure the crown's MD and BL diameters, while the "polyline" software option was used to measure the length of the roots, due to their variable morphology and curvature. The measurements were given in millimeters.

A dental caliper was used to measure the dimensions of the extracted teeth: crown length (from the crest of the buccal cusp or cusps to the crest of curvature at the cementoenamel junction), root length (from the crest of curvature at the crown cervix to the apex of the root), tooth length (from the crest of the buccal cusp or cusps to the apex of the root), the MD diameter of the tooth crown (from the crest of the curvature on the mesial surface (mesial contact area) to the crest of the curvature on the distal surface (distal contact area), the MD diameter of the crown cervix (from the junction of the crown and root on the mesial surface to the junction of the crown and root on the distal surface), the BL diameter of the crown (from the crest of the curvature on the buccal surface to the crest of the curvature on the lingual surface), and the BL diameter of the crown cervix (from the junction of the crown and root on the buccal surface to the junction of the crown and root on the lingual surface) (14). The measurements were also given in millimeters.

### *Ethics Statement*

The study was approved by an Institutional Ethical Review Board (No. 02-3-4-59-1-4/2021).

### *Statistical Analysis*

Descriptive analysis was used to describe and present the characteristics and dimensions of the upper and lower third molars. Continuous variables were presented as means with standard deviations, and categorical variables were presented as percentages. Additionally, t-tests and one-way ANOVAs (analysis of variance) were conducted. Statistical analyses were performed using IBM SPSS software, version 23 (Chicago IL).

## Results

Patients who underwent surgery were both male and female, with a mean age of 22.8, SD 6.47.

Out of the 176 third molars included in the study (61 maxillary and 115 mandibular), 89 were impacted and 87 were partially impacted. The frequency of upper and lower third molars in relation to diagnosis, angulation, crown and root morphology, and depth of impaction is shown in Table 1 (A and B).

### *Root Morphology*

According to the Alavi classification for upper third molars, the most frequent finding for upper third molars is a fusion of three roots (Class IV) (Table 1 A). The Machado classification system states that the fusion of roots is the most common finding for lower third molars (Table 1 B).

The number of roots found on OPG images and the number of roots detected on extracted teeth is shown in Figure 1. The dependent samples t-test showed a statistically significant difference between the average number of roots found on OPG and the actual number of roots, i.e., a statistically significant greater number of roots was found on the extracted third molars than on OPG images, $t(175) = -10.776$; $P<0.001$.The range of the average dimensions of the maxillary and mandibular third molars measured by dental and digital calipers (DC) can be found in Table 2.

Table 1. Descriptive Statistical Parameters: Diagnosis, Angulation, Crown Shape, and Depth of Impaction of Maxillary and Mandibular Third Molars

| A Maxillary third molars | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Diagnosis N (%) | | Angulation N (%) | | Shape of the crown N (%) | | Root morphology according to Alavi N (%) | | Depth in relation to occlusal plane N (%) | |
| Impacted | 39 (63.93) | Vertical | 37 (60.66) | Oval | 7 (11.47) | Class I | 4 (6.55) | A | 6 (9.84) |
| Partially impacted | 22 (36.07) | Mesioangular | 14 (22.95) | Cubic | 2 (3.28) | Class II | 5 (8.20) | B | 15 (24.59) |
| | | Distoangular | 9 (14.75) | Rectangular | 1 (1.64) | Class III | 12 (19.67) | C | 40 (65.57) |
| | | Horizontal | - | Rhomboid | 19 (31.15) | Class IV | 16 (26.23) | | |
| | | Linguoangular | - | Circular | 4 (6.55) | Class V | 2 (3.28) | | |
| | | Buccoangular | 1 (1.64) | Triangular | 22 (36.07) | Class VI | 2 (3.28) | | |
| | | | | Trapezoidal | 6 (9.84) | Class VII | 4 (6.55) | | |
| | | | | | | Class VIII | 3 (4.92) | | |
| | | | | | | Class IX | 6 (9.84) | | |
| | | | | | | Class X | 7 (11.48) | | |
| Total | 61 (100) | Total | 61 (100) | Total | 61 (100) | Total | 61(100) | Total | 61 (100) |
| B Mandibular third molars | | | | | | | | | |
| Diagnosis N (%) | | Angulation N (%) | | Shape of the crown N (%) | | Root morphology according to Machado N (%) | | Depth in relation to occlusal plane N (%) | |
| Impacted | 50 (43.48) | Vertical | 71 (61.74) | Oval | 44 (38.26) | Convergent | 16 (13.91) | A | 39 (33.91) |
| Partially impacted | 65 (56.52) | Mesioangular | 32 (27.82) | Cubic | 19 (16.52) | Parallel | 25 (21.73) | B | 55 (47.83) |
| | | Distoangular | 4 (3.48) | Rectangular | 12 (10.43) | Fused | 43 (37.39) | C | 21 (18.26) |
| | | Horizontal | 3 (2.61) | Rhomboid | 4 (3.48) | Single | 4 (3.47) | | |
| | | Linguoangular | 5 (4.35) | Circular | 7 (6.09) | Dilaceration | 19 (16.52) | - | - |
| | | Buccoangular | - | Triangular | 5 (4.35) | Divergent | 8 (6.95) | | |
| | | | | Trapezoidal | 24 (20.87) | | | | |
| Total | 115 (100) | Total | 115 (100) | Total | 115 (100) | Total | 115 (100) | Total | 115 (100) |

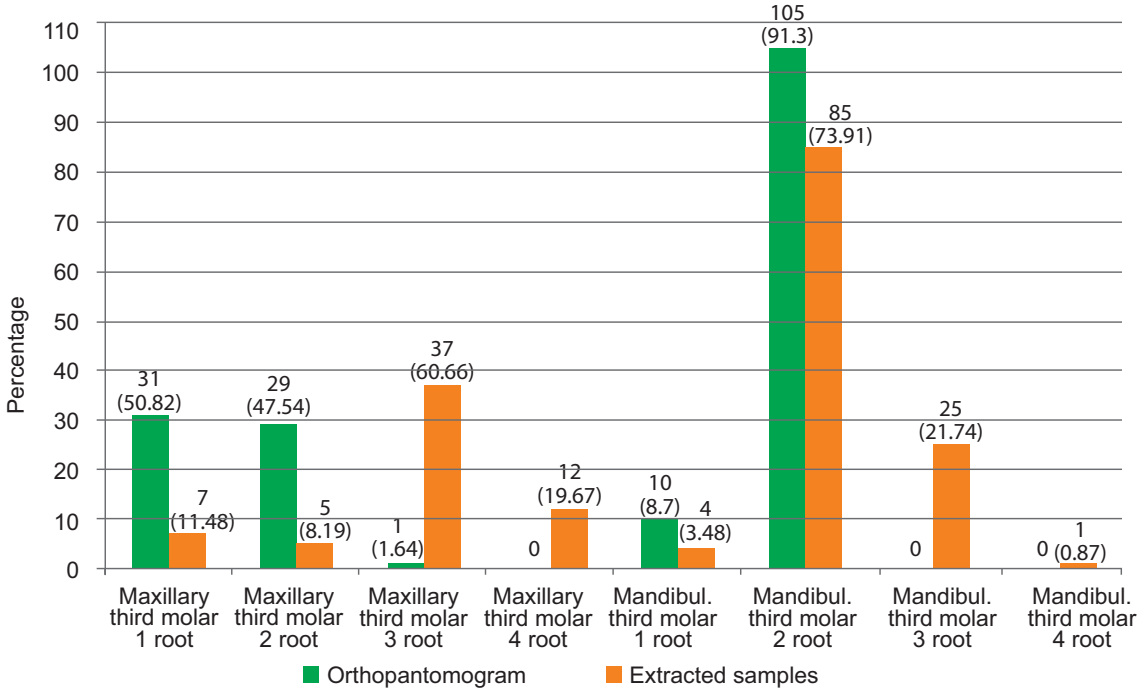


Figure 1. The frequencies of the number of roots of the upper and lower third molars based on the orthopantomogram and extracted samples.

Table 2. Upper and Lower Third Molar Average Dimensions in mm Measured with a Dental and Digital Caliper

| Dimension | Maxillary third molars (mm) | Mandibular third molars (mm) | P |
|---|---|---|---|
| Total length | 17.86 | 18.11 | >0.05 |
| Length of the crown | 7.23 | 7.65 | <0.05† |
| Length of the root | 10.76 | 10.71 | >0.05 |
| Mesiodistal diameter of the crown | 9.53 | 9.70 | >0.05 |
| Mesiodistal diameter of the crown at the cervix | 9.07 | 8.97 | >0.05 |
| Buccolingual diameter of the crown | 8.61 | 8.63 | >0.05 |
| Buccolingual diameter of the crown at the cervix | 8.27 | 7.93 | >0.05 |
| Length of the root DC | 10.65 | 10.52 | >0.05 |
| Mesiodistal diameter of the crown DC* | 9.38 | 9.57 | >0.05 |
| Buccolingual diameter of the crown DC* | 8.47 | 8.50 | >0.05 |

*Digital caliper; †Independent samples t-test.

### *The Average Dimensions of Lower Third Molars in Comparison to the Available Space between the Mandibular Ramus and Second Molar*

The position of third molars according to the Pell and Gregory classification is shown in Table 3. One-way between group ANOVA analysis showed a statistically significant difference in the mesiodistal diameter of the crown of lower third molars (measured with a dental caliper) within the Pell and Gregory classes, F (2, 105)=5.016; P<0.01. The post hoc Scheff test revealed a distinction between classes I and III. The mean mesiodistal diameter of the crown in class I (M=9.51; SD=0.91) was smaller than the mean mesiodistal diameter of the class III crown (M=10.50; SD=0.96), P=0.023.

One-way between group ANOVA revealed a statistically significant difference in the mesiodistal diameter of the crowns measured with a digital caliper for the Pell and Gregory classes, F (2, 105)= 5.706; P<0.01. The post hoc Sheff test revealed differences between classes I and II, as well as classes I and III. The mean mesiodistal diameter of the class I crowns (M=9.34; SD=0.83) measured with a digital caliper was significantly smaller than the mean mesiodistal diameter of the class II crowns (M=9.80; SD=0.83), P=0.038. The mean mesiodistal diameter of the class I crowns measured with a digital caliper was smaller than the mean mesiodistal diameter of the class III crowns (M=10.37; SD=0.97) P=0.016 (Table 3).

Table 3. Average Dimensions of Lower Third Molars in mm with Respect to Pell and Gregory's Classification

| Dimension | Pell & Gregory's classification of mandibular third molars | | | |
|---|---|---|---|---|
| | Class I (N=32) | Class II (N=76) | Class III (N=7) | P |
| Total length | 17.87 | 18.40 | 20.00 | >0.05 |
| Length of the crown | 7.47 | 7.93 | 7.86 | >0.05 |
| Length of the root | 11.19 | 10.52 | 11.80 | >0.05 |
| Mesiodistal diameter of the crown | 9.52 | 9.94 | 10.50 | <0.01† |
| Mesiodistal diameter of the crown at the cervix | 8.73 | 9.10 | 9.00 | >0.05 |
| Buccolingual diameter of the crown | 8.54 | 8.68 | 9.14 | >0.05 |
| Buccolingual diameter of the crown at the cervix | 7.80 | 8.14 | 8.28 | >0.05 |
| Length of the root DC | 10.66 | 10.47 | 11.77 | >0.05 |
| Mesiodistal diameter of the crown DC* | 9.34 | 9.81 | 10.37 | <0.01† |
| Buccolingual diameter of the crown DC* | 8.46 | 8.38 | 9.10 | >0.05 |

*Digital caliper; †One-way between groups ANOVA.

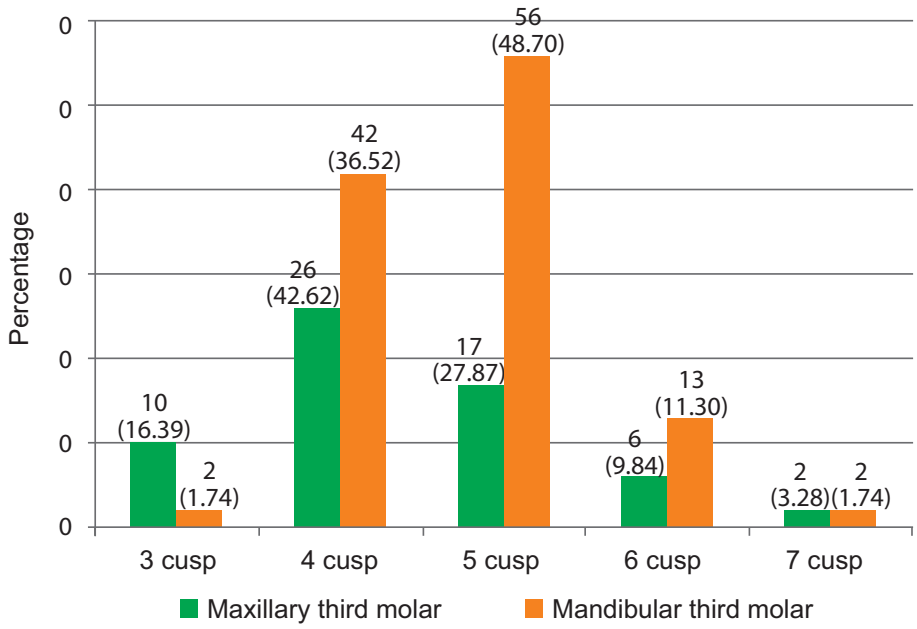


Figure 2. The frequency and percentages of the number of cusps of upper and lower third molars.

### *Crown Dimensions of the Third Molars*

Using an independent samples t-test, measurements with a dental caliper revealed a statistically significant difference in the crown length of the upper and lower third molars. The crown of the upper third molars was smaller than the crown of the lower third molars: $t(174)=-2.277$; $P<0.05$ (Table 2).

### *The Number of Cusps and Crown Shape*

The analysis of the number of cusps on the occlusal surface of third molars established five types of cusp morphology: Type-1 (three cusps), Type-2 (four cusps), Type-3 (five cusps), Type-4 (six cusps), and Type-5 (seven cusps). Type-2 was most often found in the upper third molars, while Type-3 was most commonly found in the lower third molars (Figure 2).

Maxillary third molars were found most often to have a triangular crown shape. The crowns of the lower third molars were mostly oval (Table 1). An analysis of the relationship between the number of cusps and the number of roots revealed that third molars with three cusps usually had three roots, whereas third molars with 4, 5, 6, and 7 cusps mostly had two roots (Table 4).

Table 4. The Relationship between the Number of Cusps and the Number of Roots of the Upper and Lower Third Molars

| Cusps | Number of roots | | | |
|---|---|---|---|---|
| | One | Two | Three | Four |
| Three | 3 | 2 | 6 | 1 |
| Four | 6 | 35 | 24 | 3 |
| Five | 2 | 40 | 25 | 6 |
| Six | 0 | 10 | 7 | 2 |
| Seven | 0 | 3 | 0 | 1 |

## Discussion

The population of Bosnia and Herzegovina has not been the subject of any analysis of the third molar crown and root morphology. Our study encompasses an equal number of impacted and partially impacted third molars, mostly vertically positioned, that were mainly extracted for orthodontic reasons.

This study included 176 extracted maxillary and mandibular third molars from adults of both genders. A fusion of three roots was the most

common finding for upper-third molars. Root fusion was the most common finding in lower third molars as well. The number of roots detected on extracted third molars was found to be statistically significantly greater than the number of roots seen on OPG images. The mesiodistal diameter of the crown of lower third molars differed significantly between the Pell and Gregory classes. When measured with a dental caliper and a digital caliper, Class I had a smaller mean mesiodistal diameter than Class III. The upper third molar crown was found to be statistically significantly smaller than the lower third molar crown. Type-2 (four cusps) was more common in upper third molars, and Type-3 (five cusps) was more common in lower third molars. Lower third molars were mostly oval, while maxillary third molars were mostly triangular. Third molars with three cusps typically had three roots, whereas third molars with four, five, six, or seven cusps typically had two roots.

### *Depth of Impaction*

From an oral surgeon's point of view, it is important to assess the depth of impaction accurately. The deeper the maxillary or mandibular third molar is placed within the jaw, the more complex the procedure. Our research showed that impacted upper third molars are usually in Class C (65.57%) and rarely in Class A (9.84%). Lower third molars were most commonly found in mid-deep position, Class B (47.83%) and least frequently in Class C (18.26%) (Table 1). This is in accordance with the findings of Khoury et al., who analyzed the depth of third molar impaction in the population of Lebanon (15). This outcome is contrary to that of Carvalho et al., which may be due to the larger sample size of their study. They analyzed 473 mandibular molars and found that they were in Class A in 48.4% of cases, Class B in 41% of cases, and Class C in 10.6% of cases (16).

### *Root Morphology*

One of the reasons for the complexity of third molar extraction is the variability of their root morphology, which has been the subject of many studies (11–13,17,18). Alavi et al. investigated maxillary third molars in a Thai population and established seven classes: Class I 50.9%; Class II 10.6%; Class IV 26.5%; Class VI 6.6%; Class VII 1.3%; Class IX 2%; and Class X 2%, while the remaining three classes (III, V and VII) were not present in the sample (11). In our study of 61 maxillary third molars, fusion was present in 26.23% of cases, while the rest were divided among the other classes (Table 1). Compared to the results of Alavi et al., similarity can only be noticed in Class IV. The results of our study in terms of root number and morphology were mostly in line with the study by Todor et al. They classified the morphology and the number of third molar roots into seven categories, with three fused roots being the most common (43.75%), as in our study (13). In their study of the Croatian population (56 maxillary third molars), Ćosić et al. discovered root fusion in 19 samples (33.9%) while the rest of the sample had independent roots (17). However, the comparison between studies would be more accurate if the criteria for the number of roots and their fusion were standardized.

The root morphology of lower third molars is also variable. Our study comprised a larger number of samples (N=115), and found that most mandibular third molars had fused roots (37.39%), followed by parallel roots (21.73%). Machado et al. studied 48 mandibular third molars, and discovered single and fused roots in 27.1% of samples, parallel in 33.3%, convergent in 35.4%, and divergent in 4.2% of cases (12). In contrast, no roots showed fusion in the study of a sample of 50 mandibular molars collected from a Croatia population (17). Since the Bosnian-Herzegovinian and Croatian populations are geographically close and not expected to differ to any great extent, this result may be a reflection of differences in the sample size. Saraswati et al. used a simpler root classification in their study of 100 mandibular molars. They classified mandibular third molar root morphology into three groups: group I —roots with normal morphology (12%); group II —fused roots (7%); group III —curved roots (81%) (18). This differs

from the results of our study. While curved roots were dominant in their study, our sample showed the greatest percentage of fused roots of mandibular third molars.

### *Root Number*

OPG was primarily used as a radiographic tool in preparation for surgical third molar extraction. The number of roots was counted as part of our analysis. To evaluate the accuracy of the OPG assessment, the number of roots found in the OPG images was compared to the number of roots found on the extracted specimen. Our analysis of OPG images showed that maxillary third molars mostly had a single root (50.82%), while lower third molars predominately showed two roots (91.30%). Furthermore, the extracted specimens revealed three roots in the upper third molars (60.66%) and two roots in the lower third molars (73.91%). A statistically significant difference between the number of roots assessed using OPG images and the actual number of roots is evident ($P<0.001$). In their study of the precision of three imaging techniques in assessing the number of roots of mandibular wisdom teeth, Matzen et al. found no statistically significant difference (19). They used OPG images to analyze 139 mandibular third molar root numbers, and CBCT images and stereoscanometry to examine 147 mandibular third molars. The results showed the equal reliability of the three techniques when assessing the number of third molar roots (19). Zhang et al. investigated 130 maxillary and mandibular third molars using micro-computed tomography. The results of their study on a Chinese population showed that upper third molars mostly had one root (51.5%) and lower third molars were usually two-rooted (47.7%) (20). Our results follow theirs in terms of mandibular third molar root count. Ćosić et al. examined 106 third molars, 56 maxillary and 50 mandibular teeth in Croatians. In their study, Croatians mostly had three-rooted upper third molars (83.9%), as in our study, while lower third molars mostly had single roots (56%) (17). Unlike their study, the population from B&H had predominantly two-rooted lower third molars. Our study had twice the sample size, which could be a reason for the discrepancy between two geographically close nations. By analyzing CBCT images, Park et al. discovered that a Korean population mostly had two-rooted mandibular third molars (56.5%), then one (37.9%), and three roots (1.9%) (21). As in our population, two rooted mandibular third molars were found most often.

In a study by Bell et al. from the United Kingdom, the number of roots was analyzed on the basis of OPG scans, and the accuracy of the OPG scan in estimating the actual number of roots was assessed. The results of that study showed a statistically significant difference between the number of roots shown on OPG and the actual root number, which brings the reliability of OPG into question (22). Our results confirm the results of Bell et al., especially in terms of assessment of the number of maxillary third molar roots. Although OPG is routinely used preoperatively, it has low diagnostic accuracy and is not a good tool to assess root number and curvature.

The number of roots in the B&H population ranged from one to four for the maxillary and mandibular third molars. In his review article, Ahmed demonstrated that maxillary third molars may have one to five roots, and mandibular one to four roots (5). In the American study by Sidow et al., 17% of mandibular molars had one root, 77% had two roots, 5% had three roots, and 1% had four roots. Out of 150 maxillary third molars, 15% had one root, 32% had two roots, 45% had three roots, and 7% had four roots (3). In accordance with the present results, lower third molars were mostly two-rooted, and upper third molars were three-rooted.

## The Position of Third Molars

One of the characteristics of impacted third molars assessed preoperatively using OPG images is their position within the jaw bone, most commonly according to Winter's classification. Winter classified third molars on the basis of their inclination towards the long axis of the second molar

as vertical, horizontal, distoangular, mesioangular, transversal, or inverse (8). In our sample, vertical angulation was found most frequently in the maxilla (60.66%) and mandible (61.74%), followed by mesioangular, linguoangular, distoangular, and horizontal angulation. (Table 1). The results of our study are in accordance with the results of Carvalho et al., who analyzed 473 mandibular third molars and found them predominantly in a vertical position (49.5%) (16). Meanwhile, Bokindo et al., established that mandibular third molars were mostly in a mesioangular position (21.9%), followed by horizontal (2.9%), vertical (1.3%), and distoangular positions (1%) (23). Sampieri et al. also found the mesioangular position to be the most frequent (53.8%) in their sample of Brazilians (N=1205 mandibular third molars) (7). In their study of 181 upper and lower third molars in a population from Lebanon, Khouri et al. found the most mesioangularly positioned third molars, followed by the distoangular, horizontal, and vertical positions (15).

## Crown Dimensions of Third Molars

A discrepancy between tooth size and available space is a possible etiological factor for impaction or partial impaction. The present study compared the crown dimensions of third molars with the available space in the sampled B&H population. A statistically significant difference between the crown length of maxillary and mandibular third molars was found, while there was no difference between their root lengths (Table 2). Our results agree with the results of Zhang et al. in a Chinese population (20). It is evident from odontometric measurements that Chinese people have shorter crowns than Bosnians (20). Ahmed et al. also studied the average dimensions of third molars, and noticed the length of third molars to be 14 mm to 22 mm, with an average of 17–19 mm (5). In our study, the average length of maxillary third molars was 17.86 mm, and the average length of mandibular third molars was 18.1 mm. The clinical importance of these measurements is that they may be helpful when choosing the length of instruments during endodontic treatment.

## The Average Dimensions of Lower Third Molars in Comparison to the Available Space between the Mandibular Ramus and Second Molar

The average dimensions of lower third molars were compared in relation to Pell and Gregory's classification of the position of lower third molars, i.e., the available space between the mandibular ramus and the second molar. We discovered a significant difference in the mesiodistal diameter of the crowns between Pell and Gregory's Classes I, II, and III. The mesiodistal diameter of the crowns of the lower third molars in Class I was notably smaller than the MD diameter of the crowns of the third molars in Classes II and III (Table 3). This was an attempt to see if tooth dimensions lead to the occurrence of impaction or partial impaction. In a recent study, Orafi et al. questioned the connection between the MD diameter of the crown of third molars and the available space for their eruption (24). This study found three categories by size (the impacted tooth's mesiodistal diameter in relation to its normal space). S1: the MD diameter is lower than the available space for the third molar eruption; S2: the MD diameter is greater than the available space for the third molar eruption; and S3: the MD diameter equals the available space for the third molar eruption (24). Our results are in agreement with the results of Orafi et al. and can be used to assess the possibility of the eruption of third molars. For accurate measurement of unerupted teeth, a 3D imaging technique such as CBCT should be used (24).

## Crown Morphology

The study established seven types of crown morphology with regard to the geometric shape it resembles. The occlusal surface of the maxillary third molars was mainly triangular, while the occlusal surface of the mandibular third molars was mostly oval. This differs from the results of a study by Todor et al. in Romanians, who found six possible geometric shapes of maxillary third molars, with the rectangular shape being dominant (28.18%).

Conversely, this shape was the least common in our study (1.64%). This suggests that there are differences in the crown morphology of maxillary third molars between different populations (13). In our analysis of the relationship between the root number and the number of cusps on the occlusal surface of the third molars, we established the following: a three-cuspid crown is usually followed by three roots, while crowns with four, five, six, and seven cusps are usually followed by two roots. This suggests that the number of cusps is not a reliable indicator of the root number.

## Study Limitations and Future Research Suggestions

Considering that our study was based on the morphology of crowns and roots, our sample had to be intact. As a result, many of the samples were ineligible due to mechanical defects, or their position necessitated operative separation. This was mostly the case with horizontally positioned lower third molars and molars in unusual positions that could not be extracted as a whole. This affected the results concerning the position of mandibular third molars. For future research, it would be interesting to note all the positions of third molars that require separation in order to be extracted. This would be especially helpful to inexperienced oral surgeons, as it would assist them in deciding when to separate the tooth during the procedure.

## Fi - Index Tool

This manuscript has been checked with the Fi-index tool and obtained a score of 0.20 for the first author only on the date 24 July 2023 according to SCOPUS® (25). The fi-index tool aims to ensure the quality of the reference list and limit any auto-citations.

