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**EVALUATION OF THE EFFECTS OF THE VOLUMES OF THE
POSTERIOR AND ANTERIOR VERTEBRAL MUSCLES
ESTIMATED FROM THE COMPUTED TOMOGRAPHY IMAGES
ON THE LUMBAR LORDOSIS**

PhD Dissertation

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ÖZET
OMURLARIN ÖN VE ARKASINDAKİ KASLARIN HACİMLERİNİN LUMBER
LORDOZ ÜZERİNE ETKİLERİNİN BİLGİSAYARLI TOMOGRAFİ
GÖRÜNTÜLERİ ÜZERİNDEN İNCELENMESİ

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Bu çalışmada, Lomber Lordosis tanısının radyolojik görüntüler üzerinde kantitatif olarak hesaplanarak konulmasını sağlayan PAL tekniği (The projeksiyon area per length squared) ile prevertebral ve postvertebral kas hacimlerinin karşılaştırmalı olarak incelenmesi ve takibinin yapılması amaçlanmıştır.

Samsun Ondokuz Mayıs Üniversitesi Hastanesi Radyoloji Bölümü Arşiv Sistemi'nden bilgisayarlı tomografi (BT) görüntüleri toplandı ve bu incelemede kullanıldı. Veri toplama işlemi sırasında, yaşları (19-84) olan hastalar için sırtüstü pozisyonda 62 başlıklı BT cihazı taranarak görüntüsü elde edildi. Bu çalışmada ilk olarak görüntü bankamızdaki dosyaların görüntülenmesini sağlayan “OsiriX” programı kullanılmıştır. Bu yazılım ile dosyalardaki görüntüler sagittal, koronal ve enine düzlemlerde tek bir pencerede gösterilecek, yönelimi düzeltilmiş görüntüler DICOM dosyasına aktarıldı. İkinci yazılım uygulaması ImageJ ile açı ve kesit yüzey alanları ölçmeleri yapıldı. Ön (psoas majör) ve arka (paraspinal, multifidus) kaslarının hacimleri kesitlerdeki kesit yüzey alanlarının toplamının kesit kalınlığı ile çarpılması ile stereolojir olarak hesaplandı. PAL değerleri ise literatürde tarif edilen uzunluk ve alan ölçümlerini ilgili formüle yerleştirilerek hesaplandı.

Toplam ön hacim, toplam arka hacim ve toplam PAL'den bağımsız olarak değişkenler arasında anlamlı bir ilişki olmadığını gösterilmiştir. Ayrıca Pearson korelasyon testine göre her iki cinsiyette ön hacim, arka hacim ve PAL arasında istatistiksel olarak anlamlı bir ilişki yoktur.

Bulgular doğrultusunda vücut kitle indeksi, boy ve kilo, aktivite durumu ve fiziksel koşulların bilinmesi, bel ağrısı öyküsü ve bu faktörlerin önemine bağlı olarak yaşa bağlı kas hacmindeki yağ değişimlerinin bilinmesi ve bunların vücut kitle indeksi ile doğrudan ilişkisinin bilinmesini düşünmekteyiz. Kasların hacmi, ileride yapılacak çalışmalarda verilere dahil etmek için dikkate alınacaktır.

Anahtar kelimeler: Lomber lordoz, uzunluk başına düşen alanın karesi, psoas major, prevertebral kaslar, postvertebral kaslar, bilgisayarlı tomografi, stereoloji, hacim

ABSTRACT

EVALUATION OF THE EFFECTS OF THE VOLUMES OF THE POSTERIOR AND ANTERIOR VERTEBRAL MUSCLES ESTIMATED FROM THE COMPUTED TOMOGRAPHY IMAGES ON THE LUMBAR LORDOSIS

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The lumbar lordosis is an anatomical curvature formed by the lumbar vertebrae. An increase in the lordosis or straightening of it results in backpain. Several reasons may responsible for the changes of normal curvature range of the lordosis. In the present study, we aimed to observe the effect of the prevertebral and postvertebral muscle volumes over the degree of lumbar curvature using the computed tomography (CT) images. The CT scan images were collected from image archives of the Department of Radiology, Ondokuz Mayıs University in Samsun. Sixty-two CT scan images for patients aged from (19 to 84) were obtained in supine position. OsiriX software is used to view the files in the image bank. The images in the files displayed in a single window in sagittal, coronal and transverse planes, and images converted to orthogonal plane exported to DICOM files.

The prevertebral (psoas major) and postvertebral (psoas major) muscles were viewed in another software, the ImageJ. The sectional surface areas of the muscles were measured by the program multiplied by the interval between images. Therefore, the volumes of the muscles were obtained stereologically. The sagittal images were viewed in the ImageJ and the degree of the lumbar lordosis measured by the projection area per length squared (PAL) method. The relations among the volumes and lumbar lordosis analyzed. The mean total volumes of the prevertebral and postvertebral muscles were $230.34 \pm 91.45 \text{ cm}^3$ and $598.03 \pm 154.69 \text{ cm}^3$ in both sexes, respectively. The mean degree of the lumbar lordosis was $4.08 \pm 1.86 \%$ in both sexes.