## Conclusion

Orthopantomogram imaging is not a precise diagnostic method to assess the third molar root count. Our study of a Bosnian and Herzegovina population showed that maxillary third molars usually had three fused roots (Alavi Class IV), while mandibular third molar roots were mostly fused. Both maxillary and mandibular third molars were mostly vertically positioned. Lower third molars were typically classified as Pell and Gregory Class II. The crowns of upper and lower third molars differ in shape: mandibular third molar crowns are mostly oval, and maxillary crowns are triangular. The number of cusps on the upper and lower third molars cannot be used to predict the number of roots. Knowing the morphological characteristics of wisdom teeth as well as their position is important for clinical practice in assessing the potential risk of impaction, difficulty of extraction, and increased susceptibility to caries and periodontal disease.

**What Is Already Known on This Topic:**
*Various classifications and scoring systems have been identified in studies to categorize impacted third molars on the basis of their position and degree of impaction. These classifications aid in treatment planning and extraction decision-making. Radiological evaluation also aids in determining the relationship between the impacted tooth and adjacent structures, which is important for surgical planning and lowering the risk of complications. Furthermore, assessing crown and root morphology helps predict extraction difficulty, determine the need for preoperative procedures, such as sectioning or bone removal, and to identify the risk of postoperative complications. Overall, clinical and radiological evaluation is important in assessing impacted third molars, facilitating personalized treatment plans, and reducing associated risks and complications.*

**What This Study Adds:**
*The prevalence, eruption patterns, and anatomical characteristics of wisdom teeth differ between ethnic groups and populations. This is the first study of wisdom teeth in the Bosnian and Herzegovinian population, and it focuses on wisdom tooth position, as well as crown and root morphology. This study's findings will have an impact on dental care and treatment decisions in the fields of oral surgery, restorative dentistry, and endodontics.*

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**Conflict of Interest:** The authors declare that they have no conflict of interest.

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# Pneumomediastinum: Experience with 87 Patients

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**Abstract**

**Objective.** The aim of the present series was first to present our experience in the management of 37 patients with spontaneous pneumomediastinum (SPM), and further to indicate the necessity of identifying true SPM cases as they are currently inadequately defined. **Methods.** This is a single-center, retrospective study, conducted in a university hospital. Consecutive adult patients with pneumomediastinum (PM) between January 2009 and March 2020 were involved in the series. The data about age, gender, symptoms, signs, treatment, length of hospital stay (LOS), and in-hospital mortality were evaluated. **Results.** In total, 87 cases with pneumomediastinum (37 with spontaneous and 50 with secondary PM) were analyzed. Patients in both groups were of similar ages (P=0.4). Sufferers with secondary PM were more likely to have: an associated pneumothorax (19% vs 58%, P<0.05), a chest tube placed (18.9% vs 58%, P<0.05), an associated pleural effusion (0% vs 18%, P<0.05). They presented with a longer LOS (3.9 vs 5.3 days, P<0.05), and were more likely to die (0% vs 10%, P<0.05). Additionally they showed a higher prevalence of radiologic subcutaneous emphysema (49% vs 74%, P<0.05). **Conclusion.** Spontaneous pneumomediastinum is an onset of clinical importance with a low mortality rate, short LOS and good longterm prognosis. It often presents with chest pain, dyspnea and/or subcutaneous emphysema. However, secondary causes of mediastinal air must be ruled out, due to their potential devastating outcome if not diagnosed promptly. A consensus aimed at an update of the classification guidelines is more than indispensable.

**Key Words:** Pneumomediastinum ▪ Spontaneous vs Secondary ▪ Classification ▪ Treatment ▪ Outcomes.

## Introduction

Pneumomediastinum (PM) is defined as the presence of air in the mediastinal cavity, and can be a potentially catastrophic complication. According to the pathological cause, it is further divided into two entities: spontaneous pneumomediastinum (SPM), without any obvious primary cause, and secondary pneumomediastinum, with a specific responsible pathological event, such as trauma, intrathoracic infections, or violation of the aerodigestive track.

SPM was originally described by Louis Hamman in 1939 (1) and is generally described as a benign condition, presenting mainly in young adults exposed to a sudden pressure change within the intrathoracic cavity. The pathogenesis of SPM is characterized by a sudden increase in intrathoracic pressure, along with intraalveolar pressure (2). The difference in pressure created within the pulmonary parenchyma leads to alveolar rupture, with further leakage of air throughout the interstitium and bronchovascular tissue toward the mediastinum. In fact, SPM usually occurs after several precipitating events, triggering a strong Valsalva maneuver (2, 3).

On the other hand, secondary pneumomediastinum (secondary PM) is found in the majority of patients with pneumomediastinum. In most cases, there is a precipitating event, such as a penetrating

or blunt trauma, rupture of a hollow viscus, esophagus or trachea, tissue dissection originating from a spontaneous pneumothorax, or pulmonary or mediastinal infection by gas-forming organisms (4). Despite the rare incidence of SPM, we report here one of the largest series of PMs available in the literature, to the best of our knowledge (5, 6).

The purpose of the present study was on the one hand to present our experience in the management of 37 individuals with SPM, and on the other to point out the importance of recognizing true spontaneous pneumomediastinum cases as long as they are poorly defined in the current literature. Their clinical presentation, diagnostic evaluation, radiologic findings, and clinical outcomes were analyzed and compared with those from 50 patients suffering from secondary PM.

## Materials and Methods

### *Patients Selection*

The present study is a single-center, retrospective analysis incorporating patient data from all consecutive patients diagnosed either with SPM or secondary PM, treated in our hospital from January 2009 to March 2020. The search was conducted covering the aforementioned time period in databases of the Departments of Radiology, Thoracic and Cardiovascular Surgery, and Accident and Emergency, using the following keywords and their combinations in the documented diagnoses: "Pneumothorax", "Pneumomediastinum", "Pneumopericardium", and "Subcutaneous Emphysema".

Since definitions of primary and/ or spontaneous PM are interchangeably and arbitrary used, we followed the widely accepted "common" practice and classified as SPM all these "otherwise healthy" cases in which SPM occurred in the absence of clinically apparent underlying lung disease, penetrating or blunt trauma, iatrogenic causes, or complications due to surgery and mechanical ventilation.

### *Primary and Secondary Endpoints*

All data regarding baseline characteristics, pathological characteristics, along with imaging and the hospital course, were prospectively collected. The parameters evaluated for comparison between the two groups included: age, sex, diagnostic chest radiograph, associated pneumothorax, pleural effusions, atelectasis, subcutaneous emphysema, length of stay (LOS), and in-hospital mortality. In-hospital mortality was the primary endpoint and LOS was the secondary endpoint.

### *Laboratory and Radiologic Analyses*

All patients underwent laboratory blood tests for hematocrit, hemoglobin, white blood cells, neutrophils, electrolytes, urea, creatinine, and c-reactive protein. Radiology images upon admission included chest radiograph in 95% of patients (35 of 37) and chest CT-scan in 81% (30 of 37).

### *Statistical Analysis*

The results were analyzed using GraphPad Prism 8.4.3 for Mac (GraphPad Software, San Diego, CA). Normal distribution of the continuous data was tested by application of the D'Agostino and Pearson Omnibus normality tests. Comparisons of continuous variables were performed with the two-tailed unpaired t-test for parametric data and the Mann-Whitney U-test for nonparametric data. The categorical outcomes were tabulated in 2x2 tables and were assessed by performing the Chi square test. Differences were deemed significant with a $P \leq 0.05$.

## Results

### *Baseline Characteristics*

A total of 87 patients were included (SPM group: 37 patients; secondary PM group: 50 patients). SPM patients' baseline characteristics are presented in Table 1. Regarding the SPM group, the most frequently reported symptom was chest pain in 38% (14 of 37), followed by dyspnea in 35% (13 out of 37) and cough in 30% (11 out of 37). Pneumothorax was present in 19% (7 out of 37) upon admission and atelectasis in 14% of the cases

(5 out of 37). The pneumothoraces were small and evident only on the chest CT scan. No pathological lung abnormality (eg, bleb, cavity, bullae) was identified as the etiology of the pneumothorax. Laboratory analysis included complete cell count, electrolytes, and arterial blood gases. The white blood cell count was elevated in 43% of patients (16 out of 37). The remainder of the laboratory work performed was otherwise unremarkable. Radiology images upon admission included chest radiograph in 95% of cases (35 out of 37) and chest CT-scan in 81% (30 out of 37). The chest x-ray (CXR) revealed mediastinal air in 57% (21 out of 37) and subcutaneous air in 38% (14 out of 37). Chest CT scan revealed mediastinal air in 100% (30 out of 30 performed scans) and subcutaneous air in 60% (18 of 30) of the examinations.

Medical history predisposing to the development of SPM included smoking in 22% (8 out of 37), asthma in 16% (6 out of 37), idiopathic pulmonary fibrosis in 5% (2 out of 37), and chronic obstructive pulmonary disease in 14% (5 out of 37) of the patients. Twenty-four cases (64.9%) appeared without any comorbidities (Table 1).

Table 1. Patient Baseline Characteristics and Clinical Findings of SPM* Patients

| Demographics | SPM* group (N=37) |
|---|---|
| Female (N; %) | 13 (35.4) |
| Mean age (years) (SD) | 54.6 (25.5) |
| Presenting symptom (N; %) | |
| Chest pain | 14 (38) |
| Dyspnea | 13 (35) |
| Cough | 11 (30) |
| Neck pain | 4 (10.8) |
| Precipating event (N; %) | |
| Cough/URI† | 14 (38) |
| Vomitting | 12 (32) |
| Physical activites | 2 (5.4) |
| Inhalational drugs | 0 (0) |
| No triggering factor | 6 (16.2) |
| Not known/ missing | 3 (8.1) |
| Comorbidities (N; %) | |
| Asthma | 6 (17) |
| IPF‡ | 2 (5.4) |
| COPD | 5 (14) |
| No comorbidities | 24 (64.9) |
| Lifestyle | |
| Smoking (N; %) | 8 (22) |

*Spontaneous pneumomediastinum; †Upper Respiratory Infection; ‡Idiopathic Pulmonary Fibrosis; §Chronic Obstructive Pulmonary Disease.

Among the suspected triggering factors in the origin of SPM, cough and upper respiratory infection were noted to be the predominant precipitating events in 38% of patients (14 out of 37). Asthma exacerbation was seen in 16% (6 out of 37) and vomiting in 32% (12 out of 37). Further triggering events observed were physical activity and panic attacks. Inhalational drugs, a well-established precipitating event for SPM, were not recorded (0%) in our cohort. There was no apparent triggering factor for mediastinal air in 6 cases (16%).

The majority of the cases were admitted to the hospital, placed on oxygen and treated expectantly. Eight (22%) of those underwent drainage through chest tube insertion. The mean length of hospital stay was 3.9 (SD=1.8) days and there were no in-hospital deaths.

The second cohort included patients (N:50) in whom pneumomediastinum developed as a result of blunt thoracic trauma in 44% (22 out of 50), barotrauma in 36% (18 out of 50), esophageal perforation in 8% (4 out of 50), surgical intervention (tracheostomy in 10% [N:5] and thyroidectomy in 2% [N:1]). This group of 50 sufferers with secondary PM was compared with the original cohort with SPM. Comparing the two groups (SPM vs secondary PM)showed that: individuals were of similar age (P=0.4), while secondary PM cases were more likely to have an associated pneumothorax (19% vs 58%, P<0.05), a chest tube placed (18.9% vs 58%, P<0.05), and an associated pleural effusion (0% vs 18%, P<0.05). Additionally, they presented a higher prevalence of radiologic subcutaneous emphysema (49% vs 74%, P<0.05) (Table 2).

Regarding outcomes, they presented longer LOS (3.9 vs 5.3 days, P<0.05) (Figure 1), and higher in-hospital mortality (0% vs 10%; P<0.05) (Table 2).

Table 2. Spontaneous Pneumomediastinum Compared with Secondary Pneumomediastinum

| Clinical parameters | SPM (N=37) | Secondary PM (N=50) | P-value |
|---|---|---|---|
| Age, mean (SD) | 54.6 (25.5) | 50.3 (21.3) | 0.40 |
| Females, n (%) | 13 (35.4) | 9 (18) | 0.07 |
| Diagnostic chest radiograph, N (%)* | 21 (56.7) | 22 (44) | 0.46 |
| Associated pneumothorax, N (%) | 7 (18.9) | 29 (58) | <0.01 |
| Associated pleural effusions, N (%) | 0 (0) | 9 (18) | 0.01 |
| Associated atelectasis, N (%) | 5 (13.5) | 16 (32) | 0.05 |
| Subcutaneous emphysema, N (%) | 18 (48.7) | 37 (74) | 0.02 |
| Chest tube placement, N (%) | 8 (21.6) | 30 (60) | <0.01 |
| LOS, mean (SD) | 3.9 (1.8) | 5.3 (1.9) | <0.01 |
| In-hospital Mortality, N (%) | 0 (0) | 5 (10) | 0.048 |

SPM=Spontaneous pneumomediastinum; PM=Pneumomediastinum; *The diagnosis of pneumomediastinum was made based on the Chest X-ray.

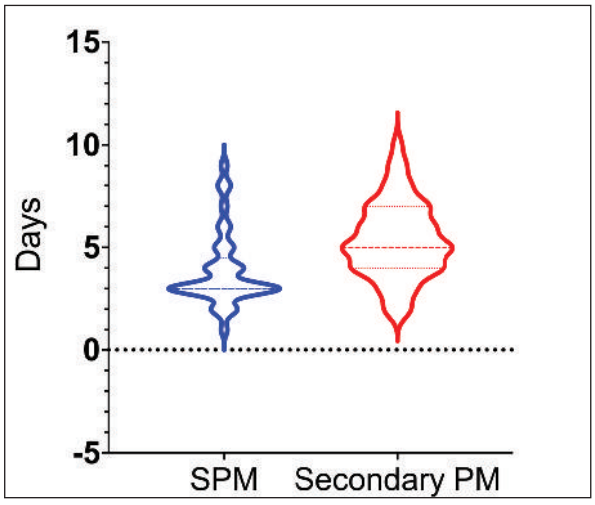


Figure 1. Comparison of length of stay (LOS).

## Discussion

Analyzing the data on the SPM cohort, we found that most affected patients were adults of younger age, which correlates with many other reviews (7–9). Nonetheless, there was no significant difference regarding age and gender distribution compared to the secondary PM group. The evaluation revealed that underlying lung diseases, mainly COPD and asthma, were frequent comorbidities among SPM individuals. This is not surprising, given the pathophysiology of the entity. In addition, we observed several precipitating factors similar to other case series (7, 10).

Concerning the clinical presentation, it was similar to other reports (10–12). In fact, most of the sufferers complained of chest pain, shortness of breath, and subcutaneous emphysema. In addition, we found an exceptionally low incidence of atelectasis, subcutaneous emphysema and pleural effusion on imaging studies, as these features are more common in cases of secondary pneumomediastinum.

Regarding diagnostic radiological tools, thoracic-CT compared to chest x-ray was more accurate in our series in establishing the diagnosis of pneumomediastinum in the SPM group (100% vs 60% of the performed scans respectively). In fact, Kaneki et al. (5) stated that up to 30% of patients with SPM present with a normal chest x-ray. Our analysis revealed that a chest radiograph is an appropriate initial study that might pose the diagnosis (in 60% of the examinations performed), while a CT scan is complementary, which is in accordance with a previous study (6). This might be explained by the fact that the patients in our series who underwent CT had more severe symptoms, typically pain, which prompted the test and hospital admission thereafter. To date there is no evidence defining which PM cases should undergo a scan. Summarizing, usually the diagnosis of SPM is established with a clinical examination and a simple chest X-ray. Nevertheless, as many as 50% of all cases might remain undiagnosed if only a posteroanterior chest x-ray is taken, a lateral view is recommended to identify the presence of air (3). However, if the diagnosis of SPM is still unclear,

or if there is a suspicion of secondary pneumomediastinum, a CT scan should be added to ensure the diagnosis. In general, the data reported in the literature underline that a high level of suspicion, supported by an individual case by case evaluation by a physician, including the close interdisciplinary collaboration of various specialties such as Emergency Medicine physicians and Thoracic Surgeons, remain the cornerstone of establishing the diagnosis.

Even so, if the diagnosis of SPM is definitely confirmed, the optimal therapeutic approach still remains under debate. Conservative management, including rest, analgesia, and close observation, is the mainstay of treatment. In approximately 10% of these cases, small concurrent pneumothoraces are present. In cases of concurrent pneumothorax, management should follow the same principles as in primary spontaneous pneumothorax sufferers.

Regarding morbidity and outcomes, the hospital course of the SPM group was benign. No death was reported and the LOS was relatively short. The chance of recurrence is small, approximately 1% (13). Few reported PM recurrences confirm its benign entity. Due to the extremely low recurrence incidence, no long-term follow-up is required, unless otherwise indicated (14).

Although SPM represents, as shown, a rare benign condition, it should be always differentiated from secondary PM, which has an ominous onset with potentially catastrophic complications. Free air in the mediastinum is a finding which may raise the concern regarding potentially devastating conditions such as abscess formation or esophageal perforation, with subsequent mediastinitis, accompanied by high morbidity and mortality rates. This was partially confirmed through the comparison in our study of the SPM and secondary PM cohorts, where the second group showed significant higher morbidity, mortality and LOS.

According to the current literature and common practice in classification, "spontaneous", or "primary" PM are considered any pneumomediastinum without any apparent precipitating clinical factor or lung disease ('sine causa'), which is not traumatic, or that develops as a complication of surgery. Nevertheless, as patients with SPM are usually found to have subtle undiagnosed pulmonary abnormalities, accompanied or not by triggering factors, the distinction between secondary PM and SPM becomes increasingly cloudy. In our series, up to 20% of the SPM had either a triggering event, or a predisposing, preexisting comorbidity for a sudden increase in intrathoracic pressure.

Asthma, one of the most commonly reported factors, was present in our study in 17% of the cases. Following the previously mentioned line of reasoning, asthmatic patients should actually be considered as having secondary PM. However, in the medical literature they are included in the SPM cohorts. In this context, although both the precipitating trigger and predisposing factors of SPM have been extensively analyzed, no distinction has been made between them, despite the fact that they are not the same. On the other hand, in our series 24 patients presented without any predisposing pulmonary disease and only 6 without any triggering factor. These would correspond to 27.5% and 6.9% respectively of the total population of PM patients, meaning that, "true" SPM cases (without any predisposing and precipitating factors!!) are extremely rare. Summarizing, the current definitions for SPM and secondary PM, as well the common practice in distinguishing between the subgroups, create confusion and cause conceptual difficulty. The question arises whether it is time for a consensus for a change of classification, introducing among others the term "idiopathic" PM, as proposed by some groups (15, 16). This would lead to greater accuracy in order to achieve appropriate diagnosis, treatment or management, and reliable prognosis estimation.

### *Limitations of Study*

This retrospective non-randomized series refers to a single-center regional experience; thus, the results may not be generalizable to the entire population, since there are significant differences between institutions and countries. Additionally, the relatively small size of 87 cases may have limited the power for comparison between spontaneous and secondary PM.

## Conclusions

Spontaneous pneumomediastinum is a benign and self-limiting onset of clinical importance with good prognosis, as shown by the extremely low mortality, as well as the relative short LOS in our case series. In the absence of significant pathology, the treatment focuses on symptom relief. The entity often presents with chest pain, dyspnea and/or subcutaneous emphysema. Due to its clinical presentation, mimicking many other respiratory pathologies and clouding the differential diagnosis, it is often under-diagnosed. Therefore diagnosis requires a high level of suspicion given that a significant proportion of patients present without any precipitating factor, or it may be missed on a plain chest radiograph. However secondary causes of mediastinal air must be ruled out, because they may have a devastating outcome if not diagnosed promptly. A consensus targeting an update of the classification guidelines is more than necessary. This would enable more accurate diagnosis resulting in appropriate treatment and reliable prognosis estimation.

**What Is Already Known on This Topic:**

*Pneumomediastinum (PM) is in general a self-limiting condition with good outcomes. Its presenting clinical signs are nonspecific, thus the identification of predisposing risk factors is essential for better management and prognosis. If there is no significant pathology, the treatment focuses on symptom relief. The entity is further divided into two groups: spontaneous pneumomediastinum (SPM), without any obvious primary source, and secondary PM, with a specific responsible pathologic event, such as trauma, intrathoracic infections, or violation of the aerodigestive track. SPM usually presents with chest pain, dyspnea and/or subcutaneous emphysema. However secondary causes of mediastinal air must always be ruled out, in order to prevent complications with devastating outcome.*

**What This Study Adds:**

*Despite the rare incidence of SPM, our study represents one of the largest series of PM available in the literature. The comparison of SPM patients with secondary PM cases revealed findings similar to those reported by other authors. However, the series underlines, on the one hand, the necessity of a high level of suspicion in establishing the SPM diagnosis as many cases present without any precipitating factors, or may be missed on plain chest radiograph, and on the other hand it illustrates that the current PM classification into spontaneous and secondary PM may create confusion and cause conceptual difficulty. The question arises whether it is time for a consensus to seek amendment of the classification for the sake of greater accuracy.*

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**Conflict of Interest:** The authors declare that they have no conflict of interest.

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# A Review of the Typical Course of the Musculocutaneous Nerve into the Coracobrachialis Muscle: Its Variability and Possible Clinical Implications

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**Abstract**

**Objective.** This literature review highlights the prevalence of the typical course of the musculocutaneous nerve (MCN) through the coracobrachialis muscle (CB), and evaluates the distance from the entrance point of the MCN to the CB, taking the coracoid process (CP) as a landmark. **Methods.** PubMed (MEDLINE), Scopus, and CINAHL online databases were searched in December 2022 for studies reporting the prevalence of the MCN's typical course and the distance between the CP and the MCN entrance point to the CB. **Results.** Twenty-eight studies were included (including 2846 subjects) investigating the MCN's typical course, and eliciting a prevalence of 93.4%. The mean distance of the CP to the entrance point of the MCN's main trunk into the CB was 5.6±2cm (median 6.1cm, in 550 subjects). In 76.12% of cases the MCN's accessory branches entered the CB proximally to the MCN's main trunk. The mean distance from the CP to the entrance point of the MCN's proximal branches to the CB was 3.8±1.2cm (median 3.7cm, in 140 subjects). **Conclusion.** In the vast majority of cases, the MCN had a typical course through the CB. In cases of altered anatomy, the MCN was either absent or passed medially to the CB (without piercing it). The average entrance point of the MCN into the CB from the CP is 5.6 cm. Proximal motor branches of the MCN to the CB are common and usually arise at a mean distance of 3.8cm from the inferior border of the tip of the CP. Surgeons should be aware of both the MCN's typical and its atypical course and these distances to avoid possible complications when operating in the area.

**Key Words:** Musculocutaneous Nerve ▪ Arm ▪ Coracoid Process ▪ Prevalence ▪ Review Literature.

## Introduction

The musculocutaneous nerve (MCN) arises from the brachial plexus (BP) lateral cord and contains fibers from the 5th to 7th cervical spinal nerves (C5-C7). It courses posterior to the pectoralis minor muscle, above the subscapularis muscle tendon, and pierces the coracobrachialis muscle (CB). After exiting the CB, it heads downwards between the biceps brachii and brachialis muscles, and crosses the lateral side of the humerus between the brachioradialis and the lower part of the biceps brachii (BB). During MCN's course, it gives off the motor branches to the CB, BB, and brachialis muscles (1, 2). At the elbow joint, lateral to the BB tendon insertion, the MCN becomes the lateral antebrachial cutaneous nerve, innervating the skin on the lateral side of the forearm (1). Several procedures include the mobilization of muscles inserted into the coracoid process (CP), such as CP transfer and fixation to the anterior part of the glenoid for treating anterior shoulder instability with significant bone loss (3-7) – the Bristow-Latarjet procedure and its modifications - and CB transfer in reconstructive surgery (8, 9). The MCN may also be injured, especially by a medial retractor in the standard anterior deltopectoral approach (10, 11). The MCN, before piercing the CB, may give off motor branches proximal to it. These branches are characterized as accessory innervation. Protection of the MCN is crucial in these operations, and so the distance

of CP-MCN penetration into the CB is frequently recorded as between 5-8 cm (1, 3, 12, 13). In addition, MCNs with higher penetration into the CB have also been reported (14-17). The current study reviews the data literature and estimates the prevalence of the MCN's typical course through the CB.

We refer to the atypical course of the MCN in relation to the CB as either the absence of the MCN or its medial course without piercing the CB. On a secondary basis, the distances between the CP and the entrance point of the MCN into the CB, and between the CP and the point of origin of the proximal branches, as well as the safe zone in order to avoid damaging the MCN intraoperatively, are evaluated.

## Methods

A narrative literature review was performed in a systematic manner according to the PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*) guidelines (18).

### *Search Strategy*

The narrative literature review was conducted in PubMed (MEDLINE), Scopus, and CINAHL databases, up to December 19th, 2022, to identify eligible studies, through different combinations of the following search terms: "coracobrachialis", "variation", "main trunk", and "proximal branches" (Supplementary Material 1). The research was conducted independently by two researchers (IP and MP) and in the case of any discrepancies, consultation with a third (AS) was sought. The inclusion criteria were the following: *i. cadaveric or surgical or imaging studies, ii. studies reporting both the MCN absence and CB non-perforation, iii. studies reporting measurements between the CP and the entrance point of the MCN's main trunk or proximal branches to CB, iv. studies providing numerical information on the abovementioned measurements, v. studies published in English, Spanish, or Greek*. Hence, studies that did not meet the criteria (such as those that only investigated the MCN's absence or CB non-perforation by the MCN, but not both) were excluded.

### *Data Extraction*

The following data were extracted from each of the eligible studies: i. First author, ii. Year of publication, iii. Type of study, iv. Study population, v. Mean age with standard deviation (SD) and range, vi. The number of cases of the MCN piercing the CB, vii. The number of cases recording the MCN's absence, viii. The mean distance, SD, and range from the CP to the entrance point of the MCN's main trunk to the CB, iv. The mean distance, SD, and range from the CP to the entrance point of the MCN's proximal branches to the CB, v. The number of cases and proportion of the total population with MCN proximal branches, vi. Point of measurement from the CP.

### *Risk of Bias Assessment*

The Anatomical Quality Assessment (AQUA) Tool (19) was used to assess the included studies' quality, reliability and risk of bias. This tool consists of 25 questions, divided into 5 areas: 1. Objectives and Subject Characteristics, 2. Study Design, 3. Methodology Description, 4. Descriptive Anatomy, and 5. Results Reporting. If all questions had affirmative replies in each domain, the risk of bias was rated as 'low', otherwise as 'high'. A study's overall risk of bias was defined as 'low' if all domains were at low bias risk, 'moderate/ some concerns' if at least three domains were at low bias risk, and otherwise as 'low'.

## Results

A total of 126 studies were identified, 28 of which were assessed as full-text articles (Figure 1). Out of these, 23 manuscripts (1, 2, 15, 20-38) were used for estimation of the MCN's typical course, 10 (6, 12, 15, 17, 27, 34, 36, 39-41) for calculation of the distance between the CP and the entrance point of the MCN into the CB, and 7 (2, 6, 12, 15, 17, 36, 40), for computation of the distance between the CP and the point of origin of the proximal branches.

Out of the 28 studies included, four studies were considered of low risk of bias, 23 of moderate risk, and one of high risk. The risk of bias analysis for each domain of all the studies is summarized in Figure 2.

The MCN was found to be piercing the CB in a total of 2,661 subjects, leading to estimation of the unweighted prevalence of the MCN's typical course of 93.4% (Table 1). In cases of atypical

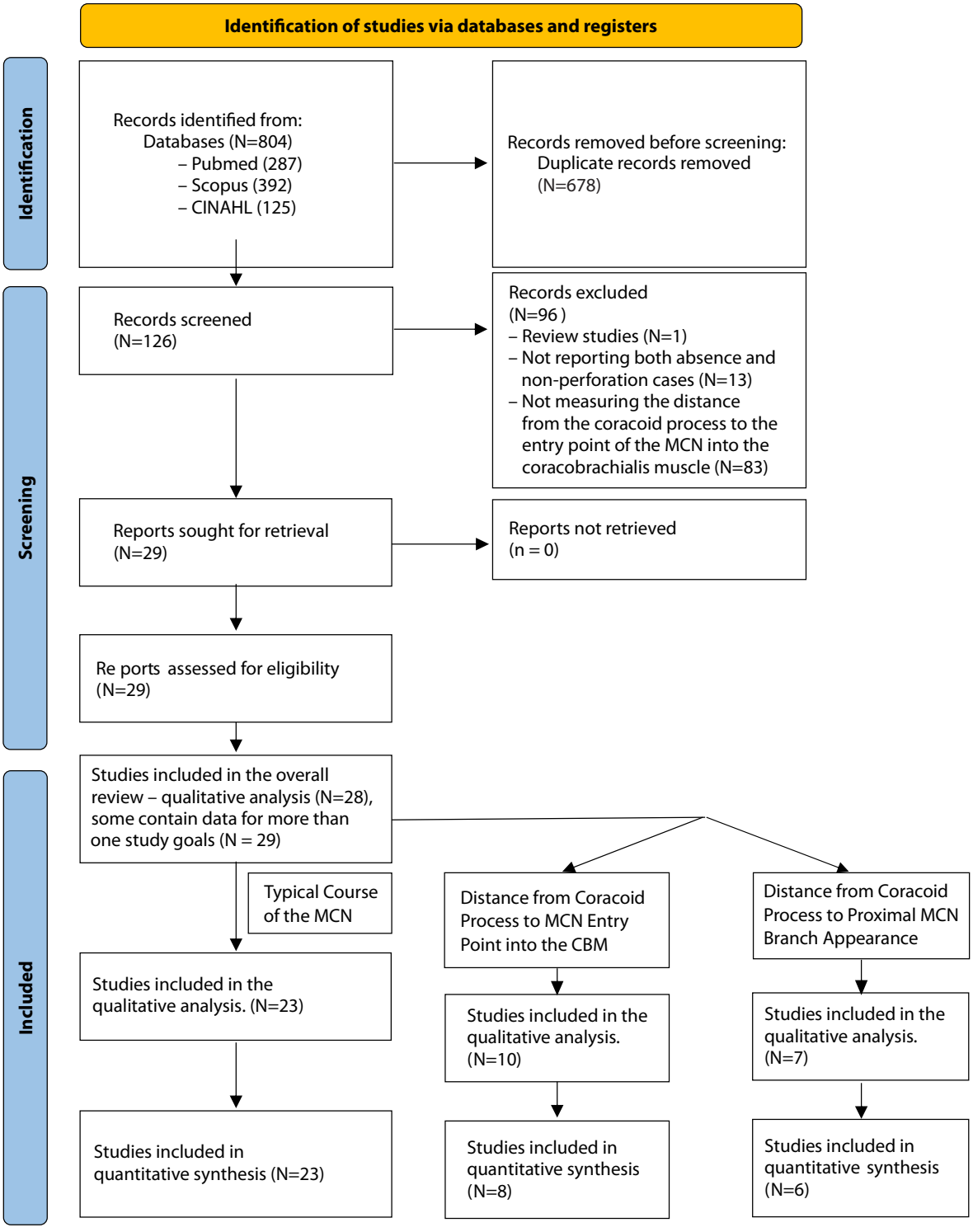


Figure 1. PRISMA 2020 flow diagram for new reviews which included searches of databases and registers only.

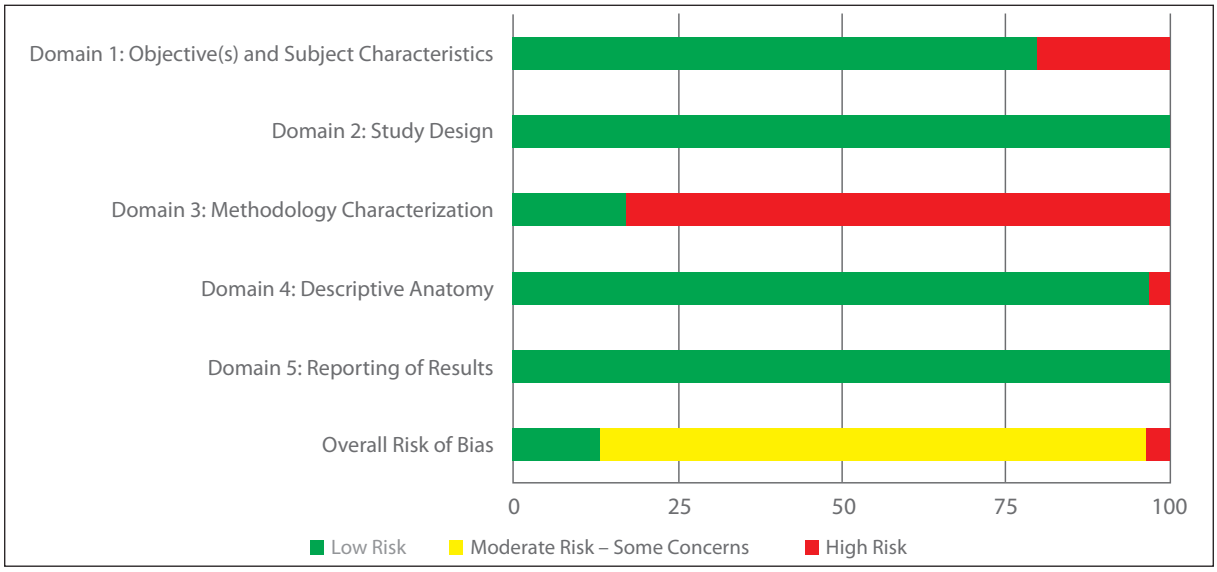


Figure 2. Risk of bias assessment according to the AQUA tool domains.

Table 1. Basic Characteristics of Studies Included (23) in the Review Concerning the Typical Course of the Musculocutaneous Nerve (MCN) in Relation to the coracobrachialis muscle (CB)

| Author (s) | Year | Type of Study | Population/ Country | Population (N) | No piercing of CB (N) | MCN absence (N) | MCN typical course (N) | Percentage of typical course |
|---|---|---|---|---|---|---|---|---|
| Loukas and Aqueelah (20) | 2005 | Cadaveric | USA | 258 | 11 | 1 | 246 | 95.3 |
| Maeda et al. (21) | 2009 | Cadaveric | Japanese | 453 | 10 | 8 | 435 | 96 |
| Patel et al. (22) | 2013 | Cadaveric | Indian | 80 | 1 | 2 | 77 | 96.3 |
| Venieratos and Anagnostopoulou (23) | 1998 | Cadaveric | Greek | 158 | 3 | - | 155 | 98.1 |
| Ballesteros-Larotta et al. (24) | 2018 | Cadaveric | Colombian | 106 | 6 | 4 | 96 | 90.6 |
| Claasen et al. (25) | 2016 | Cadaveric | German | 167 | 3 | 1 | 163 | 97.6 |
| Guerri-Guttenberg and Inglotti (26) | 2009 | Cadaveric | Argentinian | 56 | 6 | 2 | 48 | 85.7 |
| Ilayperuma et al. (27) | 2016 | Cadaveric | Sri Lankan | 312 | 52 | 0 | 260 | 83.3 |
| Maiti and Bhattacharya (28) | 2018 | Cadaveric | India | 28 | - | - | 28 | 100 |
| Mori (29) | 1964 | Cadaveric | Japanese | 50 | 3 | - | 47 | 94 |
| El-Naggar (30) | 2001 | Cadaveric | Saudi Arabian | 36 | 3 | 1 | 32 | 88.9 |
| Ozturk et al. (15) | 2005 | Cadaveric | Turkish | 42 | 0 | 0 | 42 | 100 |
| Padur et al. (31) | 2016 | Cadaveric | India | 82 | 0 | 2 | 80 | 97.6 |
| Reboucas et al. (2) | 2015 | Cadaveric | Brazilian | 20 | 0 | 0 | 20 | 100 |
| Uysal et al. (32) | 2009 | Cadaveric | Turkish | 140 | 4 | 0 | 136 | 97.1 |
| Choi et al. (33) | 2002 | Cadaveric | British | 276 | 22 | 0 | 254 | 92 |
| Eglseder and Goldman (34) | 1997 | Cadaveric | USA | 54 | 16 | 0 | 38 | 70.4 |
| Pacha Vicente et al. (35) | 2005 | Cadaveric | Spanish | 46 | 3 | 0 | 43 | 93.5 |
| Latarjet (1) | 1967 | Cadaveric | French | 106 | 0 | 0 | 106 | 100 |
| Macchi et al. (36) | 2007 | In vivo | Ital.ian | 69 | 0 | 0 | 69 | 100 |
| Ferner (37) | 1938 | Cadaveric | German | 167 | 4 | 0 | 163 | 97.6 |
| Arora et al. (38) | 2005 | Cadaveric | Indian | 100 | 0 | 15 | 85 | 85 |
| Al-Sobhi et al. (39) | 2023 | Cadaveric | Saudi Arabian | 40 | 4 | 1 | 35 | 87.5 |

anatomy, the MCN was either absent or passed medially to the CB without piercing it.

The articles studying the distance from the CP to the entrance point of the MCN's main trunk into the CB included a total of 753 subjects (Table 2). Of those, 550 were included in the analysis and elicited a mean distance of 5.6±2 cm (median 6.1 cm, range 2-11.5 cm). The articles studying the distance of the MCN's proximal branches' origin to the entrance point into the CB included a total of 289 subjects. Of the total population, 76.12% (N=220) had proximal branches of accessory innervation entering the CB. One hundred and forty subjects were eligible for the analysis, eliciting a mean distance of 3.8±1.2 cm (median 3.7 cm, range 1.5-9 cm) (Table 3).

Table 2. Basic Characteristics of the Studies Included (10) Reporting the Distance from the Coracoid Process to the Entrance of the Main Trunk of the Musculocutaneous Nerve (MCN) into the Coracobrachialis Muscle (CB)

| Authors | Year | Study type | Population (N) | MCN piercing CB (N) | Length of MCN piercing (cm) | | | Measurement points of the coracoid process |
|---|---|---|---|---|---|---|---|---|
| | | | | | Mean | SD | Range | |
| Clavert et al (6) | 2009 | Cadaveric | 21 | 21 | 5.57 | 1.47 | 2.20-8.60 | The inferior border of the tip |
| Ilayperuma et al. (27) | 2016 | Cadaveric | 312 | 260 | 5.062 | 2.334 | NR | The inferior border of the tip |
| Ozturk et al. (15) | 2005 | Cadaveric | 42 | 42 | 6.20 | 1.40 | 3.20-10.4 | The inferior border of the tip |
| Macchi et al. (36) | 2007 | Cadaveric | 12 | 12 | 7.70 | 2.50 | 3.50-11.5 | The inferior border of the tip |
| Macchi et al (36) | 2007 | In vivo | 69 | 69 | 4.60 | 1.20 | 2-9 | The tip of the CP |
| Klepps et al. (40) | 2001 | Cadaveric | 20 | 20 | 6.10 | 1.80 | 3.50-10 | The CP |
| Krassnig et al. (41) | 2023 | Cadaveric | 66 | 66 | 7.10 | 1.80 | 4-11.10 | The inferior border of the tip |
| Al-Sobhi et al. (39) | 2021 | Cadaveric | 40 | 36 | 7.75 | 1.62 | NR | The CP |
| Singh et al. (17) | 2020 | Cadaveric | 24 | 24 | 5.11 | 1.44 | 1.67-7.19 | The inferior border of the tip |
| Eglseder and Goldman (34)* | 1997 | Cadaveric | 54 | 38 | 4.99 | NR | NR | The CP |
| Flatow et al. (12)* | 1989 | Cadaveric | 93 | 86 | 5.60 | NR | 3.10-8.20 | The inferior border of the tip |

*Studies not included in the quantitative analysis; N=Value reported in number; SD=Standard Deviation; NR=Not Reported; CP=Coracoid process.

Table 3. Basic Characteristics of the Studies (7) Reporting the Distance from the Coracoid Process (CP) to the Entrance of the Most Proximal Branch of the Musculocutaneous Nerve (MCN) into the Coracobrachialis Muscle (CB)

| Authors | Year | Study type | Population (N) | Cases with MCN Proximal Branch (N) | Length of MCN piercing (cm) | | | Measurement points from the coracoid process exact point |
|---|---|---|---|---|---|---|---|---|
| | | | | | Mean | SD | Range | |
| Clavert et al (6) | 2009 | Cadaveric | 21 | 16 | 4.06 | 1.89 | 1.50-8 | The inferior border of the tip |
| Ozturk et al (15) | 2005 | Cadaveric | 42 | 42 | 4.10 | 1.20 | 1.70-7.20 | The inferior border of the tip |
| Reboucas et al (2) | 2015 | Cadaveric | 20 | 20 | 3.42 | 0.59 | 2.38-4.3 | The inferior border of the tip |
| Macchi et al (36) | 2007 | In vivo | 69 | 29 | 3.30 | 0.90 | 1.50-6.50 | The tip of the CP |
| Klepps et al (40) | 2001 | Cadaveric | 20 | 16 | 4.40 | 1.80 | 2.10-9.0 | The CP |
| Singh et al (17) | 2020 | Cadaveric | 24 | 17 | 3.35 | 0.81 | 2.19-4.76 | The inferior border of the tip |
| Flatow et al (12)* | 1989 | Cadaveric | 93 | 80 | 3.10 | NR | min 1.7 | The inferior border of the tip |

*Studies not included in the quantitative, N=Value reported in number; SD=Standard Deviation; NR=Not Reported; CP=Coracoid process.

## Discussion

The current study provides evidence regarding the MCN's typical anatomy relating to the CB by identifying the prevalence of the MCN piercing the CB, and by calculating the mean distance between the CP and the point where the MCN pierces the CB. Regarding the primary goal of the

current study, in a total of 2,846 shoulders, 93.4% proved to demonstrate the MCN's typical course. In cases of variable anatomy, the MCN was either absent or passed medially to the CB without piercing it.

Developmentally, the MCN derives late during arm development. Disruption in BP differentiation may lead to the MCN's absence (24, 42, 43). In these circumstances, the MCN fibers are fused with the median nerve (MN) in a common trunk, responsible for the anterior arm compartment's motor innervation (21). In embryology "the nerve follows the muscle" and as a result a developmental problem in muscle differentiation also leads to abnormal innervation (24, 42, 43). In the current review, in cases of MCN absence, the CB is usually innervated by the MN's branches, and less frequently by a branch arising directly from the BP's lateral cord.

The CB represents the muscle group of the upper limb adductors. Developmentally, because of human's upright stance, its role became insignificant because gravity contributes to humeral adduction from an abducted position, in conjunction with the latissimus dorsi and the pectoralis major muscles, when active motion is required (30, 44). McMinn and El-Naggar were the first to suggest that the CB is two-headed (30, 44, 45). The superficial (anterior) head originates from the CP, from the medial border of the tendon of the BB's short head, while the deep (posterior) head arises from the lateral border of the BB's short head (CP base) (30). After a short course, the two heads fuse, entrapping the MCN that courses between them. In cases of an MCN that does not pierce the CB, it appears that the CB's deep head is missing. The origin of the CB's two heads from both sides of the short head of the biceps brachii suggests another role for it – that of enhancing the BB, putting the tendon of its short head in the optimal axis for its action (30).

The average distance from the inferior border of the tip of the CP to the entrance point of the MCN's main trunk into the CB is 5.6 cm (median 6.1 cm). The classically described safe zone for the MCN of less than 5 cm from the CP places the MCN in danger. Without considering the MCN's proximal twigs of accessory innervation, three of the studies reported a mean distance of less than 5cm for the MCN's main trunk. MCN injury is one of the classical complications in anterior shoulder instability procedures, that include CP abutment (46-50). Flatow et al (12) reported that in 29% of cases, the MCN entered the CB at a distance less than 5 cm from the CP. This percentage rises to 74.0% in cases of the appearance of proximal branches of the MCN.

Small motor branches to the CB appear in 76.12% of cases, with an average distance of 3.8 cm (median 3.7 cm). Some studies recorded the presence of those accessory branches originating at a high-level position from the MCN's main trunk (12, 17, 36). Although this point needs further investigation, surgeons need to know this correlation when operating in this area, as MCN lesions result in reduced elbow flexion strength and sensory impairment of the forearm's radial aspect.

### *Limitations of the Study*

The main limitation of the current study is the high heterogeneity and the small subject population of some studies. Therefore, combined with the lack of a standard research protocol between the studies, this systematic search of the literature cannot be classified as a systematic review. Moreover, even if it could be statistically plausible to meta-analyze the data to obtain an estimation of the percentage occurrence of the MCN's typical course, these results would not be useful given their poor interpretation ability. Additionally, sensitivity analysis could not explain this heterogeneity and identify possible confounding factors associated with the estimated prevalence – age, type of study, sex, ethnicity, sample size. Another limitation includes the arm position when measuring the distance. Not all studies stated clearly the arm abduction at the point of measurement, which may affect the recorded value, since the MCN is anchored to the CB (8). The proportion of the distance related to the height of the body, or the humeral length can also affect the measurements. Height can affect

interpretation of the measurements, as a measurement of a distance of 5cm from the CP to the piercing point of the CB, with a humeral length of 50 cm, differs from the same measurement with a humeral length of 70 cm. Despite this limitation, because of the large sample in the current review, we believe that the current results can be interpreted as applying to the average human and modified proportionally. Further studies could follow the methodology of Krassnig et al. (41) reporting measurements in numeric values and proportional values according to the humeral length.

## Conclusion

The current literature review demonstrated that the unweighted prevalence of the MCN's typical course piercing the CB is 93.4%. The average MCN entrance point into the CB measured from the CP is 5.6cm (median 6.1cm). Small proximal branches of the MCN to the CB are common – in 76.12% of cases - and usually arise at around 3.8cm (median 3.7cm) from the inferior border of the tip of the CP. Surgeons should be aware of the prevalence of the MCN's typical course and these distances to avoid possible complications when operating in the area. Future studies need to be conducted to estimate more precisely the MCN's typical and altered courses, by the inclusion of information such as demographics in the analysis.

**What Is Already Known on This Topic:**

*The musculocutaneous nerve (MCN), on its typical course, arises from the brachial plexus (BP) lateral cord and contains fibers from the 5th to 7th cervical spinal nerves (C5-C7). It courses along the medial aspect of the upper part of the arm, passing above the subscapularis muscle and piercing the coracobrachialis muscle (CB). Variations in this course have been reported, but have not been systematically evaluated. There is lack of current literature systematically reviewing the prevalence of the MCN's typical course into the CB, combining both the MCN's absence and its medial course. Surgeons should be aware of the prevalence of typical and atypical anatomy, to avoid complications.*

**What This Study Adds:**

*This narrative literature review summarizes the existing literature, evaluating the variability of the MCN concerning the CB. It demonstrates that the typical course of the MCN exists in 93.4% of the population, which should be taken into consideration in operative procedures around that area. The review also evaluates the average distance from the coracoid process (CP), its tip or its inferior border, to the entrance point of the MCN's main trunk at 5.6cm (median 6.1cm), the presence of small proximal accessory branches from the MCN into the CB in 76.12% and the distance of their appearance from the CP as 3.8cm (median 3.7cm).*

**Authors' Contributions:** Conception and design: IP and MP; Acquisition, analysis, and interpretation of data: IP, MP and MK; Drafting the article: IP, KC, AS and GT; Revising it critically for important intellectual content: MP, KC and TT; Approved final version of the manuscript: IP, MP, CK, AS, GT, MK and TT.

**Conflict of Interest**: The authors declare that they have no conflict of interest.

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## Supplementary Material
## Search Terms

| Database | Search Term |
|---|---|
| PubMed | 1. ("musculocutaneous"[All Fields] OR "musculocutanous"[All Fields]) AND "coracobrachialis"[All Fields] AND ("distance"[All Fields] OR "distances"[All Fields]) |
| | 2. ("musculocutaneous"[All Fields] OR "musculocutanous"[All Fields]) AND "coracobrachialis"[All Fields] |
| | 3. ("musculocutaneous"[All Fields] OR "musculocutanous"[All Fields]) AND (("main"[All Fields] AND ("torso"[MeSH Terms] OR "torso"[All Fields] OR "trunk"[All Fields] OR "trunk s"[All Fields] OR "trunks"[All Fields])) OR (("proximal"[All Fields] OR "proximalization"[All Fields] OR "proximalize"[All Fields] OR "proximalized"[All Fields] OR "proximalizes"[All Fields] OR "proximalizing"[All Fields] OR "proximally"[All Fields] OR "proximals"[All Fields]) AND ("twigs"[All Fields] OR ("branch"[All Fields] OR "branch s"[All Fields] OR "branche"[All Fields] OR "branched"[All Fields] OR "branches"[All Fields] OR "branching"[All Fields] OR "branchings"[All Fields] OR "branchs"[All Fields])))) |
| Scopus | 1. TITLE-ABS-KEY (coracobrachialis AND (variation OR variations)) (ALL (musculocutaneous) AND ALL (coracobrachialis) AND ALL (distance)) |
| | 2. (ALL (musculocutaneous) AND ALL (coracobrachialis)) |
| CINAHL | 1. TX musculocutaneous AND TX coracobrachialis AND TX distance |
| | 2. TX musculocutaneous AND TX coracobrachialis |
| | 3. TX musculocutaneous AND TX ((main trunk) OR (proximal AND (twigs OR branches))) |

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# Comparing Endoscopic Measurements of the Anterior and Posterior Ethmoidal Arteries with CT Measurements: A Cadaveric Study

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**Abstract**

**Objective.** To reveal the reliability of radiological measurements of the ethmoid arteries. **Method.** Five fresh frozen cadaveric heads underwent computed tomography and endoscopic sinus surgery. The lateromedial length of the anterior ethmoidal artery (AEA) and its distance to the axilla of the middle turbinate (MTA), the sphenoethmoidal recess (SR) and the posterior ethmoidal artery were measured. The posterior ethmoidal artery (PEA) was referenced to the SR. These anatomical parameters were measured both radiologically and endoscopically, and the compatibility of the two was examined. **Results.** Ten nasal cavities were dissected. We found that the distance of MTA to the AEA was 16±8 mm in dissection, 21±4 mm radiologically in the sagittal section, the distance of SR to the AEA was 14±3 mm in dissection, 19±4 mm radiologically in the sagittal section, and the distance of the AEA to the PEA was 10±3 mm in dissection, 12±3 mm radiologically in the axial section. The distance of the PEA to SR was 6±3 mm in dissection, 8±2 mm radiologically in the sagittal section. **Conclusions.** The distance of the AEA to the MTA, the distance of the AEA to the PEA and the distance of the PEA to the SR were compatible with each other in the dissection and in the radiologically evaluation, whereas the distance of the AEA to the SR was not compatible.

**Key Words:** Computed Tomography ▪ Ethmoidal Arteries ▪ Ethmoid Dissection ▪ Radiology Reports ▪ Transnasal Endoscopic Surgery.

## Introduction

Anterior and posterior ethmoidal arteries are important landmarks in functional endoscopic sinus surgery (FESS) or other skull base procedures. Iatrogenic injuries to the ethmoidal arteries during endoscopic sinus surgery (ESS) may cause serious complications. Orbital hematoma, severe bleeding, cerebral infection and serious cerebrospinal fluid leak are some of the serious complications that can occur during surgery (1).

The surgeon's recognition of the course of the ethmoidal arteries in preoperative radiological imaging, and knowing its relationship to anatomical landmarks will reduce the risk of complications (2, 3). During endoscopic sinus surgery, to prevent iatrogenic damage the anatomy (length, course, variation, angulation and etc.) of the AEA should be identified preoperatively by a CT scan of the patient (4, 5). Along with this information, to know the landmarks that can be helpful for surgery in the field of the AEA is very valuable intraoperatively (2). These anatomical landmarks have been evaluated in dissections and CT studies in many studies to date. In the CT studies, the axilla of the middle turbinate, nasal spine, nasal beak, nasion, optic foramen and nasal crest were studied (6-8). In the dissection studies, the axilla of the middle turbinate, the nasal sill, the anterior nasal spine, the lateral nasal wall, and the anterior wall of the sphenoid sinus were studied (9-12),

In this study, the distance of the anterior ethmoidal artery to the axilla of the middle turbinate

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(MTA) and the sphenoethmoidal recess, and the distance of the posterior ethmoidal artery to the sphenoethmoidal recess and anterior ethmoidal artery were measured in radiological sections taken before dissection. Then, the same measurements were measured in fresh cadaver dissections and compared with each other. We attempted to obtain anatomical measurements that would help surgeons during surgery, from the preoperative radiological sections.

We aimed to evaluate whether surgeons can reliably use preoperative radiological measurements during surgery.