Correlation analysis showed that there were no relations between the volumes of the pre/postvertebral muscle volumes and the lumbar curvature. The results were the same for males and females in details. There are still debates on the effect of exercise or use of corset for the treatment or relief of the excessive curvature or straightening of the lumbar lordosis. In the light of our finding, there is no relation between the degree of the lumbar lordosis and the sizes of the muscles surrounding the spine. For further analysis, before/after exercise program and volume changes of the muscles and curvature changes of the spine may reveal the interaction.

Keywords: Lumbar lordosis, projection area length squared, prevertebral muscles, postvertebral muscles, computed tomography, stereology, image analysis

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ABBREVIATIONS

AP	Articular Process
BMI	Body Mass Index
CT	Computed Tomography
ERS	Erector Spinae
IAP	Inferior Articular Process
ID	Intervertebral Disc
IL	Iliocostalis Lumborum
ILL	Iliolumbar Ligament
IVF	Intervertebral Foramina
LBP	Low-Back Pain
BMI	Body Mass Index
LL	Lumbar Lordosis
LLA	Lumbar Lordotic Angle
LR	Lumbar Region
LS	Lumbar Spine
LuV	Lumbar Vertebrae
MP	Mamillary Process
MRI	Magnetic Resonance Imaging
PAL	Projection Area Per Length Squared
PM	Psoas Major
PSM	Paraspinal Muscles.
SN	Spinal Nerve
SP	Spinous Process
TP	Transverse Process
VB	Vertebral Body
VC	Vertebral Column

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1. INTRODUCTION

The functional and clinical relevance of lumbar lordosis (LL) is becoming more well-acknowledged in research studies (Adam et al., 1999; Jang et al., 2009). It is generally established that LL, or the degree of lumbar curvature, plays an important role in maintaining spinal balance (Schuler et al., 2004). Based on the distinctive upright posture and lordotic lumbar curvature of the human spine, understanding the formation of the human spinal column and the specific anatomical traits that enable LL may offer insight into spine health and degeneration (Eaton et al., 2002). In the past, researchers focused their attention on the backbones, discs, and joints. Despite this, the importance of the muscular system in the stability of the lumbar spine (LS) cannot be emphasized (Cholewicki and McGill, 1996). The degree of LL is affected by vertebral body (VB) and disc shape, but it is also determined by the strength of the spinal muscles (Sinaki et al., 1996) and volume (Meakin et al., 2013).

The LS muscles are classified into two groups based on their location from the spine: anterior (prevertebral) and posterior (postvertebral). The prevertebral group includes the psoas major (PM) muscle, while the posterior group includes transversospinalis (multifidus, rotatores, interspinales, and intertransversarii) and erector spinae (ERS) (iliocostalis and longissimus) (Kanga, 2013). The PM is well-known for its function as a significant hip flexor (Bogduk et al., 1992). It may also serve as a LS stabilizer (Penning, 2000). It also serves as a LL controller when subjected to heavy lumbar stresses (Bogduk, 1987). Similarly, postvertebral muscles are important in controlling movement, providing mechanical stability, and influencing the degree of LL (Meakin et al., 2013).

Moreover utilizing computed tomography (CT) can give non-invasive morphologic information on these muscles while exposing the patient to minimal radiation (Cooper et al., 1992; Hultman et al., 1993). This advantage macroscopic signs of muscle deterioration, such as a loss in muscle size and an increase in the number of fat deposits, can be easily recognized on CT scans (Danneels et al., 2000).

The volumes of the structures can be estimated on the sections of the structure using the Cavalieri principle. The sections may be physical or the images of CT scan.

The total sectional cut surface areas are multiplied by the section thickness and the total volume of the structure is estimated. Therefore, sectional imaging modalities give the possibility to assess the size of the organ or structures of the living subjects.

The projection area per length squared (PAL), which was used in this study to quantify the degree of LL; by using direct lateral roentgenograms is a unique and straightforward methodology that may yield more representative findings than past approaches for LL measurement (Kuru et al., 2008). As a result, the purpose of this study was to compare changes in prevertebral and postvertebral muscle volumes between genders using the PAL technique, which allows the diagnosis of LL to be calculated quantitatively using radiological images, to establish the diagnosis and track the progression of increase in lumbar curvature.

2. GENERAL INFORMATION AND SUMMARY OF LITLICURE REVIEW

This section discusses the theoretical aspects of this research, it explains the general anatomy of human spine, lumbar vertebrae, lumbar spine muscles, and it also provides an overview of lumbar lordosis, variations in lumbar lordosis between genders, evaluation of lumbar lordosis, measuring techniques and the muscles related to the lumbar lordosis.

2.1. The Spine

The spine in human is composed of vertebrae and intervertebral discs (IDs), it's arranged out from the skull down to the coccyx. It is involved cervical, thoracic, lumbar and sacral regions. The main functions of the vertebrae are spinal cord and spinal nerves branches protection, thorax and abdominal backing and allow pliability. It's also permits body mobility (Singh et al., 2021).

2.2. Lumbar Vertebra

Typical vertebrae comprise a VB, a vertebral arch, in addition to seven processes. The body carries most of the force put on the vertebrae. It was noted that the VBs increase in size whenever the column descends. The VB consists of "cancellous" bone, which composed the red marrow, encompassed by a thin outer layer of cortical bone (Waxenbaum et al., 2020).

(Bogduk, 2005) described the LS consist of five detached vertebrae, the names of these vertebrae are according to their location in the entire column, in order from top to bottom are known as the first (L1), second (L2), third (L3), fourth (L4), and fifth (L5) lumbar vertebrae.