## Materials and Methods

### *Radiology*

All cadavers underwent computed tomography before dissection. A multidetector CT, SOMATOM Sensation 64 model (Siemens) was used to scan the fresh frozen cadaver's paranasal sinuses. After axial sections of 1 mm were acquired, reconversions were made with an overlap of 0.75 mm. Sections were acquired from the beginning of the frontal sinus to the hard palate. Maximum Intensity Projection (MIP) was used to obtain coronal and sagittal images from the axial images.

A radiologist examined the CT images. First, on the coronal sections the medial notch, recognized as a bone protrusion in the medial orbital wall, was determined to be the anterior ethmoidal foramen (Figure 1). On sagittal sections, the anterior aspect of the middle turbinate axilla was recognized. In the sagittal section, measurements were made between the stated landmarks (Figure 1). Secondly, on a sagittal section, the sphenoethmoidal recess (SR) was identified and the distance to the AEA was measured.

After measuring the distance between the AEA and the designated landmarks, measurements related to the PEA were started. By following the ethmoidal canal, the posterior ethmoidal artery was identified according to its relationship with the ethmoid compartment on the coronal section. The distance between the PEA and the sphenoethmoidal recess, which was previously distinguished by CT, was measured in the sagittal section. Finally, the distance between both ethmoidal arteries was measured in the axial section (Figure 1).

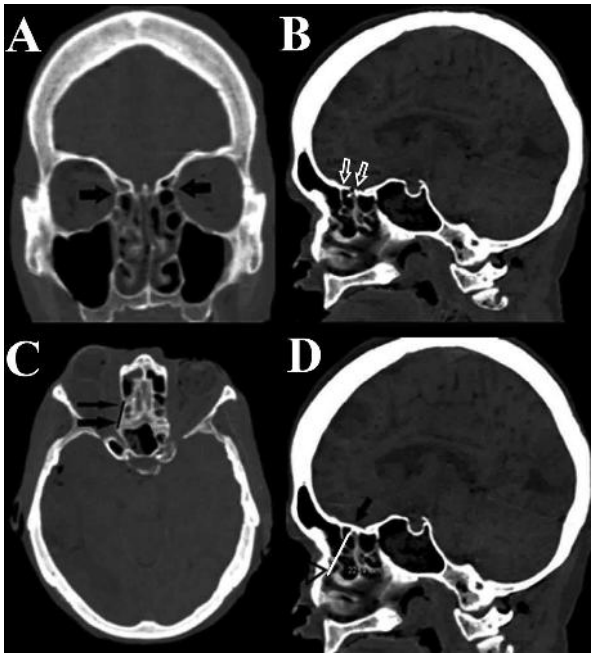

Figure 1: (A) The anterior ethmoidal foramen on the coronal section. (B) The anterior ethmoidal artery between the second and third lamellae on the sagittal section. (C) The distance between the AEA (thin arrow) and PEA (thick arrow) on the axial section. (D) The distance of the AEA to the middle turbinate axilla on the sagittal section.

### *Cadaveric Dissection*

Five fresh frozen cadaveric heads underwent endoscopic sinus surgery in the anatomy laboratory. The surgical procedure began after endoscopic evaluation of the nasal cavities. An endoscope ($0^0$, $45^0$ Storz Hopkins, Germany) and a video-endoscope system were used, alongside sinus surgery instruments (Karl Storz, Tuttlingen, Germany). The procedures were performed by an otolaryngologist who was experienced in endoscopic sinus surgery. First, an uncinectomy was performed. Then, the ethmoidal bulla was opened inferomedially, and its anterior wall was removed. The posterior ethmoidal cells were opened by exposing and

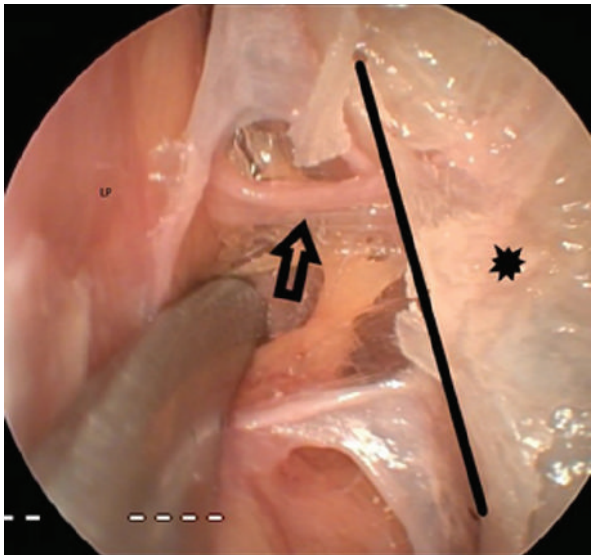


Figure 2. The entrance of the AEA from the orbit to the nasal cavity. LP=Lamina papyracea; Asterisk= Nasal cavity; Arrow=AEA; Line=Border between the lamina papyracea and nasal cavity.

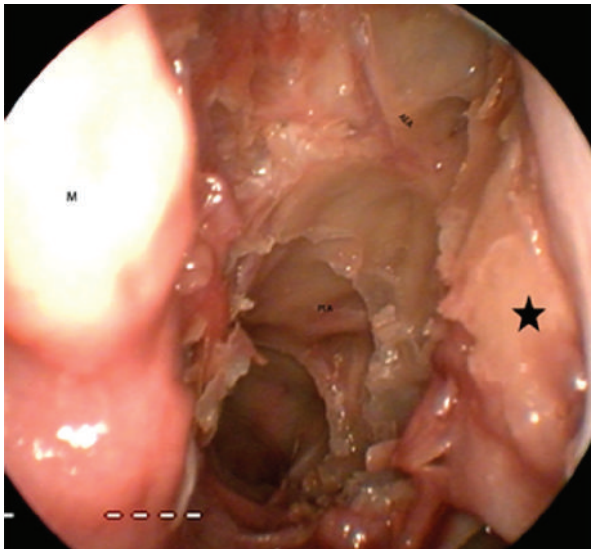


Figure 3. The AEA and PEA in dissection. M=Middle turbinate; Asterisk=Lamina papyracea.

dissecting the basal lamella. The anterior wall of the frontal recess was dissected, and the AEA was identified in the posteroanterior and lateromedial directions through the posterior wall of the frontal recess (Figure 2). After tracing from the nasal cavity to the lamina papyracea, its entry into the nasal cavity was confirmed. Then, the lateromedial length of the AEA and its distances to the MTA and the sphenoethmoidal recess were measured with a curved, calibrated seeker. The PEA was identified superior to the junction of the posterior ethmoidal cells and the sphenoid roof (Figure 3). The interarterial distance and the distance between the PEA and the SR were measured.

### *Ethics Statement*

This study was approved by the Ethics Committee of Necmettin Erbakan University (Decision No: 2023/4238 ).

### *Statistical Analyses*

Dissection and radiological measurements were compared using the dependent sample t-test. All analyses were performed with the R 3.5.3 program. P values below or equal to 0.05 were considered as statistically significant.

## Results

CTs were performed on 10 nasal cavities. The ethmoidal arteries were identifiable on all cadaver heads. The mean AEA intranasal length was 6±2 mm. The distance from the MTA to the AEA was 21±4 mm in the sagittal section, and 16±8 mm in dissection (P=0.067). The differences found were not statistically significant. As a significant finding (P< 0.05), the mean distance between the sphenoethmoidal recess to the AEA was 19±4 mm in the sagittal section and 14±3 mm in dissection. This was a significant finding (P=0.0034). The distance from the sphenoethmoidal recess to the PEA was 8±2 mm in the sagittal section and 6±3 mm in dissection (P=0.073). The interarterial distance was 12±3 mm in the axial section and 10±3 mm in dissection (P=0.16). There was no significant difference between these radiological measurements and the dissection measurements.

There was no significant difference between radiological and dissection measurements, except for the distance between the AEA and the SR, and

Table 1. Statistical Evaluation of Dissection and Radiological Measurements

| Distances | Radiology ($\bar{x}$ ± SD) mm | Dissection ($\bar{x}$ ± SD) mm | P* |
|---|---|---|---|
| AEA-SR | 19±4 | 14±3 | 0.0034 |
| AEA-MTA | 21±4 | 16±8 | 0.067 |
| AEA-PEA | 12±3 | 10±3 | 0.16 |
| PEA-SR | 8±2 | 6±3 | 0.073 |

AEA=anterior ethmoidal artery; MTA=Axilla of the middle turbinate; PEA=Posterior ethmoidal artery; SR=Sphenoethmoidal recess; *Dependent sample t-test.

it was observed that the measured values were compatible with each other. The results of the measurement are reported in Table 1. The distribution of the mean values of dissection and radiological measurements is shown in Figure 4. In Figure 5 there are box plots that illustrate the comparisons of the distances between the dissection and radiological measurements.

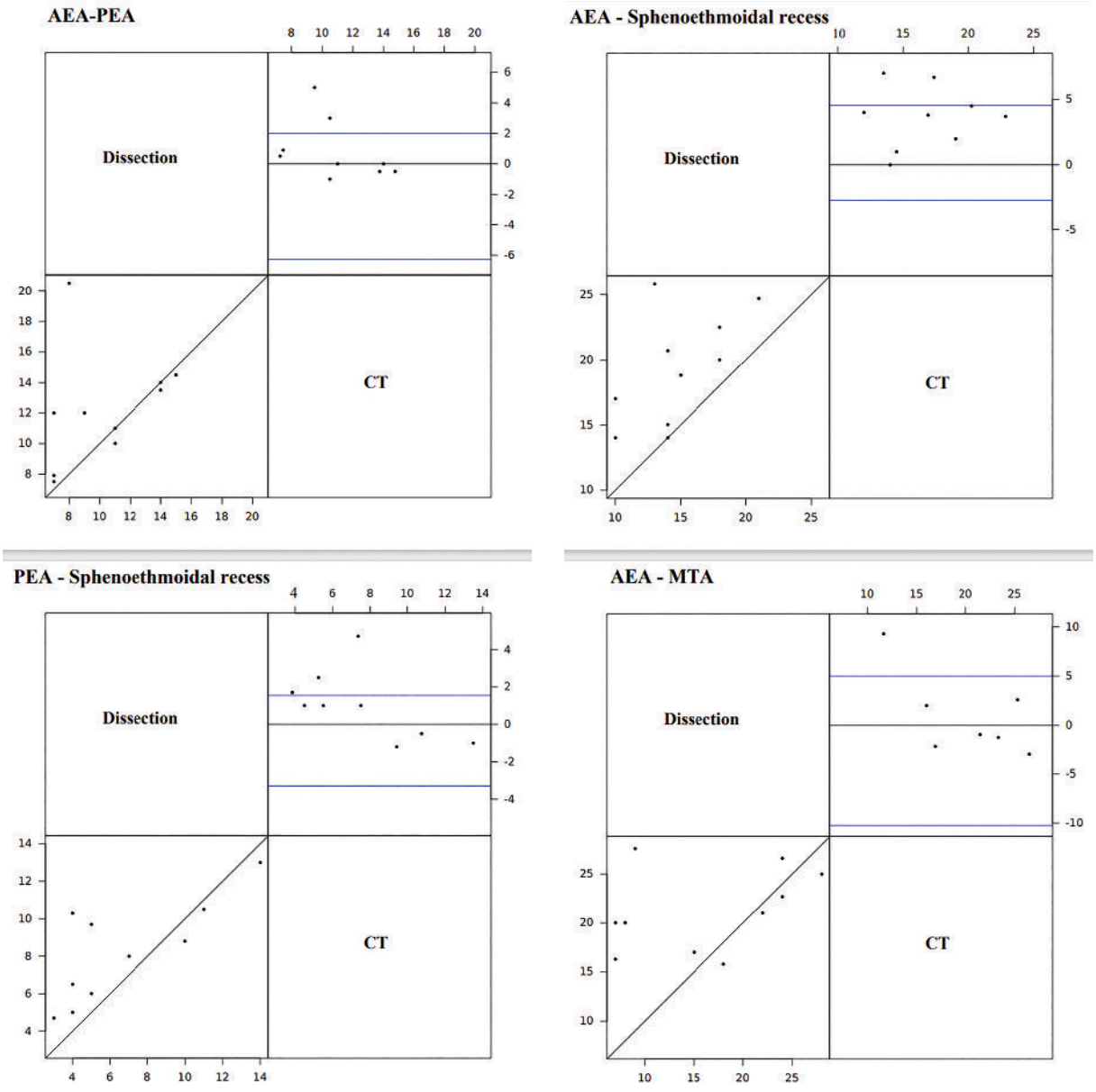


Figure 4. Distribution of dissection (X axis) and radiological (Y axis) data around the mean value. AEA=Anterior ethmoidal artery; PEA=Posterior ethmoidal artery; MTA=Axilla of the middle turbinate.

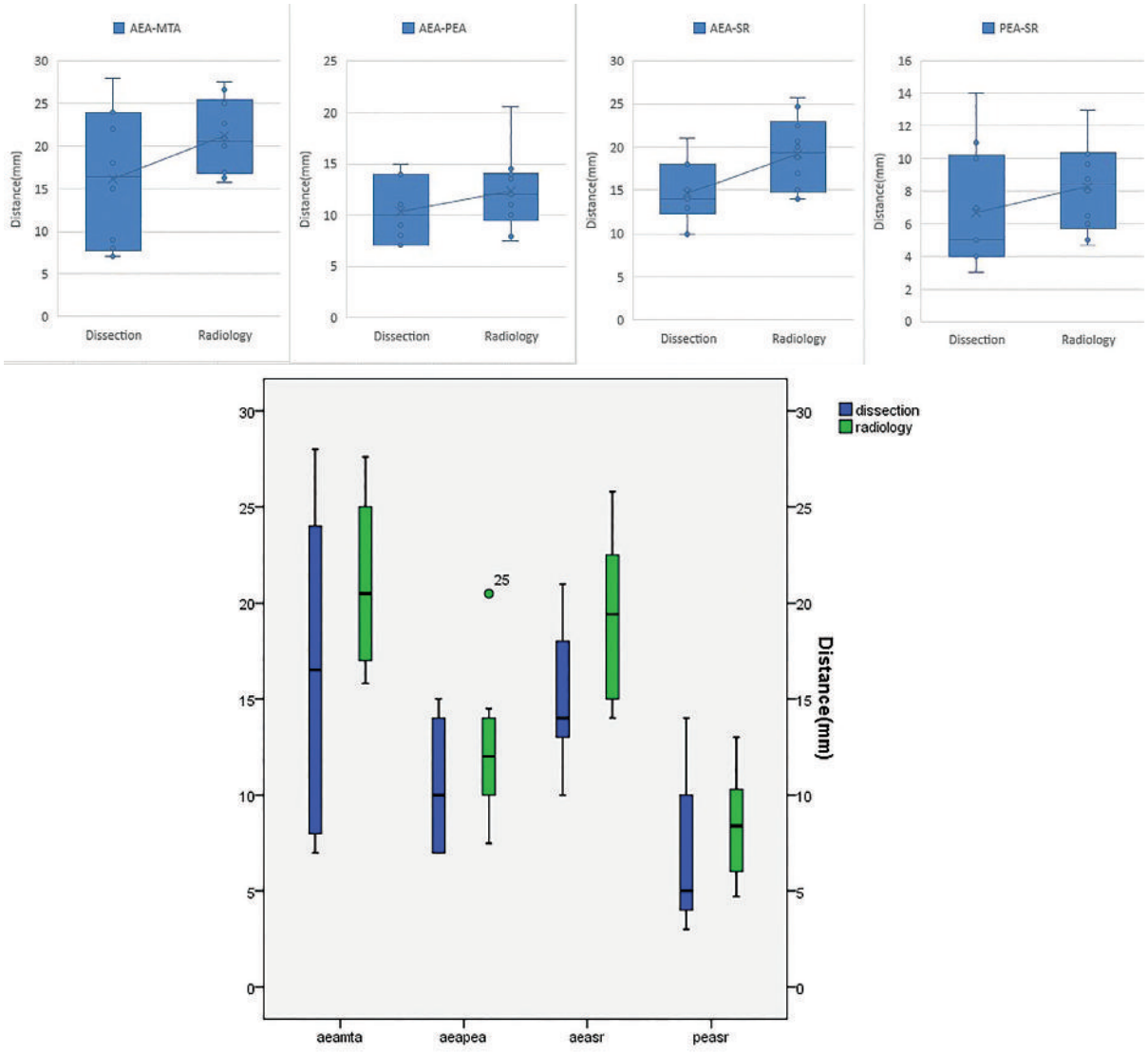


Figure 5. Box plots illustrating the comparisons of the distances. AEA=Anterior ethmoidal artery; MTA=Axilla of the middle turbinate; PEA=Posterior ethmoidal artery; SR=Sphenoethmoidal recess.

## Discussion

In this study, the mean distance of the PEA to the sphenoethmoidal recess was 6 mm in dissection, 8 mm in the sagittal section. The distance from the AEA to the PEA was 10±3 mm in dissection and 12±3 mm in axial section. There were no statistically significant differences between the radiological and dissection measurements. As a result, both the AEA and the sphenoethmoidal recess can be used for identifying the PEA. Similar to our study, in their cadaveric study Han et al. indicated that the PEA was usually 10 to 13 mm behind the AEA, while they also indicated that using the AEA as an endoscopic landmark to find the PEA might not be the most consistent landmark. Rather, the anterior wall of the sphenoid sinus can be a better endoscopic landmark for finding the PEA (10). In another radiological investigation, the average distance from the AEA to the PEA was 11.24 mm (7).

The relationship of the anterior ethmoidal artery to the sphenoid sinus has not been studied as

much as its relationship to the posterior ethmoidal artery. The distance from the sphenoethmoidal recess to the AEA was 19±4 mm in the sagittal section, 14±3 mm in dissection. The difference was statistically significant (P<0.05). The sphenoid sinus is not as reliable as the PEA for the AEA.

The mean distance of the AEA to the MTA was 16±8 mm in dissection and 21±4 mm in the sagittal section. There was no statistically significant difference between the dissection and the radiological evaluation. One of the most studied landmarks for recognition of the AEA is the MTA. Lee et al. stated that the distance from the MTA to the artery was 20 mm on average in their cadaver anatomical study, and it was accepted that it had the least variation both within and between individuals (12). Similar to this study, in another study the MTA was the most dependable anatomic landmark to localize the artery (11, 13). In addition to these studies, in a radiological study the average distance from the MTA to the AEA was 1.88 cm (6).

There is no study in which both radiological and dissection evaluations of the ethmoid arteries were performed between two points in the same subject, but the current literature includes only either radiological or dissection studies. In our study, the distances between two landmarks were measured in radiological sections taken before dissection. Then, the same measurements were measured in fresh cadaver dissection and compared with each other. The difference between published articles and our parameters can be attributed to different ethnicities and genders (11, 12). However, the MTA is an important anatomical landmark in defining the anterior ethmoidal artery.

In recent years, many scientists around the world have made a great effort to find the ethmoidal arteries, and have tried different approaches. However, the diversity of anatomical relationships between ethmoidal arteries and ethmoid cells, and their variations make it difficult to recognize the artery during surgery on the basis of these data alone (14). Therefore, we believe that the measurement of landmarks determined in the ethmoidal arteries on each patient's CT section before surgery will benefit the surgeon during the operation.

Ethmoid arteries are landmarks used in nasal surgery, endoscopic neurosurgery and control of epistaxis. In addition, in order to be protected from complications in nasal surgery, the ethmoid arteries should be recognized and protected from damage. Therefore, it is important to localize the ethmoid arteries and identify them using landmarks. In our study, we evaluated the important landmarks for the ethmoidal arteries from CT images, and showed that they can be used during surgery. We believe that this information will be a guide for sinus surgery, endoscopic neurosurgery and epistaxis interventions.

## Conclusion

In conclusion, to obtain information about the anatomic localization of the ethmoidal arteries and to measure the distances of these arteries to the stated landmarks, CT should be performed preoperatively and evaluated. Endoscopic and radiological measurements of the ethmoidal arteries are consistent and reliable with each other. It would be beneficial for surgeons to have measurements of the ethmoidal arteries in the radiology report.

**What Is Already Known on This Topic:**

*There are many studies that focus on the course of the ethmoidal arteries. In the CT studies, the axilla of the middle turbinate, nasal spine, nasal beak, nasion, optic foramen and nasal crest were studied. In the dissection studies, the axilla of the middle turbinate, nasal sill, the anterior nasal spine, the lateral nasal wall, and the anterior wall of the sphenoid sinus were studied.*

**What This Study Adds:**

*There is no study in which both radiological and dissection evaluations of the ethmoid arteries were performed between two points in the same subject, and the current literature usually includes only either radiological or dissection studies. In our study, the distances between two landmarks were measured in radiological sections taken before dissection. Then, the same measurements were measured in fresh cadaver dissection and compared with each other.*

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**Conflict of interest:** The authors declare that they have no conflict of interest.

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# Stress Response Assessment between First and Second Elective Caesarean Sections by Comparing Cortisol Levels

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**Abstract**

**Objectives.** The aim of this study was to compare the stress response produced during elective CS for the first and second time. For that goal, cortisol blood levels before, during and after childbirth were measured. **Materials and Methods.** We performed this prospective observational study during the period of September 2020 to September 2021. Blood samples were taken from all participants at three different stages. A statistical analysis was performed to compare the CS1 (first elective Caesarean) and CS2 (second elective Caesarean) groups. **Results.** At every stage, the levels of cortisol were statistically higher in the CS1 group than in the CS2 group. Therefore, CS2 generates a significantly less stressful response than CS1. Between stages, in CS2 cortisol was lowered at a faster rate than in CS1, meaning the stress response initiated was present for a longer time period in the CS1 group. **Conclusion**. A second elective caesarean section is a safe procedure that does not place an unnecessary burden upon the mother. This is an important fact that practitioners can rely upon while designing the ideal management of a pregnant woman for the stressful environment of birth.

**Key Words:** Cortisol ▪ Stress Response ▪ Caesarean Section ▪ Pregnancy ▪ Childbirth.

## Introduction

Stress is a stimulus, originating either from the environment or from the organism itself, that produces a response from the receptor organism. The response that serves as an answer to the stimuli is called the stress response (1). All living organisms face physiological stress, and nature has adapted a series of systems with the sole purpose of achieving the desired homeostasis. Two basic feedback systems provide a fast positive impact, the sympathetic nervous system (SNS) and the hypothalamic-pituitary-adrenocortical (HPA) axis. The SNS elevates blood pressure and heart rate, and stimulates hepatic glucogenolysis. The glucocorticoids produced from the HPA axis restrict the burden and time allocated by the organism to the stress response. Lengthening the time allocated to the stress response may prove harmful and be a cause of loss of stress control (2). Interestingly, it has been found that the HPA axis, as a source of stressful stimuli, holds an important place in the development of the embryo and the safe resolution of the pregnancy (3, 4).

Pregnacy requires a careful balance of the endocrine and immune systems in order for the human body to adapt to the new conditions (5). The fetus lies in an increasingly stressful environment at the end of pregnancy, foretelling the beginning of labor (6). These stress signals produce a response from the fetal HPA axis in the release of dehydroepiandrosterone sulfate (DHEAS) and cortisol (CORT) by the adrenal glands of the fetus (7). The high levels of estrogen in the blood are created from the conversion of DHEAS. The low progesterone levels, in conjunction with the high estrogen, reconstruct the cellular tissue of the

cervix, resulting in the stages of dilation. After the birth of the newborn, the levels of the corticotropin releasing hormone (CRH) return to the values before the pregnancy (8).

The correlation between prenatal maternal stress and maternal endogenous cortisol is well known (9, 10). The normal development of the fetus is dependent upon the cortisol hormone (11). The mother's cortisol levels may increase up to 2 to 4 times (4), which is necessary for the neural development of the newborn (12). On the other hand, excess maternal cortisol exposure may prove harmful to the development of the child's brain (13, 14). The effectiveness of the HPA axis is known to change during caesarean section surgery. The stress that the mother is subjected to has been recorded to decrease with the administered analgesia. Cortisol levels have been calculated to be lower in mothers undergoing caesarean delivery compared to vaginal delivery, a phenomenon worth investigating (8, 15).

The HPA axis of the pregnant woman shows the state of hypercortisolism. Pregnancy increases levels of cortisol, the adrenocorticotropic hormone (ACTH), the corticotropin-releasing hormone (CRH) and corticosteroid-binding globulin (CBG). Research suggests that the placenta secretes CRH and ACTH, increasing cortisol levels in the blood. Placental CRH is believed to be unaffected by negative feedback. In fact, the cortisol level of the fetus enhances placental CRH production. The highest CRH levels in the maternal blood are detected during the third trimester of pregnancy. Childbirth is the time point after which CRH returns to the pre-pregnancy values. Apart from this, circulating estrogens have a positive effect on CBG production by the liver. More free cortisol is bound, thus negative feedback is lessened, cortisol synthesis is increased, and the clearance rate of cortisol decreases (16).

The published literature suggests that caesarean section (CS) causes a reduced stress response in the newborn, taking into account the lower levels of cortisol in the umbilical blood (17). Knowing that there is a distinct correlation between the HPA axis of the newborn and the stressful environment of birth, it is well worth performing studies that assess the relationship between stress occurring at birth and the response of the fetus's mother (16, 18). The precise mechanisms that cause the phenomenon described here to take place are worth exploring further. For that goal, cortisol blood levels before, during and after childbirth were measured. Cortisol acts as the mediator for the "fight or flight" response in stressfull stimuli, promoting hormonal adaptations to these stimuli (19).

The aim of this study was to compare the stress response produced during elective CS for the first and second times.

## Materials and Methods

We performed this prospective observational study during the period from September 2020 to September 2021 at the "Helena Venizelou" General and Maternity Hospital in Athens.

### *Demographic Characteristics*

The women that were included in this study fulfilled a specific set of characteristics. Inclusion criteria were as follows: Aged between 20 and 44 years old; Singleton pregnancies with consent for elective CS given before going into labor; Labour did not start spontaneously; CS performed during the hours 9:00–14:00; Obstetric history (current or past) free of complications; CS performed at term. Exclusion criteria were as follows: Aged younger than 20 years old or older than 44 years old; Multifetal pregnancy; Labor started before 37 weeks or after 40 weeks; Medical history with obstetric complications in the current or past pregnancy (pregnancy hypertension, preeclampsia, gestational disorders, intrauterine growth restriction (IUGR), oligohydramnios or hydramnios, gestational/mellitus diabetes, corticosteroid treatment, autoimmune diseases, hepatic insufficiency); Conception using assisted reproduction techniques (ART).

The sample size of this study (N=40) was divided into two groups according to the number of CSs that they had undergone, CS1 for the group of

women that were undergoing elective CS for the first time (N=20) and CS2 for the group of women that were undergoing CS for the second time. All recorded CSs were performed under epidural anesthesia and did not present intraoperative complications.

### *Blood Sample Analysis*

Blood samples were taken from all participants. Samples were collected from the median antebrachial vein of the women at three different stages: Stage I: 120 minutes before childbirth; Stage II: 120 minutes after childbirth; Stage III: 48 hours after childbirth. Ethylenediaminetetraacetic acid (EDTA) test tubes were used to collect the blood samples. The test tubes were left to clot for 30 minutes at room temperature after collection. The samples were centrifuged in a refrigerated centrifuge at 4000 rev/min for 10 minutes in order to remove the clots. The blood serum was then transported to 0.5mL aliquots and stored at -80 °C.

Standard competitive enzyme-linked immunosorbent assay (ELISA) was employed for the quantification of blood serum levels of cortisol. Commercial kits were used, according to the manufacturer's instructions (cortisol parameter assay kit, provided by the R&D Systems Inc., Minneapolis, USA). 96-well microtiter plates were used for the analysis. A microplate reader (Varsamax, Molecular Devices, Sunnyvale, CA, USA) at 450 nm was used for color formation measurement. Calculations were made using SoftMax Pro software (Molecular Devices). Average values were recorded after duplicate analysis of samples (19).

### *Ethics Statement*

The Bioethics Committee of the hospital approved the study protocol and the consent form (document number: 137/12-05-2020) in accordance with the Helsinki Declaration. Oral instructions about the process and goals of the study were given to all women whose participation was approved. All women included in the study signed a written consent form.

### *Statistical Analysis*

Statistical analysis was performed to compare the CS1 and CS2 groups regarding the levels of cortisol. In addition, data from the patients' clinical records were compared, that is, maternal age, gestational age and birth weight. Data were expressed as mean±SD and the Shapiro-Wilks test examined the normal distribution of the parameters. Homogeneity between groups was performed using the independent samples t-test. We used the two-way Mixed ANOVA model using as factors "caesarean delivery" (between groups) and "time" (within the group) for analysis of the biochemical markers. Since there was statistically significant interaction between these factors, we used univariate analysis, e.g. comparison between groups for each stage separately and comparison of stages for each group separately, making the appropriate adjustment of P-values based on the Bonferroni correction. More specifically, a one factor Repeated Measures ANOVA model was used for comparison of the different stage measurements of biochemical markers for each group, and the independent samples t-test was used for the between groups comparison at each stage separately, making all the necessary adjustments of P-values. Sensitivity analysis concerning the baseline-balance between the two groups was performed using the analysis of covariance model (ANCOVA) considering the absolute change from Stage I to Stage II and Stage III respectively as dependent variables, the group (caesarean delivery 1 vs. caesarean delivery 2 ) as a factor and the Stage I value as a covariate. All tests are two-sided, and statistical significance was set at $P<0.05$. All analyses were carried out using the statistical package SPSS vr 21.00 (IBM Corporation, Somers, NY, USA).

## Results

40 women participated in the prospective study presented. Twenty were primigravida that delivered via caesarean section, and twenty underwent caesarean section for the second time. There was no statistically significant difference between

the maternal ages (P=0.331) and the babies' birth weights (P=0.280) in the two groups, whereas there was a difference in the gestational age (P=0.014), but due to the small and similar standard deviations in the two groups, in effect, the difference in the gestational age was 0.5 weeks, or 3.5 days (Table 1).

There was statistically significant interaction between "caesarean delivery" and "time" factors F(2.76)=7.6 , P=0.001. There were statistical significantly differences between "caesarean deliveries" at Stage I t(38)=4.8 , P<0.0005 , Stage II t(38)=9.2 , P<0.0005 and Stage III t(38)=4.8 , P<0.0005 respectively (Table 2, 3).

There was a statistically significant difference between stage measurements for the "caesarean delivery 1" group (P<0.0005). Pairwise comparisons presented a statistically significant difference between Stage I and Stage II (P<0.0005) Stage III (P<0.0005) respectively and Stage II and Stage III (P<0.0005).

There was a statistically significant difference between stage measurements for the "caesarean delivery 2"" group (P<0.0005). Pairwise comparisons presented a statistically significant difference between Stage I and Stage II (P<0.0005) and Stage III (P<0.0005), respectively, and Stage II and Stage III (P<0.0005) (Figure 1).

The absolute change in cortisol levels from Stage I to Stage II was statistically significantly lower for "caesarean delivery 2" than "caesarean delivery 1" -F(1.37)=45.2 ; P<0.0005. The absolute changein cortisol levels from Stage I to Stage III was statistically significantly lower for "caesarean delivery 2" than "caesarean delivery 1" F(1.37)=16.7; P<0.0005 (Figure 2).

Table 1. Demographic Characteristics

| Characteristics | Caesarean delivery 1 | Caesarean delivery 2 | Mean difference (95% CI) | P-value* |
|---|---|---|---|---|
| Age | 28.65±4.68 | 30.20±5.25 | -1.55 (-4.73–1.63 ) | 0.331 |
| Gestation period | 38.29±0.61 | 37.81±0.58 | 0.49 ( 0.10–0.87 ) | 0.014 |
| Birth weight | 3159.50±382.82 | 3030.25±362.62 | 129.25 (-109.44–367.94 ) | 0.280 |

*Independent samples t-test.

Table 2. Comparison of Cortisol between Groups during the Observation Period

| Group | Stage I | Stage II | Stage III | P-value (wg) |
|---|---|---|---|---|
| | ($\bar{x}$±SD) | | | |
| Caesarean delivery 1 | 225.6±11.3 | 127.9±9.8* | 105.1±7.1*,† | <0.0005 |
| Caesarean delivery 2 | 210.6±8.3 | 102.4±7.7* | 94.1±7.4*,† | <0.0005 |
| P-value (bg) | <0.0005 | <0.0005 | <0.0005 | - |

P-value (wg)_within groups; P-value (bg)=between groups; *P<0.0005 vs Stage I; †P<0.0005 vs Stage II; Analyses (wg) were performed using the one factor Repeated Measures ANOVA model and the Bonferroni test; Analyses (bg) were performed using the Independent samples t-test.

Table 3. Maca Stage Comparison

| Group | Maca* Stage I to II | Maca* Stage I to III |
|---|---|---|
| Caesarean delivery 1 (mean±SE†) | -91.1±2.3 | -112.6±1.9 |
| Caesarean delivery 2 (mean±SE†) | -114.8±2.3 | -124.4±1.9 |
| P-valuebg‡ | <0.0005 | <0.0005 |

*Mean absolute change adjusted from Stage I: †Standard Error; ‡Analysis of Covariance model (ANCOVA model).

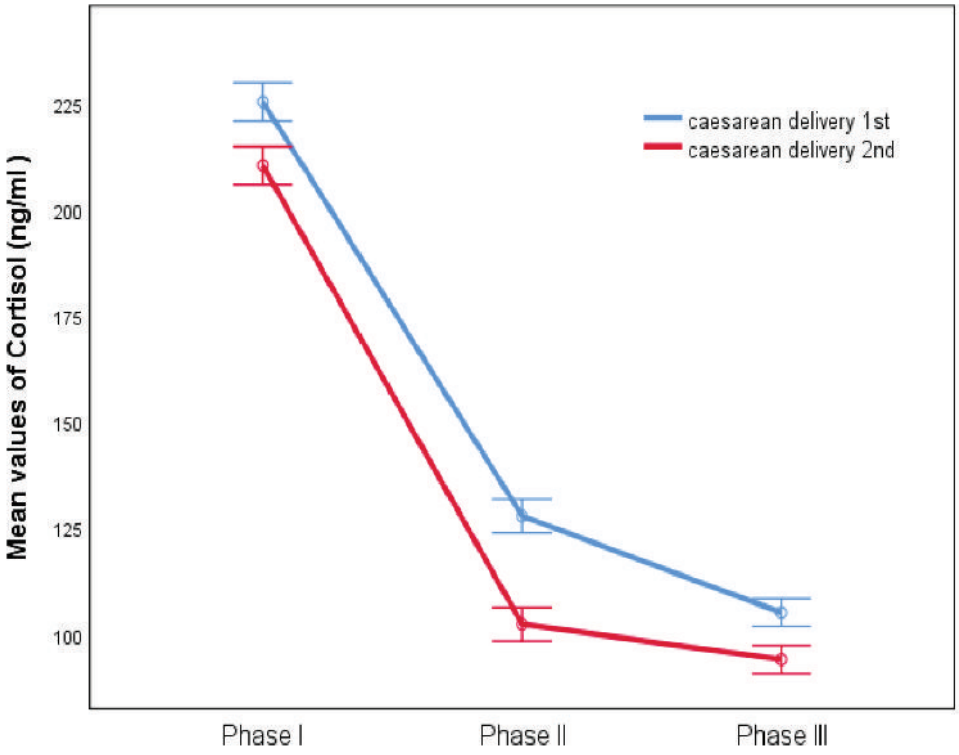


Figure 1. Mean values of Cortisol levels between groups during the observation period.

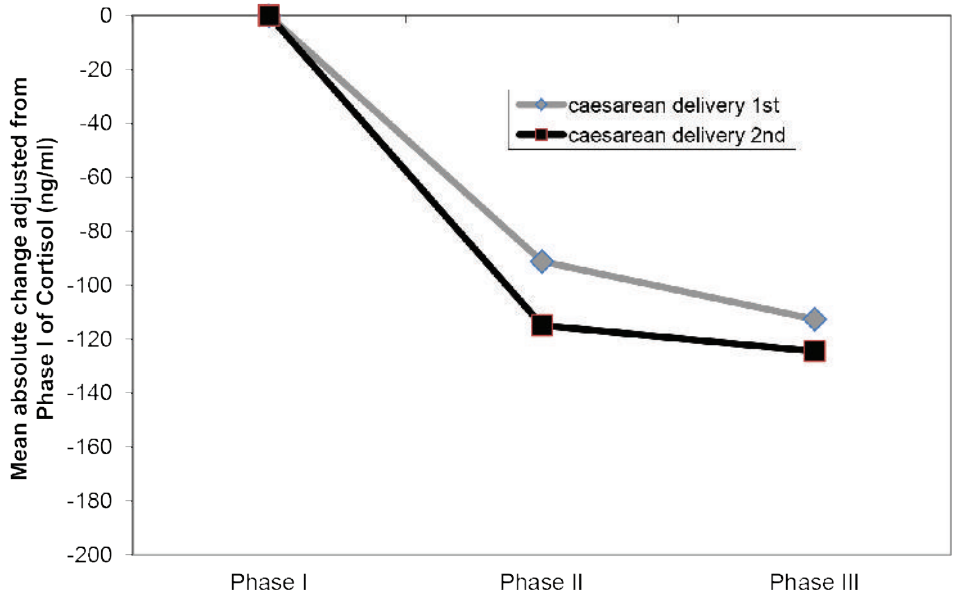


Figure 2. Absolute change in Cortisol levels adjusted from Stage I between groups during the observation period.

## Discussion

In this prospective study, we attempted to assess the stress response created by caesarean sections for the first and second time. This attempt was performed by comparing the levels of cortisol between two groups of women. To our knowledge, this is the first study attempting to correlate the cortisol levels in these two groups. As such, our results could serve as a point of reference for future studies. First, we examined whether cortisol fluctuated in the same way in both groups. The results of the study presented statistically significant interaction between the two groups at every stage, pointing to the fact that cortisone levels do not change in the same way in the two groups. At every stage the levels of cortisol were statistically higher in the CS1 group than in the CS2 group, showing that CS2 generates a significantly less stressful response than CS1.

Next, we made a pairwise comparison between stages to determine the variations in the rhythm of cortisol in the two groups. We detected that cortisol levels were statistically lower between stages, from Stage I to Stages II and III, as well as that in CS2 cortisol decreased at a faster rate than in CS1. The conclusion drawn is that the initiated stress response is present for a longer time period in the CS1 group.

From the above findings, it may be concluded that a second caesarean section is a safe procedure that does not place an unnecessary burden on the mother. This is an important fact that practitioners can rely upon while designing the ideal management of a pregnant woman for the stressful environment of birth. All women participating had to adhere to the set of criteria mentioned above, however a limitation of the study was that the measurements of cortisol were taken from different women. It is worth considering whether pregnant women with different biocharacteristics could affect the fluctuation rate of cortisol.

A credible indication exists in the method of analgesia. A considerable number of women are reluctant to be subjected to the laborious condition of childbirth without anesthesia. Findings suggest that the benefits of the advancements in analgesia procedures have a positive effect on stress management and the mental health of the prospective mother (15, 20), as well as postpartum depression, although evidence is conflicting at best (21). An organized study with the goal of cataloguing the experiences and mental states of women undergoing a second caesarean section could yield intriguing results.

### *Limitations of Study*

A major limitation of the study is its small sample size and the lack of sample size estimation.

In addition, recruitment was performed using convenience sampling of the patients attending the hospital without randomization. Lastly, our study, being the first of its kind, has no direct comparison to draw from. More studies in this area of expertise could yield useful data.

## Conclusion

The conclusions derived from this study could also be of benefit to practitioners when performing follow-up of high-risk pregnancies. It is currently unknown whether the cortisol rate behaves the same way in the management of high-risk pregnancies. This study indicates this finding, but research specifically constructed to target this goal could prove invaluable.

**What Is Already Known On this Topic:**
*Stress is a stimulus, originating either from the environment or from the organism itself, that produces a response from the receptor organism. The published literature suggests that caesarean sections (CS) cause a reduced stress response in the newborn, taking into account the lower levels of cortisol in the umbilical blood.*

**What This Study Adds:**
*The aim of this study was to compare the stress response produced during elective CS for the first and second times. For that goal, cortisol blood levels were measured before, during and after childbirth. The analysis showed that it may be concluded that a second caesarean section is a safe procedure that does not place an unnecessary burden on the mother. This is an important fact that practitioners can rely upon while designing the ideal management of a pregnant woman for the stressful environment of birth.*

**Author Contributions:** Conception and Design: NK; Methodology: NK; Acquisition,analysis and interpretation of data: DG and CB; Drafting the article: DG, PKK and AS; Revising it critically for important intellectual content: NK, FA and ID; Approved final version of the manuscript: NK and AM; All authors have read and agreed to the published version of the manuscript.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

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# Physical Activity Level Alterations Due to the Lockdowns: A Multi-Center Greek University-Based Study

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**Abstract**

**Objective**. This cross-sectional study determines the impact of the pandemic lockdowns on physical activity, and evaluates the factors associated with physical activity cessation on students and personnel of eight Greek Higher Education Institutions. **Materials and Methods.** A total of 6,380 volunteer participants completed a survey reporting their physical activity levels and perceptions during the COVID-19 pandemic. The survey was made available through an online platform. **Results.** Both the conduct and intensity of physical activity were significantly reduced from the pre-pandemic era to the second lockdown ($P<0.001$). Walking was the most frequently selected type of physical activity, in all periods except for the second lockdown. Loss of interest (52.4%) was the main, self-reported factor for cessation of physical activity. Females had a 31% lower probability of ceasing physical activity during lockdowns. **Conclusion.** The conduct and intensity of physical activity decreased significantly during the pandemic. Female gender, annual checkup attendance, and specific physical activity types during the pre-pandemic era were associated with a reduction in the risk of pausing physical activity during lockdowns. Lockdowns may be implemented in future health crises, hence measures for maintaining the physical activity of the general population, such as online group sessions and support from healthcare professionals, should be prepared.

**Key Words** Exercise ▪ Survey ▪ Pandemic ▪ Musculoskeletal Health.

## Introduction

Following the declaration of the COVID-19 pandemic by the World Health Organization (WHO) on March 11, 2020 (1), various restrictive measures were put in place to curb the spread of the SARS-CoV-2 virus. These measures included the cancellation of mass gatherings, the closure of public areas, and the mandatory use of protective masks. The first infection in Greece was recorded on February 26th, 2020, and from then, the Greek government implemented strict preventive measures in good time, including two national lockdowns, to prevent the spread of the coronavirus (2). The main concern in Greece was the endurance of the aged national health system under the pressure of the country-level epidemic. A depiction of the COVID-19 pandemic timeline in Greece is presented in Figure 1. This confinement may have led to several modifications in everyday activities that might have eventually resulted in the adoption of sedentary behavior, predisposing to a variety of diseases, such as obesity, and cardiovascular

[a] Authors' equal contribution

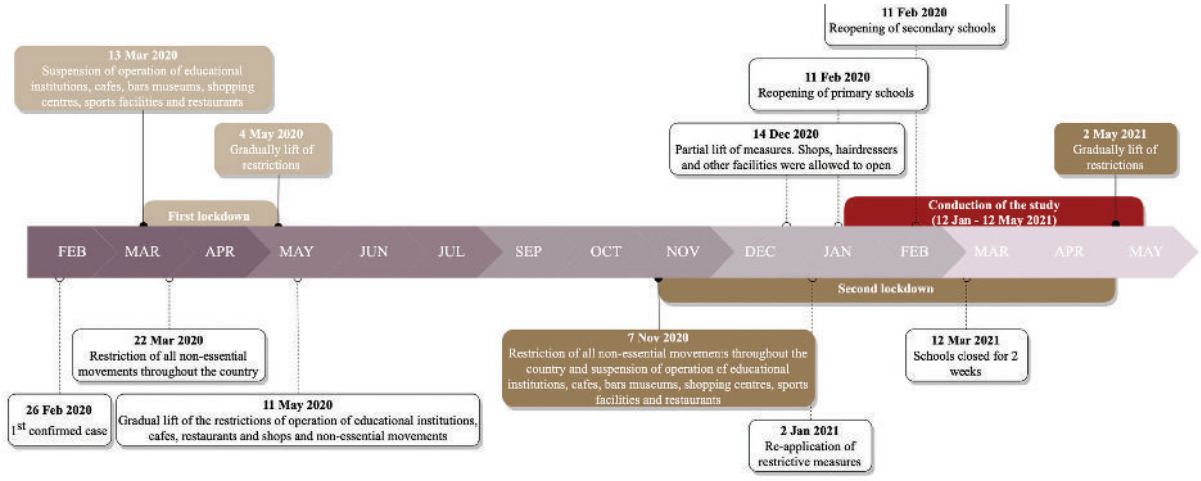


Figure 1. The COVID-19 pandemic timeline in Greece.

and osseous diseases (3, 4). Regardless of the levels of physical activity (PA), recent research suggests a correlation between sedentary behavior and mortality (5-11). Additionally, excessive sedentary behavior and a lack of PA are connected to psychological distress and mental health disorders, including depression (12, 13).

The current questionnaire-based multi-center study aimed to record the alterations in PA levels in Greece during the pandemic-related lockdowns, and to identify the factors associated with physical inactivity.

## Materials and Methods

### *Study Design*

From January 12, 2021, to May 12, 2021, a cross-sectional multi-center study was conducted in Greece. The study involved students and personnel from eight Greek Higher Education Institutions. A total of 26 Institutions were invited to participate, and 8 out of 26 (30.8%) agreed. The collaborating Institutions posted an announcement on their official website, which included details about the study and a link to the questionnaire. Any adult over 18 years who was involved with any of the collaborating Greek Highest Education Institutions on an academic or occupational level was considered eligible, regardless of gender, academic year, full-time/part-time employment, or academic program.

### *Questionnaire Development*

The questionnaire consisted of 34 questions, with each question representing a different study variable. The questions were divided into 4 domains. Prior to beginning the study, the questionnaire underwent testing for validity and completeness. On the basis of input from expert academics who were not involved in the study, changes were made to improve it. The first set of questions focused on standard sociodemographic factors, including age, gender, height (in centimeters), weight (in kilograms with no decimal approximation), living conditions (living with others, number of household members, and permanent residency), educational attainment, employment status, and smoking habits. For the study purposes, smoking was defined as having smoked at least one cigarette every 1-3 days for six months. Former smokers were those who had quit tobacco for at least a year, while occasional smokers fell between these two categories. Alternatives such as IQOS® or electronic cigarettes were also available as options. For all former smokers, the duration of smoking cessation (in months) was also required. The second domain was related to the participants' health status. Questions related to any history of underlying diseases (occurrence and type of disease), the effect of the diseases on performing PA (restriction), and the preventive measures taken for participants with such diseases (advice from a physician about PA and regular follow-up attendance). The third

domain was related to the participants' PA level. PA was defined according to WHO recommendations for adults aged between 18–64 years as the conduct of at least 150 minutes of moderate-intensity PA per week (14). The participants were asked to report information regarding their PA engagement (yes or no), the frequency (average number of times within a week), and the type of PA in four distinct periods: during the pre-pandemic era, the first lockdown, between the lockdowns, and during the second lockdown. The fourth and final domain contained 4 Likert-scale questions related to the participants' perspective regarding the relationship of the pandemic with PA. A sample of the questionnaire is provided in the Supplementary material.

### *Data Collection*

The questionnaire was made available to the participants via the Google Forms platform (Google LLC, United States) by creating a separate link for each of the participating Greek Higher Education Institutions. Since the present study was conducted on a voluntary and anonymous basis, no emails or other personal data of the respondents were collected. However, double replies from the same participant were prevented by activating the "limiting replies" to a once-per-person function in Google Forms. The total number of individuals associated with these 8 Greek Higher Education Institutions and hence, those who could access and complete the questionnaire, was calculated to be 121,065 (110,514 students, 6,409 academicians, and 4,142 administrative officers). Incomplete questionnaires were not considered eligible. During the questionnaire's availability (a 5-month period - January to May 2021), a total of 6,380 valid questionnaires were gathered (5.3%). A map chart displaying the administrative regions that were declared as the respondents' permanent residences, and the frequency of replies per Higher Education Institute is presented in Figure 2.

### *Ethics Statement*

The study was approved by the Ethics Committees of the National and Kapodistrian University of Athens, Greece, and the Aristotle University of Thessaloniki, Greece (N/2020/0567). The research was conducted following the principles of the 1964 Declaration of Helsinki and its later amendments.

### *Statistical Analysis*

Statistical analysis was performed with the STATA statistical software (Release 14.0, Stata Corp., TX, USA) for macOS. The Shapiro–Wilk test, the evaluation of skewness and kurtosis values, as well as the visual interpretation of the histograms produced were used to assess data normality. In the case of normally distributed quantitative variables, mean and standard deviation (SD) values were used, otherwise, the median and interquartile range (IQR) were provided. All qualitative variables, except smoking cessation, were translated into categorical ones. The ages were subdivided into 5 groups (group 1: 18-24 years, group 2: 25-34 years, group 3: 35-44 years, group 4: 45-54 years, and group 5: 55-64 years), the height and weight into BMI levels (underweight: BMI score <18.5 kg/m$^2$, normal weight: BMI between 18.5 and 24.9 kg/m$^2$, overweight: BMI between 25.0 and 29.9 kg/m$^2$ and obese: BMI >30.0 kg/m$^2$), and the PA frequency into two PA intensity categories (irregular:< 5 days/week, and regular: ≥5 days/week). All qualitative variables were expressed in absolute (N) and relative (%) values. To compare ratios, Pearson's Chi-square test or Fisher's exact test were used for unpaired, and McNemar's test for paired data. The student's t-test was used to compare smoking cessation between the two groups. A stepwise multiple logistic regression analysis was conducted to investigate independently associated factors with the likelihood of ceasing the PA conduct during the pandemic. Adjusted odds ratios with 95% confidence intervals were computed from the results of the logistic regression analysis. Statistical significance was set at 0.05.

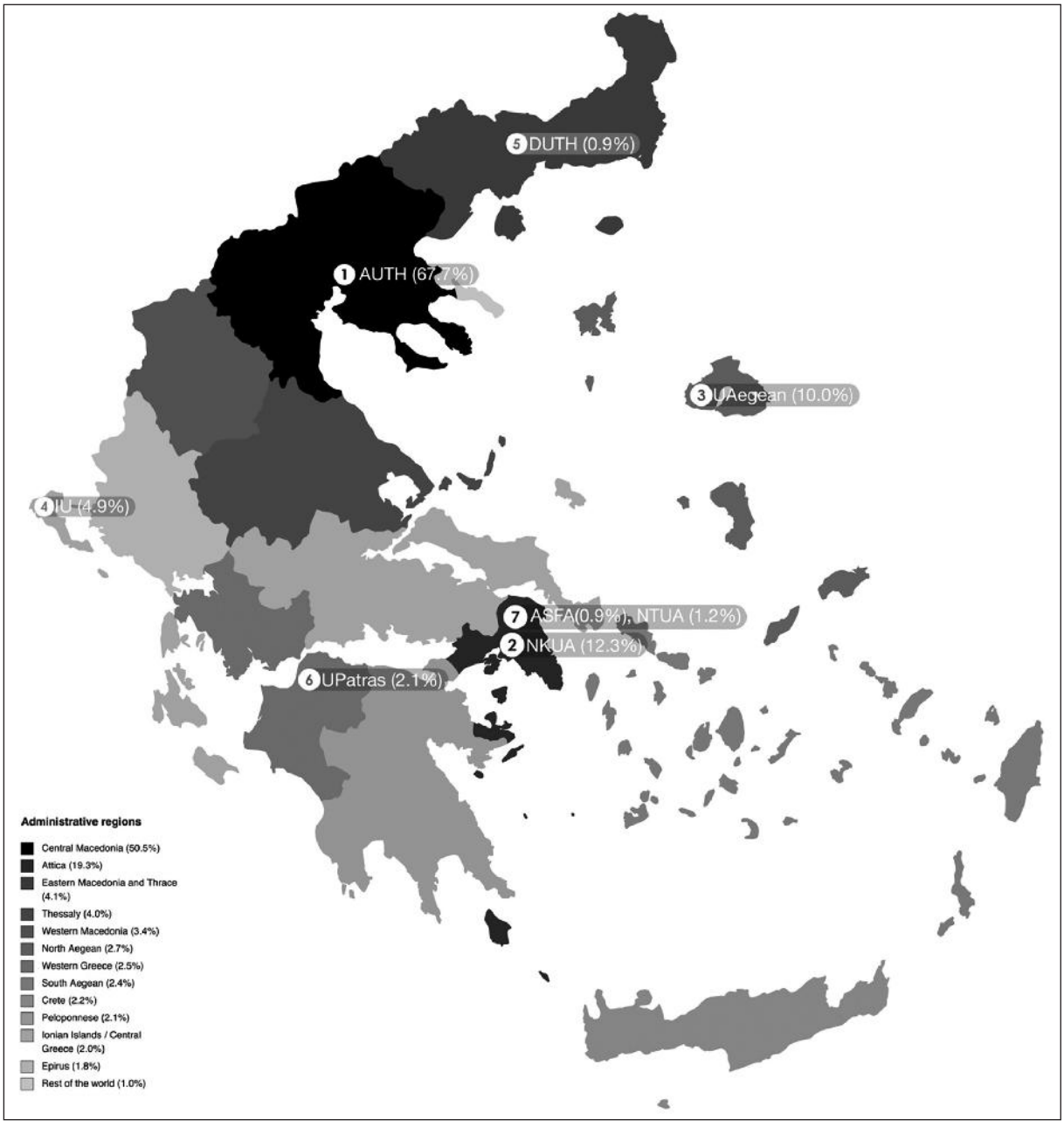


Figure 2. The mapping of the respondents per area in Greece.