The lumbar vertebrae (LuV) followed by the sacrum. Every LuV has 2 portions, the VB and neural arch. The VB located anteriorly, and its dimensions progressively increase from cranial to caudal. The neural arch located posterior to the VB and it contains of a pair of pedicles arising from the postero-lateral surface of the upper portion of VB that connects with paired laminae, which are located further posteriorly When

viewed from above, the superior surface of VB is more wide transversely and look like the kidney's shape (Ebraheim et al., 2004).

(Bogduk, 2005) also added in each VB the posterior surface is mostly flat, the major part of the upper and lower surfaces of every VB is smooth and cribriform by teeny holes. While the perimeter of every surface is characterized by a narrow border of smoother and less perforated bone, which is a little raised from the surface. This border acts the fused ring apophysis, and it considered as secondary ossification center of the VB.

Alongside with the posterior side of the VB, the arch of LuV shapes the vertebral (spinal) canal (Figure2.1), in which the spinal cord passes through. The arch comprises of two (right and left) pedicles, a cylinder portion of hard bone that bind the arch to the VB (Waxenbaum et al., 2020). As indicated by (Bogduk, 2005) The pedicles are attached to the upper portion of the VB's back; this is one attribute that causes superior and inferior aspects of the VB to be distinguished. Viewing a vertebra from the side is the easiest way to assess the proper orientation. The superior end of the body's posterior surface is where the pedicles are most tightly connected.

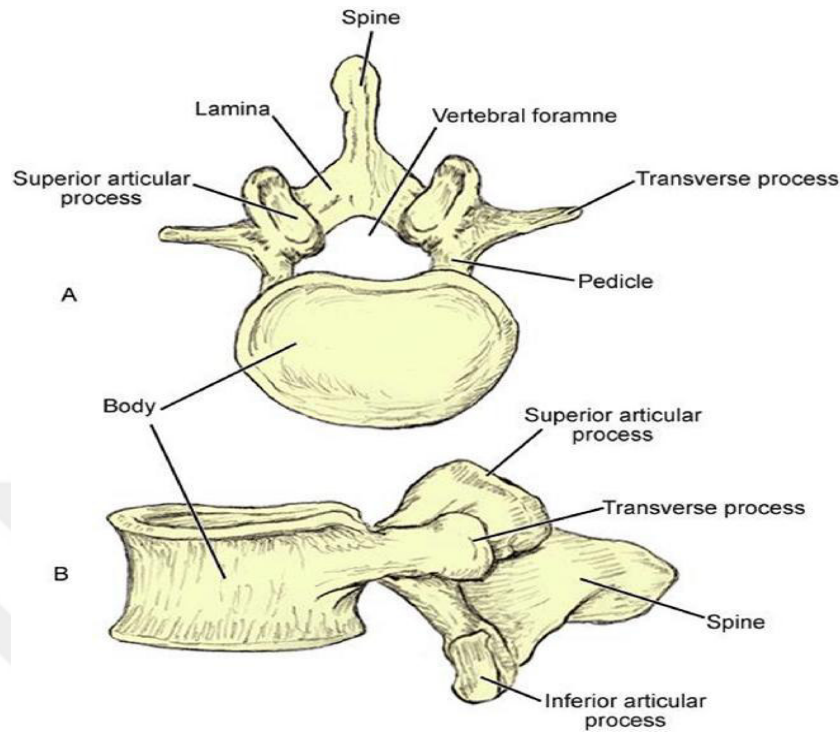


Figure 2. 1. Illustration of lumbar vertebrae showing vertebral body, pedicles, facets, transverse process, spinous process, and lamina (Sions et al., 2017)

The lamina, flattened bone segments form most of the arch, binding the transverse and spinous processes (SP) (Waxenbaum et al., 2020).

Inside views of the LuV are superior and inferior to both pedicles, vertebral notches can be seen among the superior and inferior articular processes posteriorly and the parallel projections of the VB anteriorly. Hence, the spinal nerves (SNs) come up from the spine from these foramina (intervertebral foramina) (IVF), which are shaped by the superior and inferior vertebral notches of neighboring vertebrae as well by the IDs that link them. Additionally, these foramina also house the spinal (posterior root) ganglia (Keith, 2014).

(Van De Graaf, 1995) coincided with (Keith, 2014) that the SP and two transverse processes (TPs), as well as the two superior and two inferior articular processes (APs), acts as muscle attachments that keep the spine from twisting. The four APs emerge from the lamina-pedicle junction. From The lumbar vertebral arch of all seven of these processes arises. The SP protrudes inferiorly from the vertebral arch in a posterior inferior direction. Around the same time, the TPs spread laterally from both sides of the

vertebra, and at the lamina-pedicle junction. The superior APs of the vertebrae connect to the inferior articular processes (IAPs), each bearing an articular surface (facet).

(Cramer and Darby, 2017) added The L4 and L5 SPs, mainly the L5 SP, are shorter than the other lumbar SPs and not easy to palpate. L4's SP is the most inferior one with palpable movement through trunk flexion and extension. The posterior margin of the LuV's SPs varies from those of the thoracic vertebrae in that they have more flat surface. He also mentioned that The L4 SP was once thought to be in a horizontal plane with the superior margin of the iliac crests (the supra-cristal plane), though the tops of the iliac crests were thought to be associated with the L5 SP in around 20% of the population. The tips of the LuV's TP are about 5 cm laterals to the midline and are normally not palpable.