## Results

### *Sociodemographic Factors and Health Status*

Among the 6,380 respondents, 67.7% (4,316 subjects) were females and 61.8% (3,943 subjects) were aged from 18 to 24 years. Most of the respondents (69.8%, 4.451 subjects) attended the Higher Education Institutions as undergraduate students, 90.3% of the study population had no history of underlying disease, 73.6% were non-smokers (4,693 individuals) and 50.2% of them did not regularly attend any annual check-ups by a physician. 73.6% of the participants had no restriction on performing PA. The sociodemographic characteristics of the participants and their health status are summarized in Table 1.

Table 1. Participants' Characteristics (socio-demographic Factors) in the Study, PA-Physical Activity

| Studied variables | Number of participants (%) |
|---|---|
| Age groups (years) | |
| 18-24 | 3,943 (61.80) |
| 25-34 | 772 (12.10) |
| 35-44 | 530 (8.31) |
| 45-54 | 700 (10.97) |
| ≥ 55 | 435 (6.82) |
| Gender | |
| Males | 2,064 (32.35) |
| Females | 4,316 (67.65) |
| Housing- living with other people | |
| No | 2,128 (33.35) |
| Yes | 4,252 (66.65) |
| People living with | |
| 1 person | 421 (9.90) |
| <5 people | 3,783 (88.97) |
| ≥5 people | 48 (1.13) |
| Permanent residency | |
| Hometown | 3,950 (61.91) |
| Other | 2,430 (38.09) |
| Highest level of education | |
| High school diploma | 2,603 (40.80) |
| Bachelor's degree | 760 (11.91) |
| MSc degree | 875 (13.71) |
| PhD degree | 2,142 (33.57) |
| Occupation | |
| Undergraduate student | 4,451 (69.76) |
| Academician | 707 (11.08) |
| Administrative officer | 1,110 (17.39) |
| Other (professor emeritus etc.) | 112 (1.75) |
| Smoking status | |
| Non-smokers | 4,693 (73.56) |
| Never smoked | 3,891 (82.91) |
| Smoked in the past | 791 (16.85) |
| Duration of smoking cessation* | 94.16±103.48† |
| Alternatives (i.e., electronic cigarettes) | 11 (0.23) |
| Smokers | 1,687 (26.44) |
| Daily | 822 (48.73) |
| Occasionally (i.e., social smoker) | 865 (51.27) |
| BMI level | |
| Normal | 4,134 (64.80) |
| Underweight | 322 (5.05%) |
| Overweight | 1,466 (22.98) |
| Obese | 458 (7.18) |
| Difficulty maintaining weight | |
| No | 3,185 (50.28) |
| Yes | 3,149 (49.72) |
| History of underlying disease | |
| No | 5,762 (90.31) |
| Yes | 618 (9.69) |
| Disease (type) | |
| Endocrine | 190 (30.74) |
| Circulatory system | 189 (30.58) |
| Cancer | 20 (3.24) |
| Respiratory system | 66 (10.68) |
| Blood and the blood forming organs | 28 (4.53) |
| Digestive system | 32 (5.18) |
| Other (i.e., musculoskeletal disease) | 93 (15.05) |
| Restrictions on performing PA | |
| No | 455 (73.62) |
| Yes | 163 (26.38) |
| Preventive measures- Participants free of history of disease- annual check-up attendance | |
| No | 2,088 (50.18) |
| Yes | 2,073 (49.82) |
| Participants with history of disease- advice from physician about PA | |
| No | 195 (31.55) |
| Yes | 423 (68.45) |
| Regular follow-up attendance | |
| No | 2,687 (46.63) |
| Yes | 3,075 (53.37) |

*In months; †Median±IQR.

### *Physical Activity Conduction, and Intensity*

A significant decrease (P<0.001) in both the conduct and intensity of PA was recorded between the pre-pandemic and the 2nd lockdown era. In particular, before the pandemic most respondents performed PA for a duration of more than an hour (92.4%) and were engaged in PA less than three times per week (61.3%), while during the 2nd lockdown, fewer respondents were engaged in PA (58.9%) and were performing PA irregularly (63.6%). Concerning the type of PA, walking was most frequently chosen in all periods (P<0.001), except during the second lockdown, when home

Table 2. Physical Activity (PA) Status of Survey Participants (N=6380). In Brackets, the Percentage of Each Reply per Question Category (the Percentage of Each Overall Reply to the Total Replies) and in Parentheses, the Distribution of Each Reply in Preview and New Cases (the Percentage of Previews and New to Overall Cases) Are Reported

| Physical activity (PA) status | | | Examined period | | | |
|---|---|---|---|---|---|---|
| | | | Pre-pandemic era N (%) | First lockdown N (%) | Between lockdowns N (%) | Second lockdown N (%) |
| Engagement in PA | No | Previous cases* | - | 121 (15.9) | 450 (25.0) | 1,463 (55.9) |
| | | New cases† | - | 640 (84.1) | 1,350 (75.0) | 1,156 (44.1) |
| | | Overall‡ | 488 [7.6] | 761 [11.9] | 1,800 [28.2] | 2,619 [41.1] |
| | Yes | Previous cases* | - | 5,252 (93.5) | 4,269 (93.2) | 3,424 (91.0) |
| | | New cases† | - | 367 (6.5) | 311 (6.8) | 337 (9.0) |
| | | Overall‡ | 5,892 [92.4] | 5,619 [88.1] | 4,580 [71.8] | 3,761 [58.9] |
| | **Total** | | 6,380 [100.0] | 6,380 [100.0] | 6,380 [100.0] | 6,380 [100.0] |
| PA Intensity | Irregular | Previous cases* | - | 3,219 (89.8) | 2,566 (92.6) | 2,055 (85.9) |
| | | New cases† | - | 367 (10.2) | 205 (7.4) | 337 (14.1) |
| | | Overall‡ | 3,614 [61.3] | 3,586 [63.8] | 2,771 [60.5] | 2,392 [63.6] |
| | Regular | Previous cases* | - | 2,033 (100.0) | 1,703 (94.1) | 1,369 (100.0) |
| | | New cases† | - | - | 106 (5.9) | - |
| | | Overall‡ | 2,278 [38.7] | - | 1,809 [39.5] | - |
| | **Total** | | 5,892 [100.0] | 5,619 [100.0] | 4,580 [100.0] | 3,761 [100.0] |
| PA Type | Walking | Previous cases* | - | 2,020 (90.9) | 1,743 (100.0) | 1,134 (93.0) |
| | | New cases† | - | 202 (9.1) | | 86 (7.0) |
| | | Overall‡ | 1,956 [33.2] | 2,222 [39.5] | 1,743 [38.1] | 1,220 [32.4] |
| | Running | Previous cases* | - | 651 (96.7) | 547 (100.0) | 515 (90.7) |
| | | New cases† | - | 22 (3.3) | | 53 (9.3) |
| | | Overall‡ | 454 [7.7] | 673 [12.0] | 547 [11.9] | 568 [15.1] |
| | Sport | Previous cases* | - | 94 (96.9) | 82 (100.0) | 54 (10.00) |
| | | New cases† | - | 3 (3.1) | | |
| | | Overall‡ | 724 [12.3] | 97 [1.7] | 82 [1.8] | 54 [1.4] |
| | Gym | Previous cases* | - | - | - | - |
| | | New cases† | - | - | - | - |
| | | Overall‡ | 1,517 [25.7] | - | - | - |
| | Home workout | Previous cases* | - | 2,077 (94.8) | 1,564 (100.0) | 1,237 (91.8) |
| | | New cases† | - | 115 (5.2) | | 110 (8.2) |
| | | Overall‡ | 598 [10.1] | 2,192 [39.0] | 1,564 [34.1] | 1,347 [35.8] |
| | Other | Previous cases* | - | 410 (94.3) | 333 (51.7) | 484 (84.6) |
| | | New cases† | - | 25 (5.7) | 311 (48.3) | 88 (15.4) |
| | | Overall‡ | 643 [10.9] | 435 [7.7] | 644 [14.1] | 572 [15.2] |
| | **Total** | | 5,892 [100.0] | 5,619 [100.0] | 4,580 [100.0] | 3,761 [100.0] |

*As previous, all cases identified during the preceding period of the examined one (i.e., as per the conduction of PA the cases of the pre-pandemic era (121 cases) when the 1st lockdown is examined (overall cases: 761) are reported; New cases; †As new, all cases identified during the examined period [i.e., as per the PA conduction, the cases of the first lockdown (640 cases) when the 1st lockdown is examined (overall cases: 761)] are reported; ‡As overall, the total number of cases (sum of previous and new cases) are reported and indicated with brackets [ ]. Small brackets ( ) indicate the prevalence of each variable in previous status and new cases.

workout was preferred. The participants' PA levels during each period are summarized in Table 2.

### *Factors Associated with Conducting Physical Activity*

Most of the respondents reported a loss of interest (52.4%) and various other factors, mainly the self-perceived improvement of their physical condition and overall health status (58.1%), as the primary factors related to the cessation or the continuation of the PA conduct, respectively. The perspective of surveyees on the relationship of the COVID-19 pandemic with the PA is depicted in Figure 3. The results of the univariable and multivariable logistic regression analyses (Table 3) indicate that a) female gender, b) annual checkup attendance, and c) some types of PA during the pre-pandemic era are significantly associated with a decrease in the likelihood of stopping PA during lockdowns. Specifically, the likelihood of cessation of engagement in PA during the lockdowns decreased by 31.0% for female over male participants (OR, 0.69; 95% CI, 0.49-0.98; P=0.041), 47.0% for participants that attended checkups on an annual basis (OR, 0.53; 95% CI, 0.38-0.75; P<0.001) over the ones who did not, and 52.0% or 91.0% for participants choosing running (OR, 0.48; 95% CI, 0.23-0.98; P=0.044) or home workout (OR, 0.09; 95% CI, 0.02-0.36; P=0.001) over walking, as the preferred type of PA before the pandemic.

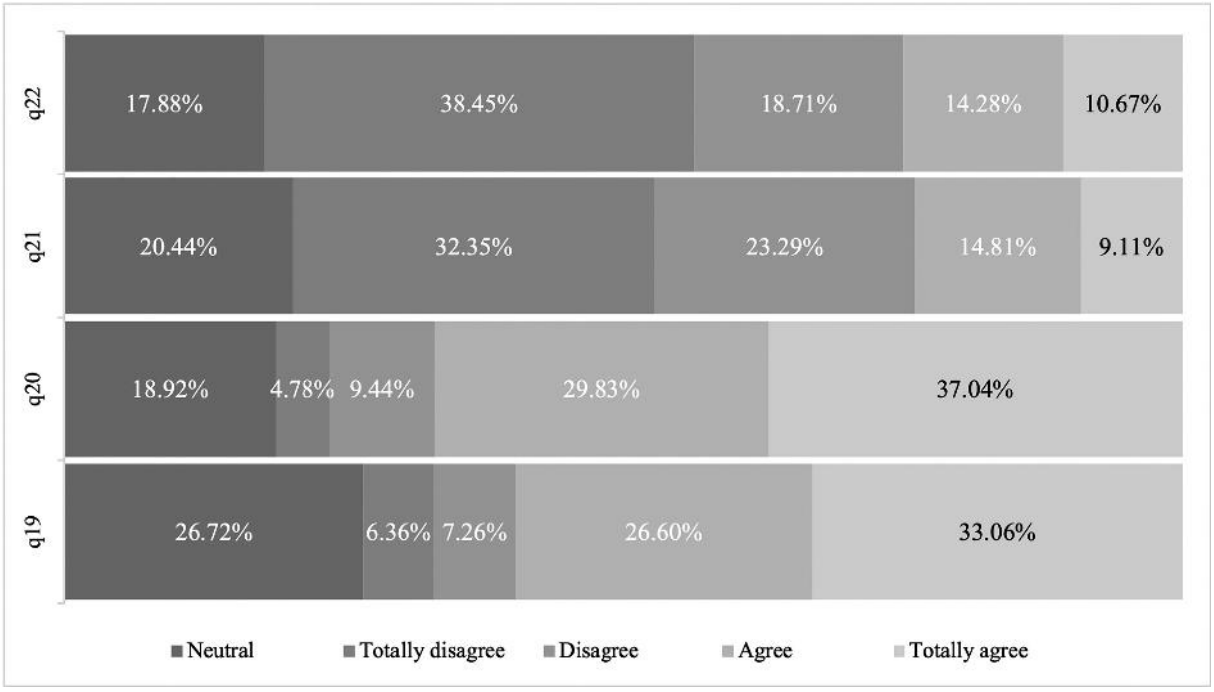


Figure 3. The perspective of surveyees regarding the relationship of the pandemic with physical activity according to their replies in the following questions (q19-q22), section 4 of the Likert scale.

q19 What is your position (on a scale of 1 to 5) on the phrase "After the end of the 2nd lockdown I am going to perform more physical activity"?

q20 What is your position (on a scale of 1 to 5) on the phrase "Today's lifestyle affects the ability to perform physical activity"?

q21 What is your position (on a scale of 1 to 5) on the phrase "The pandemic helped me to discover new forms of physical activity"?

q22 What is your position (on a scale of 1 to 5) on the phrase "The pandemic helped me to add physical activity into my daily routine"?

Table 3. The Output of the Univariable and Multivariable Logistic Regression Analyses regarding the Factors Associated with Physical Activity (PA) Cessation during the Lockdowns

| Variables | Univariable models | | | Multivariable model | | |
|---|---|---|---|---|---|---|
| | OR* | P-value† | 95% CI | OR* | P-value† | 95% CI |
| Age | | | | | | |
| 18-24 (ref.) | 1.00 | - | - | 1.00 | - | - |
| 25-34 | 0.88 | 0.641 | (0.53 -1.48) | 0.92 | 0.781 | (0.51 - 1.66) |
| 35-44 | 1.47 | 0.123 | (0.90 - 2.40) | 1.36 | 0.398 | (0.67 - 2.74) |
| 45-54 | 1.6 | 0.024 | (1.06 - 2.40) | 1.67 | 0.168 | (0.81 - 3.47) |
| ≥ 55 | 1.01 | 0.998 | (0.57 - 1.75) | 1.08 | 0.858 | (0.45 - 2.64) |
| Gender | | | | | | |
| Male (ref.) | 1.00 | - | - | 1.00 | - | - |
| Female | 0.76 | 0.070 | (0.56 - 1.02) | 0.69 | 0.041 | (0.49 - 0.98) |
| BMI level | | | | | | |
| Normal (ref.) | 1.00 | - | - | 1.00 | - | - |
| Underweight | 1.13 | 0.747 | (0.54-2.37) | 1.47 | 0.322 | (0.68-3.17) |
| Overweight | 1.71 | 0.002 | (1.22-2.39) | 1.23 | 0.319 | (0.82-1.84) |
| Obese | 2.19 | 0.003 | (1.31-3.67) | 1.45 | 0.274 | (0.75-2.83) |
| Housing (living with other people) | | | | | | |
| No (ref.) | 1.00 | - | - | - | - | - |
| Yes | 0.83 | 0.244 | (0.61-1.13) | - | - | - |
| Number of people living with | | | | | | |
| 1 person (ref.) | 1.00 | - | - | - | - | - |
| < 5 people | 0.82 | 0.494 | (0.46-1.46) | - | - | - |
| ≥ 5 people | 0.74 | 0.778 | (0.09-5.92) | - | - | - |
| Permanent residency | | | | | | |
| No (ref.) | 1.00 | - | - | - | - | - |
| Yes | 0.87 | 0.381 | (0.64-1.18) | - | - | - |
| Highest level of education (degree) | | | | | | |
| High school (ref.) | 1.00 | - | - | - | - | - |
| PhD | 0.85 | 0.501 | (0.54-1.35) | - | - | - |
| MSc | 0.87 | 0.547 | (0.55-1.38) | - | - | - |
| Bachelor | 0.84 | 0.348 | (0.59-1.21) | - | - | - |
| Occupation | | | | | | |
| Undergraduate student (ref.) | 1.00 | - | - | 1.00 | - | - |
| Academician | 1.13 | 0.582 | (0.73-1.74) | 0.68 | 0.312 | (0.32 - 1.45) |
| Unemployed | 1.47 | 0.416 | (0.58-3.73) | 1.41 | 0.501 | (0.52 - 3.85) |
| White collar workers | 1.36 | 0.099 | (0.94-1.97) | 0.96 | 0.897 | (0.51 - 1.80) |
| Difficulty maintaining weight | | | | | | |
| No (ref.) | 1.00 | - | - | 1.00 | - | - |
| Yes | 1.72 | 0.002 | (1.23 - 2.41) | 1.47 | 0.065 | (0.98 - 2.22) |
| Smoking | | | | | | |
| No (ref.) | 1.00 | - | - | 1.00 | - | - |
| Yes | 1.33 | 0.086 | (0.96 - 1.85) | 1.11 | 0.564 | (0.77 - 1.61) |
| Smoking cessation (in months) | 1.01 | 0.892 | (0.96 - 1.05) | - | - | - |
| History of underlying diseases | | | | | | |
| No (ref.) | 1.00 | - | - | - | - | - |

Continuation of Table 3.

| Variables | Univariable models | | | Multivariable model | | |
|---|---|---|---|---|---|---|
| | OR* | P-value† | 95% CI | OR* | P-value† | 95% CI |
| Yes | 1.22 | 0.41 | (0.76 - 1.95) | - | - | - |
| Follow-up attendance | | | | | | |
| No (ref.) | 1.00 | - | - | - | - | - |
| Yes | 0.70 | 0.581 | (0.20 - 2.50) | - | - | - |
| Restriction | | | | | | |
| No (ref.) | 1.00 | - | - | - | - | - |
| Yes | 1.49 | 0.428 | (0.56 - 3.99) | - | - | - |
| Advice | | | | | | |
| No (ref.) | 1.00 | - | - | - | - | - |
| Yes | 0.99 | 0.982 | (0.37 - 2.63) | - | - | - |
| Annual checkup attendance | | | | | | |
| No (ref.) | 1.00 | - | - | 1.00 | - | - |
| Yes | 0.54 | <0.001 | (0.39 - 0.74) | 0.53 | <0.001 | (0.38 - 0.75) |
| Type of PA before the lockdown | | | | | | |
| Walking (ref.) | 1.00 | - | - | 1.00 | - | - |
| Running | 0.4 | 0.010 | (0.20 - 0.80) | 0.48 | 0.044 | (0.23 - 0.98) |
| Sport | 0.82 | 0.395 | (0.52 - 1.30) | 1.04 | 0.878 | (0.63 - 1.73) |
| Gym | 0.72 | 0.088 | (0.49 - 1.05) | 0.83 | 0.384 | (0.54 - 1.27) |
| Home workout | 0.07 | <0.001 | (0.02 - 0.28) | 0.09 | 0.001 | (0.02 - 0.36) |
| Other | 0.81 | 0.392 | (0.51 - 1.31) | 0.98 | 0.936 | (0.58 - 1.65) |

*Odds ratio; †Stepwise multiple logistic regression analysis.

## Discussion

The current study, performed in eight Higher Educational Institutions, evaluated the effect of COVID-related lockdowns at a national level. It recorded and identified the impact of the pandemic-related lockdowns on PA by examining two lockdowns, as well as the between-lockdown period. This fact allowed us to examine this impact from a broader perspective, given that PA was recorded in all possible periods with the between-lockdown period acting as an "atypical" follow-up to the first lockdown. Lockdowns, utilized worldwide during COVID- 19 pandemic, had numerous effects on public health, the economy, and industry (1). Lockdowns may be applied in the future in medical and/or other crises. This is why the current study remains important not only for its conclusion concerning the effects of this pandemic, but also for adopting preventive measures in future.

The present study demonstrated a significant reduction in PA levels due to COVID-related lockdowns. Furthermore, it showed that female gender, adherence to an annual checkup attendance, and some types of PA during the pre-pandemic era, were associated with a more active lifestyle. Reductions in PA levels were also highlighted in the majority of published studies (15-24), while others (25-28) concluded with contrasting results. This disparity could be attributed to the variability of the factors examined (e.g., the subjects' employment status) that further exhibit different outcomes in terms of PA-level maintenance. Additionally, the studies that concluded that there was an increase in PA during the pandemic enrolled mainly health professionals (25-28), while the current study's population was not necessarily limited to such individuals. In the meanwhile, socio-demographic factors, such as the place of permanent residency, that were found to significantly influence PA levels during

the COVID-19 pandemic in other studies (29-33), failed to be significantly associated in the current one. Concerning the association of PA with gender, most studies (34-38) found complementary results to those in the present study. The interpretation of this discrepancy may be attributed to the explanation provided by the study by van Uffelen et al. (39): women, as opposed to males, in their sixties, may perceive the lockdown as an opportunity to improve their external appearance, and this may act as a motivating factor for engagement in PA. Additionally, in relation to the association of the relationship between annual checkup attendance and the type of PA during the pre-pandemic era with the level of PA activity during the pandemic, to the best of our knowledge, no similar studies were identified, since several studies only highlight the increased engagement in home workout during and not prior to the lockdown.

### *No Engagement with Physical Activity and Effects*

The current study concluded that there was quite a high percentage (41.1%) of no engagement with PA during the 2nd lockdown. As PA is beneficial for the population's general health, the long-term decrease in PA, and particularly no engagement at all, may lead to increased morbidity, obesity, high blood pressure, diabetes, musculoskeletal and psychological disorders, as well as a reduction in skeletal strength and endurance, and cardiorespiratory capacity (40, 41). Furthermore, the loss of lean mass, muscle function, and motor control may lead to sarcopenia, cardiometabolic disorders, and the emergence and/or worsening of other comorbidities, with significant impacts on the population and especially the elderly (42). These may affect the healthcare system, especially during long periods of lockdowns, such as COVID-related ones.

### *Measures for Maintaining Physical Activity at Beneficial Levels*

Measures for maintaining PA in similar situations in the future may include: a) participation in online group training courses, which may be age and PA-level specific, and may be performed at local gyms by their members, b) proper public awareness of this issue, c) the ability to exercise in open areas (during possible lockdowns), and d) proper psychological support from professionals. It has been documented that PA supervision is recommended to improve the effects of exercise at home (42). This is possible through weekly visits, or telephone or online video calls. Health professionals, including physiotherapists, nutritionists, physical trainers, general and sports medicine physicians, psychologists, and health assistants should organize multidisciplinary programs aimed at promoting and maintaining PA, reducing functional losses during lockdowns, maintaining the general population's autonomy and life quality, in order to minimize morbidity and the burden on the healthcare systems.

### *Limitations of the Study*

Although efforts to achieve a homogenous sample were made through the study design (inclusion of all individuals involved with each university regardless of their age), most of the respondents were students aged between 18-24 years of age residing in the two largest cities in Greece (Athens and Thessaloniki). This could potentially lead to a lower perception of other age groups and rural areas. Additionally, only subjective measures were used to record all the variables used, such as body weight, height, and PA conduct. Hence, PA may be overrepresented since subjective assessment was employed. Furthermore, the impact on PA engagement and its intensity, in all periods (the pre-pandemic, the first lockdown, the between-lockdowns, and the second lockdown) were recorded and compared, on the basis of the restrictive measures that were imposed in Greece during the pandemic. Hence, the potential difference in the restrictive measures between countries should be taken into consideration when interpreting the results.

Recall bias could have also influenced the study population's replies. To reduce the possibility of recall bias, all questions that were included were carefully selected to limit the effort of memory

needed to answer (for instance, the participants were asked to report the frequency of the PA months prior and after the time the responses were collected – during the lockdowns) and were asked for all individuals at the time that they joined the study. Yet, despite all efforts the possibility of the existence of recall bias should not be overlooked and should be taken into consideration when interpreting the results. Nevertheless, to the best of the authors' knowledge, this is the first study of this kind of the Greek population. Another limitation is the inclusion of respondents that were all related to universities, who were therefore undergoing a higher level of education, as well as the low response rate of participants (5.3%). Thus, the results might not apply to people with lower educational levels, or may be influenced by the fact that individuals that were not conducting PA refused to participate (non-response bias).

## Conclusions

PA conduct and intensity were significantly reduced from the pre-pandemic era to the second lockdown. Female gender, annual checkup attendance, and the type of PA during the pre-pandemic era were significantly associated with a decrease in the likelihood of stopping PA during lockdowns. PA may be beneficial for the population's health. Therefore, measures such as online group training sessions and public awareness, should be implemented in cases of future lockdowns to avoid PA reduction during such periods.

**What Is Already Known on This Topic:**
*Physical activity (PA) is beneficial for the population's general health. Long-term decreases in PA may lead to increased morbidity, including obesity, high blood pressure, diabetes, musculoskeletal and psychological disorders, as well as a reduction in skeletal strength, and endurance and cardiorespiratory capacity. The loss of lean mass, muscle function, and motor control may lead to sarcopenia, cardiometabolic disorders, and the emergence and/or worsening of other comorbidities, with significant impacts on the population and especially the elderly. These may affect the healthcare system, especially during long periods of lockdowns, such as COVID-related ones.*

**What This Study Adds:**
*The current survey showed that physical activity (PA) conduct and intensity were reduced from the pre-pandemic era to the second lockdown to a statistically significant degree. Female gender, annual checkup attendance, and the type of PA during the pre-pandemic era are significantly associated with a decrease in the likelihood of stopping PA during lockdowns. PA may be beneficial for the population's general health. Therefore, measures, such as online group training sessions and public awareness, should be implemented in cases of future lockdowns to avoid reductions in PA during such periods. Health professionals, including physiotherapists, nutritionists, physical trainers, general and sports medicine physicians, psychologists, and health assistants, should organize multidisciplinary programs aimed at promoting and maintaining PA, reducing functional losses during lockdowns, maintaining the general population's autonomy and quality of life, and to minimize morbidity and the burden on the health-care system.*

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**Conflict of Interest:** The authors declare that they have no conflict of interest.