Three joints are formed as two consecutive LuV are articulated. The two VB join to form one. The IAPs of one vertebra articulate with the superior APs of the vertebra above, forming the other two joints. The anterior intervertebral joint also called intervertebral symphyses joint or intervertebral amphiarthroses, is the joint that connects the VBs. Simply by stacking two consecutive VBs on top of one another, an intervertebral joint may be formed. Therefore a joint like this could support a lot of weight while still allowing for gliding motions between the two bodies (Nikolai Bogduk, 2005). As indicated by (Ombregt, 2013) the two adjacent VBs are linked by an ID (Figure 2.2). Together with the accompanying facet joints, they form the "functional unit of Junghans". The disc consists of an annulus fibrosus, a nucleus pulposus and two cartilaginous endplates, annulus fibrosus is made up of 15–25 concentric fibrocartilaginous sheets or 'lamellae' each formed by parallel fibers, running obliquely at a 30° angle between the VBs. Two successive layers' fibers are directed in opposite directions. They cross each other at around a 120-degree angle. This arrangement of the annular fibers gives the normal disc great strength against shearing and rotational pressures, while angular movements remain completely possible.

The nucleus pulposus is an area in the middle of the ID, the thickness of nucleus pulposus is increase from superior to inferior in lumbar region (LR), composed mainly of mucoid material, which made up 70% to 90% water. On T2-weighted magnetic resonance imaging (MRI), in this way the nucleus pulposus shows hyperintensity signal

(white). The percentage of the water in the nucleus pulposus progressively decreases with age. Due to loss of water after the fifth decade, the nucleus pulposus becomes less distinguishable from the annulus fibrosis. The water loss in its components could be the major reason that leads to disc degeneration, and this case presented by the decrease in height of the ID (Cramer and Darby, 2017; Ebraheim et al., 2004).

(Keith, 2014) noted that the nucleus pulposus is avascular, meaning it gets its nutrients through diffusion from the anulus fibrosus and VBs peripheral blood vessels. He also mentioned that through anterior and lateral flexion and extension of the vertebral column (VC), Compression and tension occur concurrently in the same disc, in these movements, in addition during the rotary motion; the turgid nucleus serves as a semi fluid fulcrum. The lamellae of the anulus fibrosus are thinner and less numerous posteriorly than they are in anterior or lateral aspect, for that reason nucleus pulposus is not located in the center of the disc but is placed between the center and posterior aspect of disc. (Ombregt, 2013) described the superior and inferior aspects of the ID covered by upper and a lower cartilaginous endplate, they are plates of cartilage each one about 0.6–1 mm thick that attach the disc to their respective VBs. Each endplate almost completely covers the surface of the adjacent VB. Just the ring apophysis, a thin rim of bone along the circumference of the VB, is left exposed by cartilage.

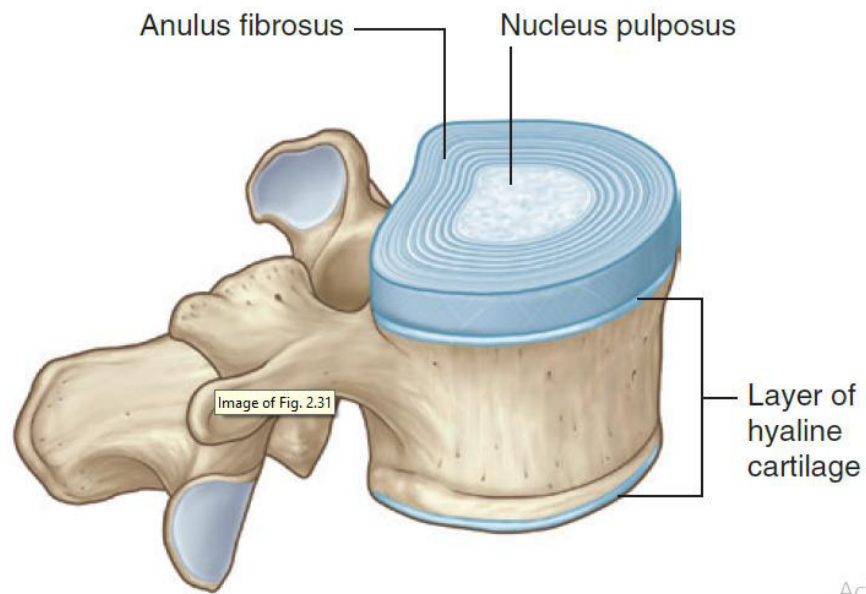


Figure 2. 2. The Intervertebral Disc in superolateral view (Drake et al., 2019)

The ID's primary functions are to facilitate movement between VBs and to transmit loads from one VB to another. Weight-bearing involves both the nucleus pulposus and the anulus fibrosus. The various components of an ID behave in different ways, both individually and cooperatively, as is obvious. The nucleus pulposus is larger in the LR than in the cervical and thoracic regions, and with the movement axis again across the nucleus, the height of the disc is one-third that of the VB. When the disc is performing its various functions, the nucleus pulposus is a pressure-sustained and transmitting structure. It is primarily engaged in weight bearing by transmitting loads and bracing the anulus fibrosus. The nucleus pulposus is not involved in any of the interbody joint's other motions. The anulus fibrosus resists these. The anulus fibrosus behaves as a ligament in all movements, limiting mobility and stabilizing the joint to some extent. As the attachments of individual collagen fibers are isolated, the fibers stretch and resist movement. . All of fibers are resistant to distraction and participate in weight bearing The overall role of the ID is to maintain a deformable space between the VBs, allowing the VC to be more flexible while serving as a shock absorber in the assimilation of compressive forces. The ID is pliable, and its thickness influences the amount of movement possible between neighboring vertebrae. The disc must be able to

augment the locomotor system's mobility in order to preserve the intervertebral space. Anulus fibrosus alone is able to stretch and allow movements to occur; however, but it reacts poorly to compressive forces (Bogduk, 2005; Humzah and Soames, 1988).

As per (Ombregt, 2013) the connection of the lower and upper AP are known as zygapophyseal joints, "facet joints" or "apophyseal joints" (Figure 2.3). They are real synovial joints, with cartilaginous articular surfaces, synovial fluid, synovial tissue, and a joint capsule. Moreover, the superior articular surface is slightly concave and faces medially and posteriorly. The convex inferior articular surface points laterally and partially anteriorly. (Almeer et al., 2020) described the inferior facet of the vertebra above articulates with the superior facet of the vertebra below. Facet joints are located between the pedicle and lamina of same vertebra forming articular pillars that give mechanical stability to the entire VC. In reality two adjacent VBs, an ID, and two facet joints make up the functional unit of the VC. The motion segment is the name for this unit. (Ebraheim et al., 2004) pointed out Hyaline cartilage covers the articular surfaces in facet joints, allowing sliding motion in the spinal column's posterior arch, thin articular capsules, with a synovial membrane within and a fibrous membrane outside, they are connected to the facet joints' articular surfaces on the periphery. The most common aging-related changes in the LR are narrowing of the joint space, thinning of the articular cartilage, and hypertrophy of the subarticular cortical bone. (O'Leary et al., 2018) added The synovium, synovial folds, and fibrous capsule enclose and give a biomechanical support to the facet joint space. The synovium immediately wraps the facet joint, while the synovial fold, also known as a meniscoid fold, folds into the region between the inferior and superior facet. The synovium, synovial fold, and fibrous capsule all work together to protect and enhance the mechanical structure of the underlying articular cartilage.

The plane of facet articulation determines the form of motion directed by the posterior portion of the spinal motion segment. For example in thoracic facet joints have a coronal orientation that limits extension in the same time allows rotation, while the lumbar articular facets have a sagittal oblique orientation that limits rotation (Jaumard et al., 2011). As indicated by (Ombregt, 2013) The facet joints' main function is to direct lumbar movements and keep vertebrae in line during flexion-extension and lateral

flexion. Very little rotational motion occurs at the first four upper LuV due to the more sagittal angle of the articular surfaces. At the lumbosacral point, the joint line has a more coronal plane, which allows for rotational motions, but these are constrained by the iliolumbar ligaments. As a result, the overall range of rotation in the lumbar spine is very small, but not entirely zero.