**Data Availability:** The data sets generated and/or analyzed during the current study are available from the corresponding author on request.

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# Appendix

## Questionnaire

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Section 1 – Sociodemographic factors | | | | | | | | |
| q1 | What is your age?* | | | | | | | |
| q2 | What is your gender?* | | | | | | | |
| | ☐ | Male | ☐ | Female | ☐ | Other | | |
| q3 | Do you live with other people permanently?* | | | | | | | |
| | ☐ | Yes | ☐ | No | ☐ | Don't want to declare | | |
| q3.1 | With how many people do you live? * | | | | | | | |
| | ☐ | 1 person | ☐ | Up to 5 people | ☐ | More than 5 people | | |
| q4 | Do you live permanently in your hometown?* | | | | | | | |
| | ☐ | Yes | - | - | ☐ | No | | |
| q5 | In which of the following Greek Administrative regions do you live permanently? * | | | | | | | |
| | ☐ | Attica | ☐ | Epirus | ☐ | Thessaly | | |
| | ☐ | Central Greece | ☐ | Ionian Islands | ☐ | Western Greece | | |
| | ☐ | Central Macedonia | ☐ | North Aegean | ☐ | Western Macedonia | | |
| | ☐ | Crete | ☐ | Peloponnese | ☐ | Other | | |
| | ☐ | Eastern Macedonia and Thrace | ☐ | South Aegean | - | - | | |
| q6 | What is your educational level? (Choose based on the last level you are at now, or graduated from)* | | | | | | | |
| | ☐ | High school diploma | - | - | ☐ | Bachelor's degree | | |
| | ☐ | Master's degree | - | - | ☐ | PhD | | |
| | ☐ | Other | - | - | - | - | | |
| q7 | What is your current occupation?* | | | | | | | |
| | ☐ | Undergraduate student | | - | ☐ | Academician | | |
| | ☐ | Administrative officer | | - | ☐ | Other | | |
| q8 | Do you smoke?* | | | | | | | |
| | ☐ | Yes | ☐ | No | ☐ | Don't want to declare | ☐ | Other |
| q8.1 | How long is it since you quit smoking (in months)?* | | | | | | | |
| Section 2 – Health status | | | | | | | | |
| q9 | What is your body weight (in kg without decimal approximation)?* | | | | | | | |
| q10 | What is your height (in cm without decimal approximation)?* | | | | | | | |
| q11 | Do you find it difficult to maintain your weight?* | | | | | | | |
| | ☐ | Yes | ☐ | No | ☐ | Don't want to declare | | |
| q12 | Do you have a diagnosed underlying disease?* | | | | | | | |
| | ☐ | Yes | ☐ | No | ☐ | Don't want to declare | | |
| q12.1 | What is that disease you have been diagnosed with?* | | | | | | | |
| q12.2 | Do you attend a regular (at least annual) follow-up by a physician for this underlying disease?* | | | | | | | |
| | ☐ | Yes | - | - | ☐ | No | | |
| q12.3 | Does this underlying disease affect (restrict) your ability to perform physical activity?* | | | | | | | |
| | ☐ | Yes | - | - | ☐ | No | | |
| q12.4 | Have you received any advice from your physician about the conduct of physical activity (i.e., instructions on when and how to perform physical activity)?* | | | | | | | |
| | ☐ | Yes | - | - | ☐ | No | | |
| Section 3 – Physical activity status | | | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| q13 | Before the COVID - 19 pandemic, how many days within a week did you perform physical activity lasting at least 30 minutes each time? * | | | | | |
| | ☐ | 1 day/week | ☐ | 2 days/week | ☐ | 3 days/week |
| | ☐ | 4 days/week | ☐ | 5 days/week | ☐ | 6 days/week |
| | ☐ | Everyday | - | - | - | - |
| q14 | Before the COVID-19 pandemic, what physical activity did you perform with an average duration of more than 30 minutes? (In case many options may be chosen, please choose the most frequent one) * | | | | | |
| q15 | During the 1st lockdown, what physical activity did you perform with an average duration of more than 30 minutes? (In case many options may be chosen, please choose the most frequent one) * | | | | | |
| q15.1 | Which factor do you consider as having a positive effect on the performance of physical activity? * | | | | | |
| q17 | After the end of the 1st lockdown, did you continue to perform physical activity? * | | | | | |
| | ☐ | Yes | | | ☐ | No |
| q17.1 | Did you continue to perform physical activity with the same or a different frequency? * | | | | | |
| | ☐ | Same | | | ☐ | Different |
| q17.2 | Why did you stop? * | | | | | |
| q17.3 | Which reason helped you to continue your physical activity? * | | | | | |
| q18 | During the 2nd lockdown, did you perform physical activity? * | | | | | |
| | ☐ | Yes | | | ☐ | No |
| q18.1 | During the 2nd lockdown, did you continue to perform the same physical activity as before? * | | | | | |
| | ☐ | Same | | | ☐ | Other |
| q18.2 | What is the new physical activity you started? * | | | | | |
| Section 4 – Perspective regarding the relationship of the pandemic with physical activity | | | | | | |
| q19 | What is your position (on a scale of 1 to 5) on the phrase "After the end of the 2nd lockdown I am going to perform more physical activity" ? * | | | | | |
| | (Disagree) | 1 | 2 | 3 | 4 | 5 (Agree) |
| q20 | What is your position (on a scale of 1 to 5) on the phrase "Today's lifestyle affects the ability to perform physical activity" ? * | | | | | |
| | (Disagree) | 1 | 2 | 3 | 4 | 5 (Agree) |
| q21 | What is your position (on a scale of 1 to 5) on the phrase „The pandemic helped me to discover new forms of physical activity" ? * | | | | | |
| | (Disagree) | 1 | 2 | 3 | 4 | 5 (Agree) |
| q22 | What is your position (on a scale of 1 to 5) on the phrase "The pandemic helped me to add physical activity into my daily routine"? * | | | | | |
| | (Disagree) | 1 | 2 | 3 | 4 | 5 (Agree) |

*Manda tory field.

Short Narrative Review
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# Anatomical Variations in the Celiac Trunk: A Short Review

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**Abstract**

**Objective.** The objective of the current study was the examination of possible variants of the celiac trunk. **Methods.** An advanced review of the literature search was undertaken by means of the PubMed database and Google Scholar, searching for new studies published up to October 2022. Additional articles provided useful information in relation to the aim of this review. Hence, articles that met the inclusion criteria were included in this review and the collected data were organized into a table. **Results.** The search of the literature retrieved 10 articles that referred to the anatomical variations of the celiac trunk. According to the available literature, the most common anatomical variations are: hepatosplenic trunk where the left gastric artery originates from the abdominal aorta, hepatosplenic trunk, where the left gastric artery originates from the splenic artery, and hepatogastric trunk and splenic artery origin from the superior mesenteric artery. Many other anatomical variations of the celiac trunk may exist, such as tetrafurcation, pentafurcation and hexafurcation, that refer to the division of the celiac trunk into four, five or six branches, respectively, and should be reported as they can affect surgical approaches and the development of the appropriate treatment strategy in patients. **Conclusion.** Every visceral surgeon, interventional radiologist and abdominal imager should be familiar with these variants.

**Key Words:** Celiac Trunk ▪ Aorta ▪ Variations ▪ Surgery ▪ Anatomical Variation.

## Introduction

The celiac trunk (CT) is the anterior branch of the abdominal aorta, which arises at the level of the vertebral bodies thoracic 12 (T12) to lumbar 1 (L1) and mainly supplies the foregut (1). In general, the CT measures approximately 1.5–2 cm and supplies blood to the distal esophagus, liver, pancreas, gallbladder and spleen (1). It splits into three major branches, namely: the left gastric, which runs through the smaller curvature of the stomach; the splenic, which follows a tortuous route along the posterior superior margin of the pancreas to the spleen; and the hepatic arteries, which divide into the gastroduodenal for pancreas and duodenum vascularization (1). The hepatic artery also gives rise to the gastroduodenal artery, which later becomes the right gastroepiploic artery. This artery runs along the greater curvature and supplies the lateral stomach, with two branches of the splenic artery, the left gastroepiploic and short gastric arteries (2). This trifurcation was described by von Haller back in 1917, and is considered the classic presentation of the CT, known as "tripus Halleri" (2, 3). It is reported in approximately 89% of individuals irrespective of their sex (2, 3). Two trifurcation forms have been described to date: the first is named a "true" tripod and corresponds to cases in which the hepatic, left gastric and splenic arteries have a common origin, constituting a hepatogastrosplenic trunk (4, 5). In cases where at least one of these arteries arises before the remaining two in the course of the CT, it is called a false tripod. In most cases, the celiac trunk and the superior mesenteric artery are formed by the 10th and

13th vitelline arteries, with the remaining segments regressing before birth.

However, the ventral vertebral aorta and the celiac artery may often exhibit significant anatomical variations, as well as total absence of one of the branches, which may affect the surgical approaches performed, such as during organ transplantation or organ/tumor resection (3). In the literature, several variations of the CT have been documented (2, 6 –10). In particular, multiple studies and research have been reported that explain and assess the various forms of the CT, whereas innumerable attempts have been undertaken to characterize its consequence forms. However, each author reports their own experience and findings and, therefore, it may be difficult to include the overall knowledge up to the present.

Nevertheless, this knowledge is important for surgeons, as changes in the celiac artery may increase the difficulty and risk of performing surgical procedures, such as radical gastrectomy. Thus, as it is important to gain knowledge that will help in the preparation for a particular surgical operation and mitigate post-operative complications, we present the findings of previous studies that focused on the variations of the CT.

Our aim was to shed light on this important issue and provide the currently available knowledge to clinicians and surgeons worldwide.

## Methods

An advanced executive literature search was conducted in PubMed and Google scholar databases using the following terms: "celiac trunk AND anatomical variations OR tripus Halleri AND anatomical variations". The resulting literature was carefully screened. Only studies in English and referring to humans were included. No additional search filters, such as text availability, article type and publication date, were applied. Through the snowballing technique, further references taken from the initial articles with useful information relating to the aim of the review were also screened and taken into consideration. The extracted data were classified in a table according to the anatomical variations of the CT in adults.

## Results

The search of the literature retrieved 10 articles that referred to the anatomical variation in question in adults and they are summarized in Table 1.

An interesting work on this issue was published by Panagouli et al. in 2013. In particular in their study they presented an entirely new categorization of abnormalities of the CT, which encompassed all previously documented abnormalities (7). Especially, they examined 12,196 cases from a total of 36 studies reported up to 2013, and stated that the CT was trifurcated into the common hepatic artery, the left gastric artery, and the splenic artery in 89.42% of cases (7). A similar observation was reported in 40–94.2% of cases in previous cadaveric studies, and the figures reached 95.9% and 98.3% in radiological and liver transplantation studies, respectively (11, 20). Moreover, according to the literature, CT bifurcation (type II according to Panagouli et al.'s classification) may exist in 1.3–25% of cases (7.40% according to Panagouli et al. (7)) with the most common types of bifurcation being the following: hepatosplenic trunk (the left gastric artery originated from the abdominal aorta [3.34%]), splenogastric and hepatomesenteric trunk (1.9%) as well as the splenogastric trunk (the common hepatic artery arises from the superior mesenteric artery [1.13%]) (Figure 1). The CT may be absent (type VII according to Panagouli et al.'s classification) in 0–2.6% of cases (mean prevalence: 0.38%) (7, 12, 13).

An interesting study was conducted by Chen et al. back in 2019 (13). The authors examined the anatomic variations of the CT and the hepatic artery in a large homogeneous sample from a Japanese population. They analyzed the branching modes of the CT, as well as the anatomy of the CT and hepatic artery in 974 cadavers. Interestingly, CT trifurcation was observed in 89.8% of cases, while the normal pattern of the CT and the hepatic artery was observed in 66% and 72.4% of cadavers, respectively (13). Moreover, alternative

Table 1. Variations of Celiac Trunk in Adults

| Researchers | Year of publication | No of cases | Celiac Trunk | | | Other variations |
|---|---|---|---|---|---|---|
| | | | Bifurcation | Trifurcation | Absence | |
| Panagouli et al. (7) | 2013 | 12196 | 7.40% (903/12196) | 89.42% (10906 /12196) | 0.38% (46 /12196) | Hepatosplenomesenteric trunk 0.40% (49/12,196).<br>Celiacomesenteric trunk 0.76% (93/12,196).<br>Other variations 1.64% (199/12,196)<br>variations in the cadaveric series 14.9% (489/3278).<br>In the imaging series the 10.5% (675/6501).<br>In the liver transplantation series 4.6% (104/2261) |
| Chitra (11) | 2010 | 50 | The hepatosplenic trunk 0.02% (1/50)<br><br>The gastrosplenic trunk 0.04% (2/50) | 40% (20/50) | NA | 95.9% radiological & liver transplantation studies.<br>Division of CT into four branches:<br>the inferior phrenic artery, either one-sided or on the common trunk of both sides 20% (10/50)<br>or the additional branch was the gastroduodenal artery 2% (1/50)<br>or the middle colic artery 4% (2/50)<br>or the duodenal or the pancreatic branches 10% (5/50).<br>The left hepatic artery arising from the left gastric artery 14% (7/50).<br>The five branches of the coeliac trunk included the inferior phrenic and middle colic artery 2% (1/50).<br>The six branches of the coeliac trunk also included the duodenal branch in addition to the abovementioned branches 2% (1/50). |
| Venieratos et al. (12) | 2013 | 77 | Splenogastric trunk 1.3% (1/77) the common hepatic artery emerged directly from the aorta. | 90.9% (70/77) | 2.6% (2/77) | 5.2% (4/77) additional branches (lumbar and inferior phrenic arteries) |
| Chen et al. (13) | 2009 | 974 | Common hepatosplenic trunk 4.4% gastrohepatic trunk 0.3% | 89.8% (875/974) | NA | A common hepatic artery (CHA) arising from the superior mesenteric artery (SMA) 3.5% or directly from the aorta 0.5%.<br>A hepatosplenomesenteric trunk 0.7% (7/974) a celiomesenteric trunk 0.7% (7/974). |
| Prakash et al. (14) | 2012 | 50 | NA | NA | NA | The left gastric, common hepatic & splenic arteries were found to arise from the coeliac trunk 86% (43/50)<br>the origin of the gastric artery was proximal to the bifurcation of the coeliac trunk into the common hepatic and splenic arteries 76% (38/50) all three branches arose directly from the abdominal aorta 2% (1/50)<br>the common hepatic and left gastric arteries arose from the coeliac trunk 2% (1/50). |
| Malnar et al. (15) | 2010 | 90 | 72% | NA | NA | Anatomical variations 4.4% (4/90). |
| Grigoriță et al. (16) | 2019 | CR | NA | NA | NA | Tetrafurcation of CT:<br>- a common trunk for left & right inferior phrenic arteries<br>- an accessory left gastric artery<br>- the common hepatic artery<br>- a splenogastric trunk- |
| Srivastava et al. (17) | 2012 | 50 | 28% | 8% | 4% | Tetrafurcation 36%; pentafurcation 20%; hexafurcation 4%. |
| Pinal-Garcia et al. (18) | 2018 | 140 | 7.1% | NA | NA | Additional branches 47.9%. One or both phrenic arteries originated from the celiac trunk 41.4%.<br>Celiac trunk tetrafurcation 12.9%;<br>Pentafurcation 12.9%; Hexafurcation 1.4%; Heptafurcation 0.7%. |
| Astik and Dave (19) | 2011 | CR | NA | NA | NA | Heptafurcation of CT |

CT=Celiac trunk; CHA=Common hepatic artery; SMA=Superior mesenteric artery; NA=Not available; CR=Case report.

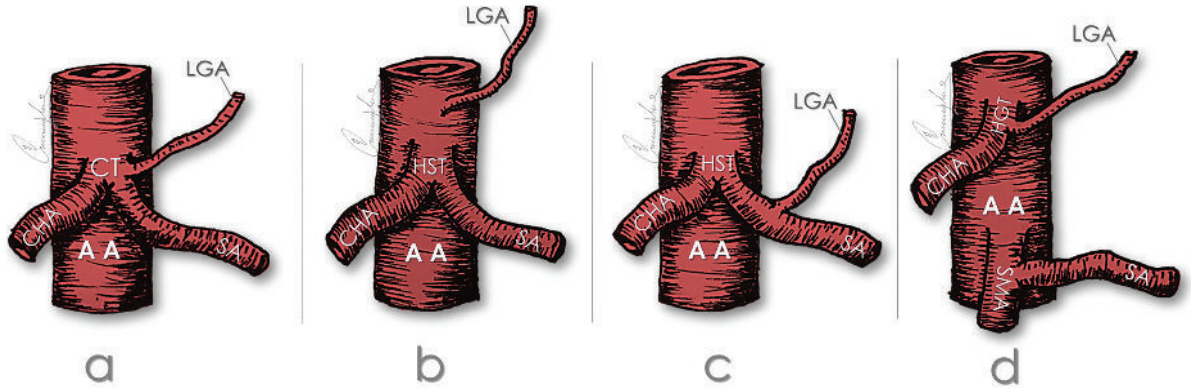


Figure 1. The most common anatomical variations of CT (the celiac trunk): a) the normal celiac trunk ("Haller's tripod") from which CHA (the common hepatic artery), SA (the splenic artery) and LGA (the left gastric artery arise), b) HST (hepatosplenic trunk) where the LGA originates from AA (the abdominal aorta), c) HST (Hepatosplenic trunk) where the LGA originates from the SA, d) HGT (Hepatogastric trunk) and SA origin from SMA (The superior mesenteric artery).

left and right hepatic arteries were observed in 11.0% and 4.9% of cadavers, respectively. In 1.5% of cases, the anatomy of the two hepatic arteries differed. Further, the gastrohepatic body part was observed in 4.4% of the cases, whereas the hepatosplenic stem was discovered in only 0.3% (13). Moreover, a common hepatic artery was observed, arising from the superior mesenteric artery (SMA) or directly from the aorta in 3.5% and 0.5% of the examined cadavers, respectively (13). Finally, a hepatosplenomesenteric trunk and a celiomesenteric trunk were encountered in 0.7% of cases.

Another interesting article was published in 2012 by Prakash et al. (14). In this study, an abdominal autopsy was performed on 50 cadavers and the corresponding structure of the vessels was recorded. All anatomical variations observed were photographed and documented. The left gastric, common hepatic, and splenic arteries were found to arise from the CT in 86% of the cadavers, similar to the prevalence rate of a normal coeliac axis reported by Song et al (89.1%) (21). According to Prakash et al., structural abnormalities were observed in 14% of cases, and can be divided into three groups: (1) a separate branching of the abdominal-hepatic aorta leading to the left stomach, common hepatic, and splenic arteries; (2) the left gastric aorta formed when the dominant hepatic and left gastrointestinal veins split from the celiac stem; and (3) the vein of the gastric system originating from the abdominal aorta (14). In their study, the division of the CT into the common hepatic and splenic arteries was the most common vascular pattern in their study, whereas the origin of the left gastric artery was relatively proximal, between the abdominal aorta and the bifurcation of the coeliac trunk in 76% of the cadavers, similar to the findings of a Croatian study published by Malnar et al, which reported a rate of 72% (15).

In terms of embryology, the above-mentioned alterations have been discussed previously (22, 23).In particular, it was highlighted that the yolk sac is nourished by a network of paired vessels, described as vitelline arteries, at the beginning of the 4th week of prenatal development. The paired vessels gradually fuse and form arteries in the dorsal mesentery of the gut. These present as celiac, superior mesenteric, and inferior mesenteric arteries during adult life (24). Moreover, it was stated that incomplete fusion or malfusion of the vitelline arteries during the developmental stage might have resulted in the observed variations (24).

Distal gastric bypass surgery with laparoscopic assistance, and open total or partial gastrectomy both require ligation and cutting of the gastric arteries, but they are different procedures. As laparoscopic surgery is performed in a small area, there is a risk that the wrong vessel will be cut or ligated, which could contribute to inflammation, ischemia, or necrotizing of the tissue or organ being irrigated (25).

An interesting Brazilian study was published in 2007, in which the authors analyzed the CT structure by measuring its diameter, length, emission, and branch variations (26). This study reported that the average arterial diameter was smaller for variable vessels, after comparing the normal and variable groups. Therefore, an interesting observation of this study was that there may be a diameter reduction of the CT main branches in the presence of anatomical variations. This may be insightful information as the knowledge of normal arterial diameters can help physicians make correct and precise radiological diagnosis of arterial aneurysms, while assessment of arterial diameters is mandatory for liver transplantation follow up (27, 28).

Further, a recent study by a Turkish team examined the prevalence of CT and common hepatic artery variations in children (29, 30). Among 174 children who underwent abdominal multi detector computed tomography angiography, either because of trauma or liver transplantation, 157 (90.2%) had normal CT anatomy, similar to other studies including adults (13, 14, 21). The hepatosplenic trunk giving rise to the branch of the left gastric artery and superior mesenteric artery was the most common variation (4%), in consistency with previous findings (7).

Apart from the aforementioned cases of variations, an unusual case of tetrafurcation of the CT was observed during the dissection of the formalin-fixed cadaver of a 60-year-old Romanian female (16). In this case, the CT gave rise to four branches: a common trunk for the left and right inferior phrenic arteries, an accessory left gastric artery, the common hepatic artery, and a splenogastric trunk (16). Along the same lines, cases of tetrafurcation, pentafurcation and hexafurcation were reported by Srivastava et al. in their CT-angiographic study in 36%, 20%, and 4% of cases, respectively (17), as well as by Pinal-Garcia et al in 32.9%, 12.9%, and 1.4% of cases, respectively (18). Importantly, the latter study also reported one case of heptafurcation. According to our findings, only one such case has been reported in the literature to date (19).

Finally, another interesting issue that should be noted is the effect of ethnicity on CT variation. Interestingly, Panagouli et al. reported that variations in the CT were more common in the Japanese and Korean populations than in Caucasians, while negro, colored and black populations presented more variations than the Indian population ($P>0.05$) (7).

## Discussion

In this study, we aimed to provide a short overview of the knowledge concerning the variants of CT reported in cadaveric and/or diagnostic imaging studies. According to our findings, cases of the absence of the CT are rare, and in these cases the common gastric, splenic and hepatic arteries originate independently directly from the abdominal aorta (7, 12, 31). This variation occurred because of the complete regression of the anastomoses of the primitive arteries. Nevertheless, the segmental arteries did not regress and emerge directly from the abdominal aorta (14, 32, 33).

Bifurcation of the CT seems to be the most common variant form. This variant is observed in approximately 11% of cases (34, 35). Among the most common bifurcation types are the hepatosplenic trunk (the left gastric artery originates from the abdominal aorta), the splenogastric and hepatomesenteric trunk, and the splenogastric trunk (the common hepatic artery arises from the superior mesenteric artery) observed in 3.34%, 1.9% and 1.13% of cases, respectively (34, 35). Interestingly, Araujo Neto et al. examined 60 patients using computed tomography and found that 8.3% of them had a splenic hepatic trunk with the absence of the left gastric artery, while only 1.7% of the participants had a hepatogastric trunk with the absence of the splenic artery (36). These findings should be considered by physicians during gastrectomy because the left hepatic artery may emerge from the left gastric artery and, therefore, there is a possibility of developing ischemia in the entire functional yellow liver lobe (9).

It is worth mentioning that Panagouli et al. stated that the CT trifurcates into the common hepatic artery, the left gastric artery and the splenic artery (Type I) in 89.42% of cases (7). This presentation

has a prevalence of 40–94.2% in cadaveric studies, but can reach 95.9% and 98.3% of cases in radiological and liver transplantation studies (11, 37, 20).

The CT may also provide >1 collateral arteries in 50% of cases. The most frequent additional branches are the single or double inferior phrenic arteries (approximately 40% of cases) (38). It has been reported that the right and left inferior phrenic arteries arose from the CT in 41% and 44% of the examined cadavers, respectively; the abdominal aorta was their origin in 49% and 47.5% of cases (18).

Further, there has been a great deal of research into the higher incidence of structural versions in the celiac stem and its branches (37). Interestingly, as Santos et al. reported, there may be differences in the anatomy of both the central part and the branches of the CT (9). Recent advances in liver transplantation have necessitated an accurate understanding of the incidence of anatomical changes in the arteries involved. Despite the fact that formalin-fixed cadavers were used, the results are trustworthy because they are comparable to those obtained in fresh cadavers or *in vivo* using non-invasive approaches to assess the vascular caliber (39). Moreover, a study by Japanese investigators stated that patients with a variable arterial anatomy had a greater rate of post-transplantation complications than those with standard arterial morphology (40). Indeed, according to Santos et al. as well patients with variable arterial anatomy may have a higher risk of problems following liver transplantation (9).

However, despite the fact that the Type IV variant (right hepatic artery source from superior mesenteric artery) has been documented, it is significantly less prevalent than the Type III variant (left hepatic artery origin from the superior mesenteric artery) (28). No data suggest that this polymorphism is related to the occurrence of two left hepatobiliary vessels splitting off from the central hepatobiliary aorta. A prevalence equivalent to that of the Type V form (which consists of two trunks from the aortic arch: a gastrosplenic and a hepatomesenteric) (3%) has been previously reported (41).

According to the literature, these differences in the rates of observed CT variations may be related to genetic factors and ethnicity (7, 29). However, no differences between sexes have been observed in previous works (12, 13), which is interesting information that should be considered by physicians.

### *Limitations of the Study*

Concerning the limitations of our study, it should be mentioned that most of the research that exists relies on case reports/small case series. Finally, it is equally important to highlight that most anatomical variations, and vascular anomalies of the celiac trunk in general, even though they are not common in the general population, should be of high clinical significance and lead to surgical vigilance.