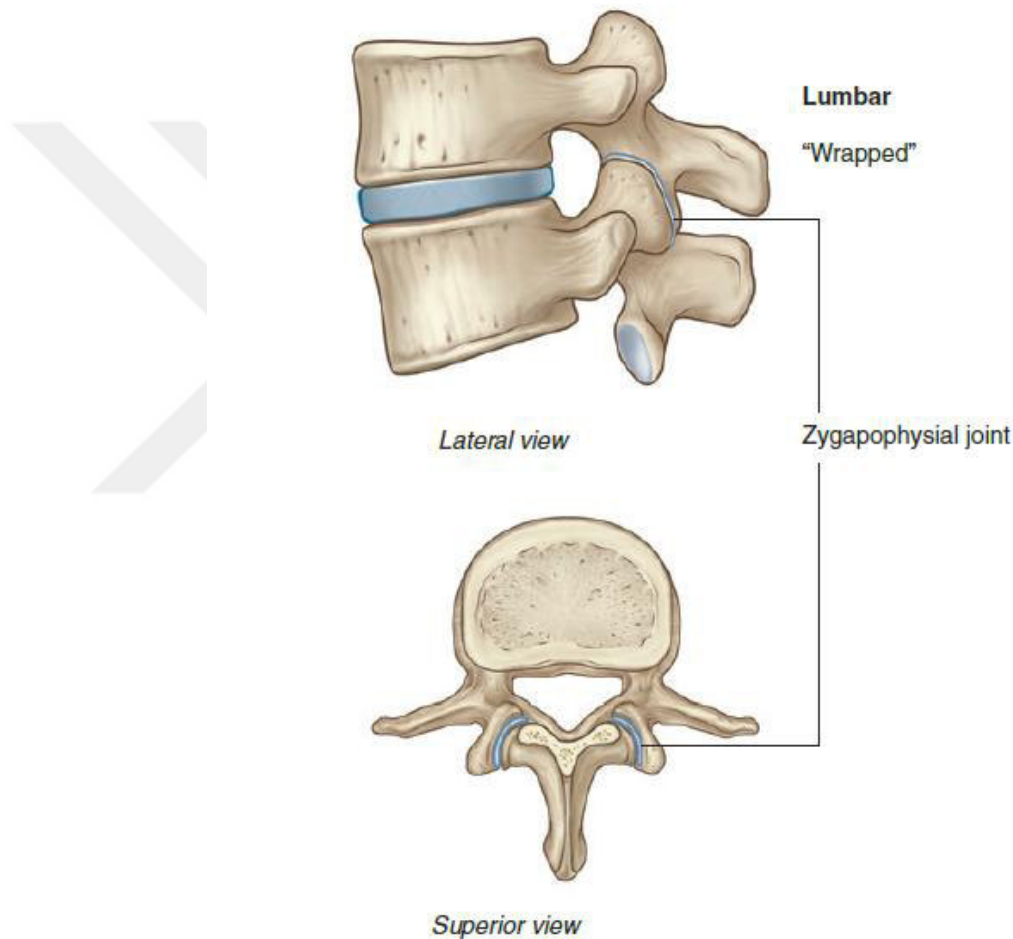


Figure 2. 3. An lateral and superior view of zygapophyseal joint (Drake et al., 2019)

The facet joints assist in carrying the loads placed on the spine, especially during extension and rotation. The facet joints are of particular interest to those who treat spinal conditions because they have been identified as a source of back pain. Facet joint pain can be caused by direct injury to the joints, or, as with any synovial joint, loss of motion or aberrant motion. Moreover, degeneration of hyaline cartilage that makes up the articular facets may cause pain (Cramer and Darby, 2017). A strong cortical area of the

posterior arch that connects the superior and inferior facet known as pars, it is small in its superomedial portion (only 2 mm) and thickest in its inferolateral part (5 to 10 mm). Beneath the pars an artery runs from the posterior anastomotic system to the spinal canal (Ouellet and Arlet, 2004).

The LS ligaments can be divided into four groups based on their topography, the first group ligaments that bind the VBs (the anterior and posterior longitudinal ligaments), The second group ligaments that bind the posterior to the anterior constituents (ligamentum flavum, the interspinous ligaments, and the supraspinous ligaments), The third group consist the (iliolumbar ligament), they are bilateral ligaments connects TPs of the fifth lumbar vertebra to the ilium on both sides. Iliolumbar ligament was originally divided into five divisions, according to their arising border from L5 TP. Anterior, posterior, superior, inferior, and the vertical iliolumbar ligament. Finally false ligaments are a term used to describe a number of structures in the LS that bear the name 'ligament' but for various reasons this is not a legitimate term. These structures include the intertransverse Ligaments, the transforaminal ligaments and the mamillo-accessory ligament (Bogduk, 2005).

2.2.1. Blood Supply of Lumbar Vertebrae

The intercostal and lumbar arteries known as segmental arteries that arise from the aorta provide the majority of the blood supply to the LS and spinal cord. The segmental artery divides into lateral and dorsal branches that supply the vertebrae, spinal cord, and cauda equine (Ebraheim et al., 2004; "Normal Anatomy Overview," 2017).

The subcostal and lumbar arteries supply the majority of the LuV. These major arteries branch into periosteal and equatorial arteries, which divide further into anterior and posterior canal branches. Branches of anterior vertebral canal send nutrient arteries through VB supplying the red marrow (Waxenbaum et al., 2020).

There are four lumbar arteries emerge in pairs from the posterior wall of the abdominal aorta in the LR, with the orifices for right and left sided branches in every level divided by just a few millimeters (Crock and Yoshizawa, 2013). Till they reach the IVF, these arteries migrate laterally to either side, staying near to the middle of front lateral side of each VB.

Two groups of branches emerge from each lumbar artery; the first one is short centrum branches that go through vascular foramina at regular intervals, adjacent to the lumbar artery. The second is the long ascending and descending branches that form a thick network in anterior and lateral margins of the VBs. The terminal branches penetrate the bone close to each vertebral endplate, even as other branches form fine vertical plexus on the surfaces of anterior longitudinal ligament and anulus fibrosus(Gilchrist, 2008) .

The fifth lumbar arteries branch off the median sacral artery at the L5 level, but furthermore, they are identical to other lumbar arteries (Bogduk, 2005). The middle sacral artery and branches of the iliolumbar arteries supply the L5 VB. The Middle sacral artery, like the lumbar arteries, arises from the abdominal aorta's posterior wall(Gilchrist, 2008).

As per (Gilchrist, 2008) and (Crock, 2013) outside IVF in the same level, each lumbar artery divides into a series of major branches. The patterns of fine arteries in these regions are extremely complex; furthermore, the IVF serve as openings for arteries and veins of the spinal canal and their contents. These include the anterior or abdominal wall branches that lie medial to the psoas muscles anterior to the lumbar plexus. They send out neural branches to the dorsal rami with per lumbar nerve in a straight line, intermediate branch of the lumbar artery divides into three subdivisions: the anterior spinal branches, nervous system branches, and posterior spinal branches. Finally, the posterior or body wall branches migrate dorsally away from the IVF, lying on the lamina's outer surface and crossing the pars interarticularis.

As per (Keith, 2014) and (Snell, 2011) Veins of the spine form dens plexuses communicate through the IVF alongside the VC, both of these plexuses are located inner and outer vertebral canal, they are known as internal vertebral venous plexuses or epidural venous plexuses, and external vertebral venous plexuses, the external vertebral venous plexus exist exterior surroundings the VC. The internal vertebral venous plexus lies inside the vertebral canal but its outer the spinal cord's dura mater.