## Conclusion

Differences in the CT are not uncommon; nonetheless, various anatomical variations have been documented. In this way, the importance of being able to recognize and account for structural changes in the celiac stem cannot be overstated. It is important to educate clinicians and surgeons appropriately so they have sufficient knowledge of the CT's anatomic patterns and variations in order to perform image-guided interventional procedures safely, as well as esophageal, gastroduodenal, hepatic, biliary, pancreatic, splenic and colonic surgical procedures.

**What Is Already Known on This Topic:**
*The CT is a major abdominal branch of the aorta arising from the T12-L1 level. However, anatomical variations may exist and should be mentioned as they can determine surgical approaches and the development of the appropriate treatment strategy in patients. Therefore, each physician should be familiar with the existence of such variants.*

**What This Study Adds:**
*This study summarizes the current literature, confirming the presence of a variety of anatomical variations of the CT. It should be underlined that the recognition of these variations is very important as the correct and early diagnosis can lead to the appropriate treatment, preventing potentially life-threatening complications.*

**Authors' Contributions:** Conception and design: DC and TT; Acquisition, analysis and interpretation of data: IV, VK,

ES, YS, GT and DC; Drafting the article: IV, VK and ES; Revising it critically for important intellectual content: DC, TT; Figure drawing, legends & revision of the article: IA. Approved final version of the manuscript: IV, VK, ES, IA, YS, DC, GT and TT.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

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# A Giant Lipoma in the Distal Forearm of a Cadaver

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**Abstract**

**Objective.** Lipomas are very common tumors which usually prefer the upper limbs and, depending on their size, may cause nerve compression, or may be asymptomatic. The current cadaveric report describes a giant lipoma in the distal forearm area. **Case Report.** A large mass (5.1 × 3.2 × 1.6 cm) was identified on the palmar surface of the distal forearm, during dissection of a 63-year-old male cadaver. The mass caused anteromedial displacement and flattening of the median nerve (MN). Despite the lack of information about the subject's medical history, MN compression was assumed on the basis of the lipoma's size, its vicinity to neural structures, and the MN displacement and flattening. **Conclusion.** The enlarged distal forearm lipoma, located adjacent to the carpal tunnel, displaced and flattened the MN. The cadaveric finding described is clinically relevant for both differential diagnosis and surgical treatment of carpal tunnel syndrome.

**Key Words:** Distal Forearm ▪ Giant Lipoma ▪ Tendon Sheath ▪ Carpal Tunnel Syndrome.

## Introduction

Lipomas, the most common tumors, often present as gradually increasing, soft and resilient non-tender masses (1). They typically appear in the fifth or sixth decade of life (2). When their size exceeds 5 cm, they are considered to be giant (3). Lipomas rarely cause symptomatic nerve compression (4, 5). Only a few cases of distal forearm-carpal lipomas have been described (1, 5-8), with some of them being completely asymptomatic (1), and others, especially the enlarged ones, causing carpal tunnel syndrome (CTS)-like symptoms (5). The prevalence of forearm-carpal lipomas varies, remaining in quite low percentages compared to lipomas in other upper limb locations (9-11).

The current cadaveric report presents an unusual giant lipoma on the palmar surface of the distal forearm, which originated from the flexor pollicis longus tendon sheath, and displaced and flattened the medial nerve (MN).

## Case Presentation

During a routine dissection of a 63-year-old male cadaver of Greek origin, a large mass was identified on the palmar surface of the left sided distal forearm. The ovoidal tumor mass measured 5.1 cm × 3.2 cm × 1.6 cm and was located between the flexor hand muscles (flexor carpi radialis and flexor digitorum superficialis), posterior to the MN, and anterior to the pronator quadratus muscle. Due to the mass, the MN was anteromedially displaced and was characteristically flattened (Figure 1). Following excision of the mass, the MN was released and the pronator quadratus muscle revealed. The mass was carefully inspected

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and characterized as a lipoma (Figure 2). No details were available in the donor's medical records related to possible clinical manifestations due to CTS during the subject's life. Furthermore, no obvious hand muscle atrophy, nor any scar indicative of prior carpal tunnel (CT) release was found.

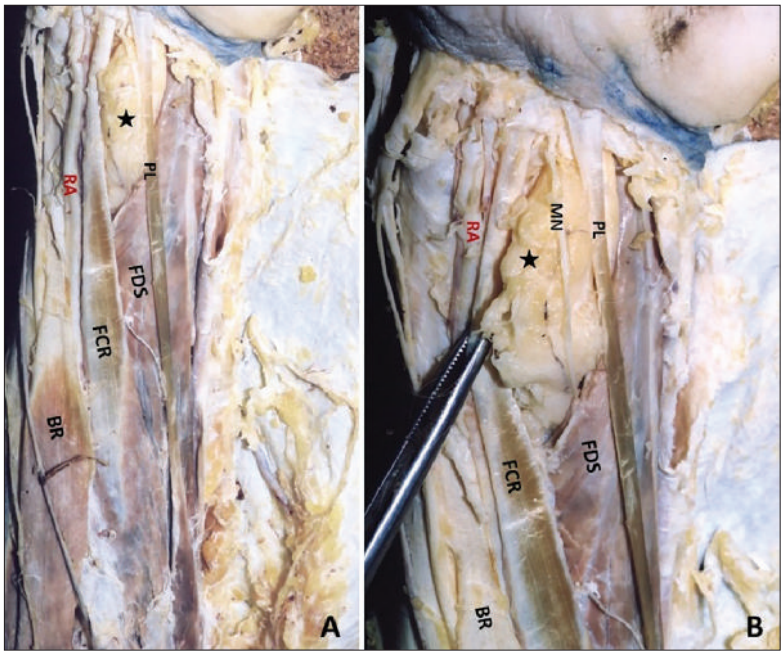


Figure 1 A and B. The tumor mass (black asterisk) located posterior to the palmaris longus (PL) muscle, between the muscles, flexor carpi radialis (FCR) and flexor digitorum superficialis (FDS), RA-radial artery, BR-brachioradialis muscle, and MN-median nerve.

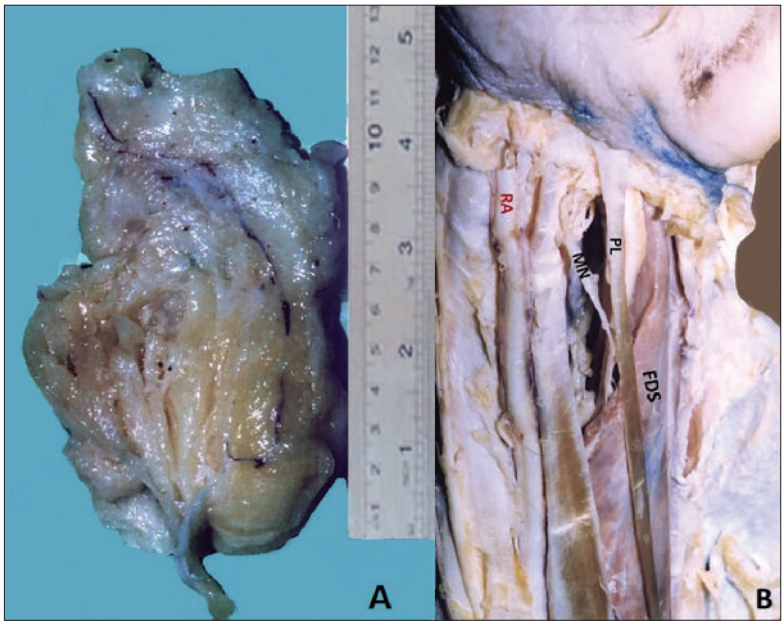


Figure 2 A. The giant lipoma after excision; B. The carpal area free of the tumor.

## Discussion

The current case is considered a synovial-related lipoma, further sub-classified as a tendon sheath lipoma. Although there were no clinical details available, the enlarged size of the lipoma (giant) provoked the MN anteromedial displacement and its flattening. Other types are: dermal, subcutaneous, subfascial, muscle-, bone- and nerve- related lipomas (12). Giant lipomas (≥5 cm) should be considered as malignant until proven otherwise (3). Lipomas are usually benign tumors and occur in approximately 2% of the population (3). Their prevalence in the forearm-carpal-palmar area is variable. Distal forearm lipomas have a variable prevalence. Yavari et al. (10) recorded a prevalence of 27.2% (3 cases out of 11 upper limb lipomas) and Elbardouni et al. (11), a prevalence of 7.7% (1 case out of 13 upper limb lipomas). Barrile (9) identified a quite low prevalence (0.21%) of palmar lipomas (1 case out of 476 upper limb lipomas).

### *Clinical Implications*

Patients with asymptomatic lipomas show a characteristic delay in seeking medical attention (3), and as a result a significant increase in the lipoma's dimensions may occur over time (1). The first symptoms that commonly alert patients are caused by nerve compression

by the mass. In the distal forearm, the lipoma may mimic CTS. Usually the MN is compressed, and the relevant symptoms include difficulty in grasping, decreased finger flexion, finger numbness and tingling, as well as power loss in MN distribution (13, 14). In 1964, Morley (6) described a carpal lipoma that was painless but with discomfort and tingling in the fingers when pressure was applied. The same symptoms were described in a giant carpal lipoma (1). Recent clinical reports refer to patients with finger numbness and swelling of the carpal area, as well as loss of muscle power in MN distribution (3, 13, 14). In addition to lipomas, entrapment neuropathy may be caused following the trans-muscular course of a MN branch in the forearm, with symptoms resembling CTS (15). Other anatomical factors causing CTS include accessory and variant muscles (elongated bellies or tendons of distal flexor muscles) in the distal forearm area, a bifid MN that may be compressed along its course, and the presence of a persistent median artery (16–18).

Surgeons, neurologists, and general practitioners should be alert to early identification of lipomas, as delayed diagnosis, particularly in cases of tumors located on the palmar surface of the distal forearm, may cause complications due to nerve compression, as well as significant disturbance in patient's life quality. Surgical excision may completely relieve symptoms (3, 5, 8, 13). Intraoperatively, surgeons should be alert for lipomas in close proximity to muscle tendons and neurovascular structures (1). In cases of recurrence, despite the transverse carpal ligament release, magnetic resonance imaging (MRI) is recommended, to investigate any aberrant soft tissue compressing the MN, within or adjacent to the CT. In such cases, imaging via MRI scan is optimal for preoperative planning (1).

## Conclusions

The current cadaveric report highlights an enlarged distal forearm lipoma, situated adjacent to the CT, displacing, and flattening the MN. The finding is clinically relevant both for CTS differential diagnosis and surgical treatment. Any case of persistent CTS that is unresponsive to treatment should alert physicians to possible nerve compression attributed to a mass.

**What Is Already Known on This Topic:**

*Lipomas are very common tumors that are considered giant when they exceed 5 cm. They are usually benign, and occur in about 2% of the population. Their prevalence in the forearm-carpal area varies, remaining in quite low percentages compared to lipomas in other upper limb locations. Distal forearm or carpal lipomas have been found to cause carpal tunnel-like symptoms, caused by median nerve compression. Specifically, they can cause tingling, numbness, loss of power, grasping difficulties, and decreased finger flexion. Usually, delayed diagnosis causes significant disturbance of the patient's life quality. Other anatomical factors causing carpal tunnel syndrome include accessory and variant muscles in the distal forearm area, a bifid median nerve that may be compressed along its course, and the presence of a persistent median artery.*

**What This Study Adds:**

*The current cadaveric report presents a large mass identified on the palmar surface of the distal forearm in a 63-year-old male cadaver. The mass caused the anteromedial dislocation of the median nerve and its characteristic flattening. Despite the lack of information on the subject's medical history, the lipoma's size and its vicinity to neural structures obviously caused nerve compression. The described finding is clinically relevant for both differential diagnosis and carpal tunnel syndrome surgical treatment.*

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**Authors' Contributions:** KN undertook the dissection of the cadaver and captured the case; VA and MP performed the acquisition, data analysis, and interpretation, and wrote the paper; TT revised the paper. All authors approved the final form of the draft paper.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

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Images in Clinical Medicine
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# The Erlenmeyer Flask Deformity on Computed Tomography

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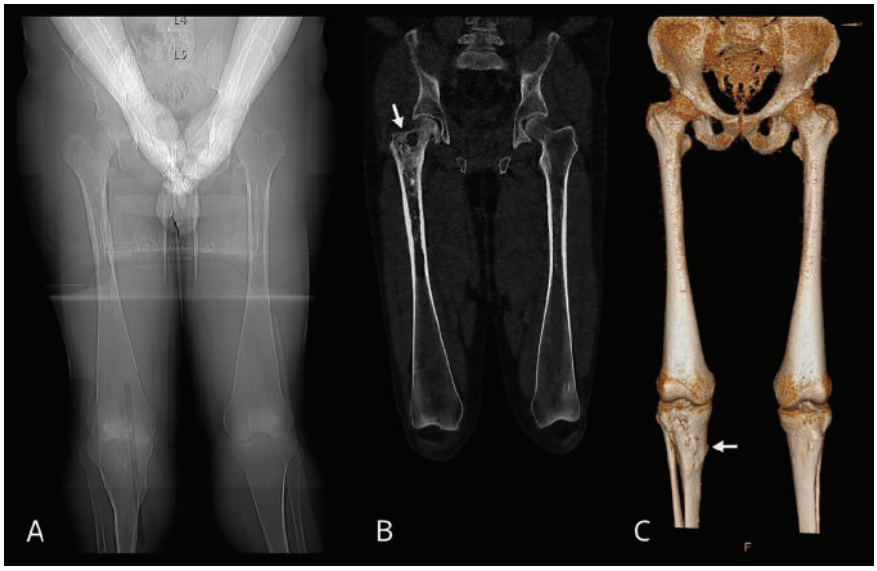
**Key Words:** Metaphyseal Flaring ▪ Gaucher Disease ▪ Bone Remodeling ▪ Computed Tomography.




A 52-year-old male was referred to the Radiology Department for a scheduled skeletal survey using a whole-body low dose computed tomography (WBLD-CT) protocol (Panel 1 A & B). He was diagnosed with Gaucher disease (GD) type 1 in early childhood and was being treated by the Hematology Department with intravenous imiglucerase. He complained of chronic right hip pain, and mentioned a right tibial plateau fracture a few weeks prior as a result of a work accident, which was treated conservatively (Panel 1 C). WBLD-CT revealed a bone infarct involving the right femoral head and trochanters (assumed to be the cause of the chronic right hip pain) (Panel 1 B). Additionally, a widened distal diaphysis and diametaphyseal region on both femora was noted, with a thin cortex and straight borders, while the proximal diaphyses were narrow, resembling a flask, also known as metaphyseal flaring, or the Erlenmeyer flask deformity (EFD) (Panel 1 C). GD is a rare autosomal recessive disease responsible for accumulation of the glycolipid glucocerebroside within the lysosomes of the macrophages, principally in the bone marrow, spleen and liver, caused by the deficiency of glucocerebrosidase activity (1). EFD is the most common bone abnormality of GD and appears in 50-80% of adult cases (2, 3). Development occurs during puberty as a result of undertubulation. It may involve all tubular bones, predominantly the femur, and is typically asymptomatic with no proven predisposition to fragility fractures (1, 2). Besides GD, EFD manifests in numerous different diseases with improper osteoclast function, such as osteopetrosis, metaphyseal dysplasia (Pyle disease), Niemann-Pick disease, achondroplasia and thalassemia (1).

**Authors' Contributions:** Conception and design: CS and SD; Acquisition of data, analysis and interpretation of data: CS; Drafting the article: CS; Revising it critically for important intellectual context: CS and SD; Approved final version of the manuscript: CS and SD.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

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# Intra-renal Arteries in Nephrectomy from a Historical Aspect, a Quest Originated by Medical Illustrations to Reach Modern Angiography

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**Abstract**
The aim of the present paper is to contribute to the understanding of the history of the anatomical study of the intra-renal arteries. The vasculature and especially the intra-renal arteries of the kidneys are an intriguing field which was first studied through art and then perfected by medicine. Angiography and microsurgery have resulted in partial nephrectomy techniques for surviving kidneys with adequate functional results. Graves' categorization dating from 1954 opened the way for innovative approaches that have resulted in modern topographical anatomy. **Conclusion:** Our understanding of the anatomy of intra-renal arteries has played a significant role in surgical anatomy and internal medicine.

**Key Words:** Graves' Categorization ▪ Kidneys ▪ Intra-renal Arteries ▪ Nephrectomy ▪ Angiography.

## Introduction

The segmental anatomy of the kidneys is a challenging issue due to the wide range of endo- or intra-renal vessel variations (1). Many scholars have tried to provide a concise system that is accepted throughout the world. The embryological development of the kidney, the topographic anatomy of the organ, the renal pyramids, and the anatomy of the segmental kidney arteries have been all used as the basis of different approaches to topographical anatomy. Nevertheless, a global consensus is fundamental since kidneys play a crucial role in surgical procedures. A cluster of dangerous situations and possible fatalities may occur, such as necrosis, during nephrectomies and alter the expected results.

The kidneys, like the lungs, liver and spleen, have a system of segmental arteries with an essential role in the surgical anatomy of these organs (Figure1). Regarding the intra-renal arteries, their study began using a scientific surgical approach during the last seven decades, even though efforts began in the 17$^{th}$ century. Despite the fact that the

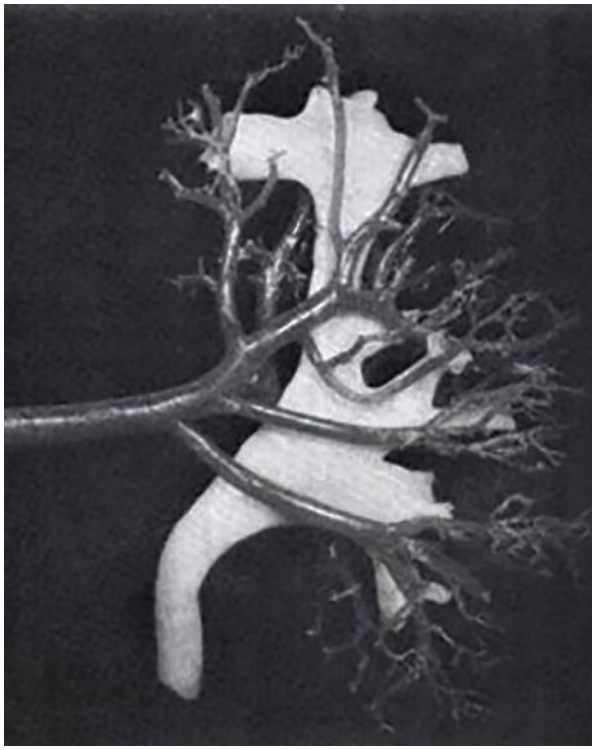

Figure 1. A figure of human kidney's blood supply and collecting system (2).

first detailed work began at the beginning of the 20th century, it is surprising that the best descriptive attempt was not provided by a physician or anatomist, but by a medical artist.

This historical vignette aims to record the story of the decade from 1950 to 1960, when it all started.

## The Painter

The German artist Max Brödel (1870-1941), who was born in Leipzig, was to become one of the greatest medical illustrators of modern times (3). He graduated from the Leipzig Academy of Fine Arts, and at a young age was brought to the John Hopkins School of Medicine to work as an illustrator for the medical authorities of the school. Brödel was credited with the development of the carbon dust technique for medical and scientific illustrations. His innovative thought, to present his illustrations in an acceptable medium that was able to demonstrate the vividness and the detailed characteristics of living tissues, paved the way for a second breakthrough in art, using clay-surfaced lithographic transfer paper (4). Those two novelties created a new era in topographical anatomy. He soon became known as an anatomist and scientist, mainly for his description of the avascular area of the kidney (which became known as Brödel's bloodless line) (Figure 2) (5) and an improved method of nephropexy using a suture that he designed (Brödel's suture) (6). His description of the vascular system of the kidneys was the best at that time (7).

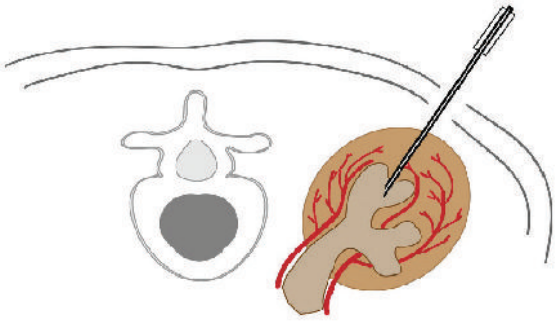

Figure 2. Brödel kidney avascular line (5).

## The Pioneer

It was F.T. Graves who presented a study on the intra-renal arteries for the first time back in 1954, which has remained in use until today (8). This gold standard approach to the anatomical study of the segmental renal arteries led to the categorization of vascular renal segments which is of great value for nephrectomies. Graves, who was a prolific researcher into the vascularization of the kidneys gave us a proposal of five vascular segments: i) the apical/superior, the upper pole in both the anterior and posterior planes, ii) the upper, central area, iii) the middle, the area between the upper and the lower pole, iv) the lower/inferior, forming the lower pole in both the anterior and posterior planes, and v) the posterior, the area between the apical and the lower pole in the posterior plane.

The intra-renal arteries are known for their diversity. However, Graves recorded what in his opinion should be followed as the "normal" pattern. Thus, according to his survey, the renal artery splits into anterior and posterior branches before the hilum. The anterior branch is divided into four segmental branches which provide blood to the apical/superior, upper, middle, and inferior segments of the kidney. The posterior branch provides blood to the posterior segment of the kidney. Furthermore, each branch supplies blood to a lobar artery, which in its turn provides hematosis to the renal pyramid. Each lobar artery is further separated into two or three more inter-lobar arteries, which arch over the base of the pyramid in order to form the various arcuate arteries. From every arcuate artery various interlobular arteries originate, and their branches constitute the glomerular capillaries which are the fundamental factors for the essential action of the kidneys, that is, filtration. We must have in mind that every segmental renal artery should be considered as the end.

Graves' studies distinguished further variations of each segmental artery. That is: a) for the apical segmental artery he recognized four types: i) Type I, arising from the upper segmental artery, ii) Type II, arising from the junction between the anterior and posterior division of the main stem

renal artery, iii) Type III, arising at the junction of the main renal artery with the aorta, entering the apical segment outside the hilum and iv) Type IV, arising from the posterior division; b) for the upper, middle and lower segmental arteries he recognized three groups: i) Group I: the lower segmental artery arises first, while the upper and middle have a common origin, ii) Group II: the upper segmental artery arises first, while the middle and lower have a common origin and iii) Group III: the upper, middle and lower segmental arteries arise in common (9-14).

### *The Reformer*

A few years after Graves' categorization, it was Boijsen who, with the use of radiology, presented an angiographic study of the renal arteries. His differentiated approach in the segmental anatomy of the kidneys sought to ameliorate or supplement Graves' efforts. Boijsen had the belief that the segmental arteries did not correspond to the kidney's parenchyma division according to the topographical view. He based this on the fact that an average adult kidney has seven pairs of Ventral-Dorsal pyramids. Therefore, he introduced the idea of dividing the kidneys into four segments based on the relationship of the segmental arteries to the renal pyramids. That is: i) Segment I containing Pyramids 1-2 Ventral and Dorsal, ii) Segment II containing Pyramids 6-7 Ventral and Dorsal, iii) Segment III containing Pyramids 3-5 Ventral, and iv) Segment IV containing Pyramids 3-5 Dorsal (15).

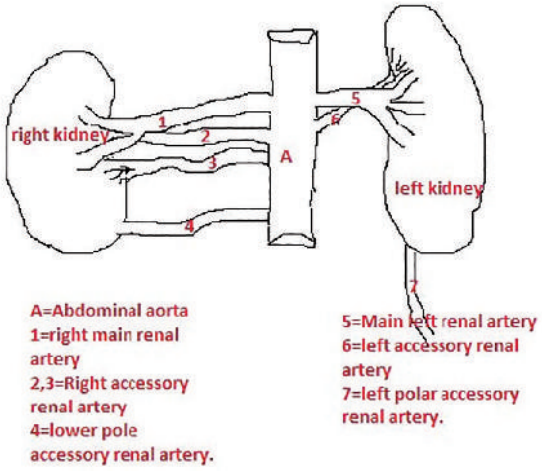


Figure 3. Vascular variations of Kidney (16).

## Discussion

Recent studies have demonstrated that in the human kidneys the arterial vasculature is frequently different from the description made by Graves 65 years ago (Figure 3) (16). Additionally, in a significant percentage of cases, a single renal segment receives two or more branches which originate from another artery leading to a different segment. Thus, in 47% of cases the arteries may derive from a common trunk. This fact should be taken into account by surgeons when performing nephrectomies (17-18). With the evolution of microsurgery and the tendency towards the saving of organ tissues rather than complete resection, partial nephrectomy is gaining more interest in oncological kidney surgery, and in polytraumatic patients. Kidney microsurgery requires mapping and a good knowledge of the vascular intra-renal anatomy for acceptable outcomes both oncologically and functionally (17-19). Thus, nephrectomy requires imaging, nephrometry scoring systems, and vascular control techniques so that the surgeon is able to maximize the remaining vascularized parenchyma, control renal function and minimize local ischemia (20). In 1998, the Terminologia Anatomica consensus homologated two branches of the renal artery: i) the anterior, and ii) posterior, while five segmental branches were recognized: i) four from the anterior branch and ii) one from the posterior branch. This partially altered Graves' categorization after almost 70 years of global acceptance (19). The modern practice of thorough presurgery mapping of the renal arterial net is the outcome of the diachronic anatomical investigation which is highlighted in this essay.

### *Epilogue*

Max Brödel introduced the idea of describing the small arteries and became known for his work in renal anatomy. Graves presented his approach to

the intra-renal vasculature, which after some reforms is still in use and mentioned by studies in the field. Partial nephrectomy is the modern form of kidney surgery and knowledge of the blood supply is a key element for success.

**What Is Already Known on This Topic:**
*A modern anatomical study on intra-renal arteries and its role in surgical anatomy.*

**What This Study Adds:**
*This study, with its starting point in the work of a painter, describes the diachronic development of the medical-anatomical study of the intra-renal arteries, and how modern medicine, with modern methods such as angiography, can help the physicians to understand their topographical anatomy in order to apply it in the surgical field.*

**Authors' Contributions:** Concept: VK and GC; Design: VK and GC; Literature search: VK, GC and PG; Data analysis: PG; Manuscript preparation: VK, GC and PG; Manuscript editing and manuscript review: EM. The final version of the manuscript has been read and approved by all the authors.

**Conflict of Interest:** The authors declare that they have no conflict of interest

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