(Gatterman, 2012) noted that the Venous plexus aligned with both posterior and anterior components of the VC. It is also can be split up into an anterior plexus that surrounds the VBs and a posterior plexus that related to the neural arches.

(Bogduk, 2005) stated that the ascending lumbar veins (ALVs) and several vertebral venous plexuses drain and surround the LS. On their path through the VBs, a lumbar vein (LV) follows lumbar arteries and drain into the inferior vena cava. The ALV, a long channel that passes in front of the bases of the TPs, communicates with LVs on either side adverse the IVF.

(Chiva and Magrina, 2018) added that the ALVs initiate from common iliac veins and connect the iliac, iliolumbar, and LVs. They rise anterior of the LuV, posterior to the psoas muscle. Almost they connect the subcostal veins, then turn medially to form the azygos and hemiazygos veins on the right and left, respectively.

2.2.2. Lumbar Spine Innervations

Several studies have looked at the innervations of the LS. The LS is connected to a number of nerves, the most important of which are the lumbar spinal nerves. The spinal nerve roots lie in the vertebral canal and they bound with to the spinal cord through the IVF (Bogduk, 2005).

As per (Cohen et al., 1990; Hasegawa et al., 1996; Rauschnig, 1987) the LR contains 11 pairs of SNs, including 5 lumbar, 5 sacral and, 1 coccygeal. In the lumbosacral area, the SNs appear under the corresponding vertebrae. The SNs emerging from the spinal canal are close to the lower-middle border of the upper pedicle and located at the top of the IVF of the LS. The IVF contains the majority of the lumbar spinal nerve ganglia, which are the enlargement of the dorsal roots. Each SN consists of ventral and dorsal roots that leave and go into the spinal cord sequentially. The ventral roots have axons of motor neurons from the anterior gray horn of the spinal cord; as well the dorsal roots have sensory axons that arise from the sensory cell bodies contained in ganglia.

Most notably, Bogduk, 2005) added Above each vertebral foramen, a pair of SN roots leave a dural sac. They penetrate the dural sac inferolaterally, forming a dural sleeve

(extension of dura mater and arachnoid mater), and the nerve roots are encased in this sleeve until they reach the IVF and the spinal nerve, where the dura mater integrates to become, the epineurium of the SN. Each nerve root's pia mater, as well as an extension of the subarachnoid space, reaches as far as the SN. As a result, before the SN, the nerve roots are enveloped in pia mater and suffused in Cerebrospinal Fluid.

2.3. Muscles of Lumbar Spine

Bone, cartilage, ligament, tendon, and muscle comprise the LS. The spine's shape and function are determined by these anatomical elements. The LS lordotic appearance is made possible by this construction. The muscles are the spine's adaptive system for mobility and stabilization. They make up available range of motion, allowing for the execution of many types of spinal movements. By absorbing axial forces, these muscles act as a backup to support the underlying lumbar spinal components (Gilchrist et al., 2003).

As indicated by (Kanga, 2013), spinal muscles are classified into 3 groups, according to their covering area and the relations with the LS, the first group is the muscles which cover the anterolateral aspects of the LS (PM muscle), the second group is the muscles that attach and cover the transverse processes (Intertransversarii laterals and quadratus lumborum), third group is a lumbar back muscles, that situated behind and covering the posterior elements of the LS.

Furthermore, there is another classification for the LS muscles it has been indicated by (Bogduk, 2005) respectively the lumbar muscles, mostly divided into flexor and extensor. Flexor muscles involve PM, intertransversarii lateralis, quadratus lumborum, and intertransversarii mediales, while extensor muscles of LS involves interspinales, multifidus, longissimus lumborum, and iliocostalis lumborum (IL).

In this study, and for fits into the research topic, the PM muscle will be highlighted as a flexor, and an example of muscles group that covering the anterolateral aspect of the LS, on the other hand, interspinalis, multifidus, longissimus lumborum, and IL muscles will be illustrated as a extensor posterior component group of the LS (Figure 2.4).

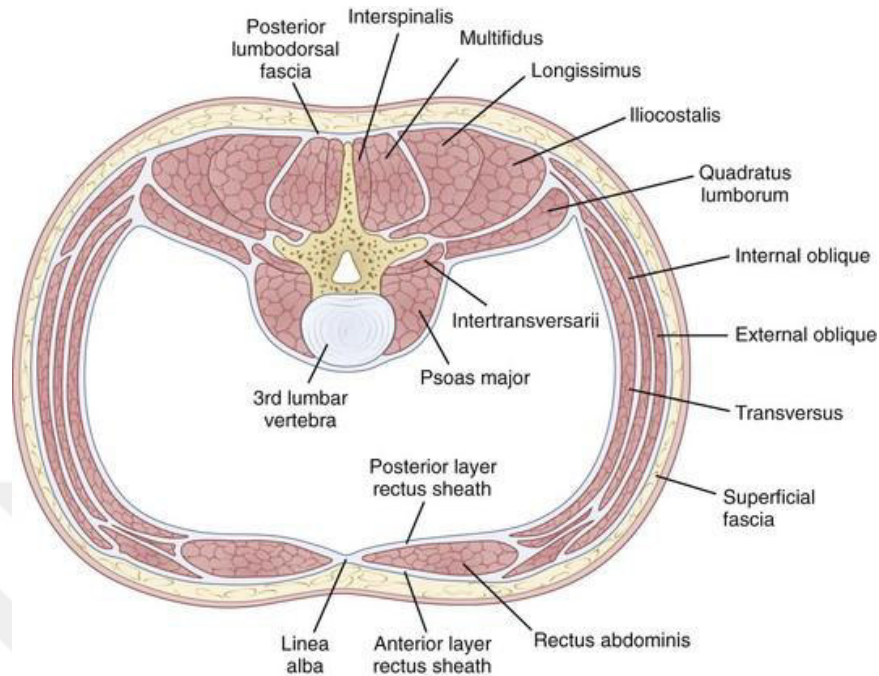


Figure 2. 4. A cross section in L3 level reveals the intrinsic spinal musculature (Finneson B: Low Back Pain, 2nd ed. Philadelphia, JB Lippincott, 1977)

2.3.1. Psoas Major and Psoas Minor Muscles

Psoas is a Greek term that means "loin muscle"(Keith, 2014) The PM is a long muscle that originates from the lumbar spine's anterolateral aspect and descends over the pelvis brim before inserting into the femur's lesser trochanter. It is a thigh muscle that performs hip flexion as its primary function (Bogduk, 2005).

As per (Gilchrist et al., 2003; Kanga, 2013) The PM attaches to the LS in various yet systemic ways. The lateral aspect of the T12 to L5 vertebral structures is the origin of PM as well as the IDs between them; it is connected to the medial three-quarters of the anterior surface of the TP, till the ID, and the borders of the VBs adjacent to the disc at each segmental stage from T12- to L5. Most notably there is an extra fascicle that emerges from the L5 VB. in this way (Rickenbacher et al., 2013) reported, Rarely accessory origins may be notice for a PM, from the twelfth rib head, from the iliolumbar ligament (ILL), the ventral sacroiliac ligament, and sometimes from the diaphragm.

The PM together with the iliacus which derives from the ilium, shape iliopsoas that passes inferolaterally, goes through the inguinal ligament to reach the insertion point, at the lesser trochanter of the femur (Drake et al., 2019; Keith, 2014).

As indicated by (Wineski, 2018) The PM is surrounded by a fibrous sheath originating from the lumbar fascia. The medial arcuate ligament is formed by thickening the sheath above. (Bogduk, 2005) added that The deepest and lowest muscle fibers bundle formed by the fibers of muscles belonging to the L4-L5 ID, the L5 VB, and the L5 TP. At higher levels these fibers are methodically overlapped between fibers from the disk, vertebral borders, and TP consecutively, therefore, the PM in cross-section is coated peripherally, by higher levels fibers forming the muscle external surface, and those from lower levels hidden successionaly, deeper inside its substance.

(Garfin et al., 2018) pointed that, in cross-section, the PM is the largest muscle at the lower levels of the LS. According to biomechanical research, PM has the capacity to flex the LS laterally, also produce compressive forces that improve stability, and generate strong anterior shear forces from L5 to S1. (Drake et al., 2019) added that, while the trunk is stabilized, PM flexes the thigh at the hip joint, and when the body is supine, it flexes the trunk against gravity.

The arterial supply of PM is from Lumbar and iliolumbar arteries, while the innervations are from lumbar plexus fibers L1- L3 directly, others from the femoral nerve (Rickenbacher et al., 2013).

As per (Drake et al., 2019; Wineski, 2018) and (Gilchrist et al., 2003) The psoas minor muscle, Associated with the PM, is a small, slender inconstant muscle, has little significance. It's Originates from the lateral aspect of the T12 - L1 and their IDs, inserting distally at the pelvic brim pectineal lines, iliopectineal eminence via the iliopectineal arch ligament. Like the PM, psoas minor is considered as a weak flexor of the LS, flexes thigh at hip joint, moreover aids in stabilizing this joint, it is located on the anterior surface of the PM and consists mainly of a long tendon. This muscle is sometimes absent, in any case when present (about 60% of individuals); it may be presented only unilaterally. Psoas minor innervated by the L1 anterior ramous.

2.3.2. Interspinales Muscle

Interspinales are segmental muscles that extend between the SPs it's found in the lumbar and cervical spine regions on a regular basis. They are usually present only at the

upper and lower ends of the thoracic spine. Vestiges on the sacrum are possible. In every segment from the first lumbar SP to the first sacral SP, the interspinales lumborum are present. The muscles are joined together by the interspinous ligament and are separated by it. Each has a muscular attachment to the upper half of one SP's lateral surface and is attached by a short tendon to the lower margin and a thin strip on the lateral surface of the next highest SP (Rickenbacher et al., 2013).

As indicated by (Kanga, 2013), In the LS, there are four pairs. While being positioned to trigger posterior and sagittal rotation of the vertebra, the interspinales are very weak and will not add significantly to the force used to shift a vertebra, nonetheless, (Drake et al., 2019) explained These postural muscles reinforce adjacent vertebrae through VC movements, allowing the large muscle groups to work more effectively. The nerve supply by the medial branch of the dorsal ramus of the SN supplies the interspinales, and getting the arterial supply by the vertebral arteries (Rickenbacher et al., 2013).

2.3.3. Multifidus

The largest, deep, and most medial of the erector spinae muscles (ERS), lies the multifidus. Short and long fibers make up this muscle. The short fibers stick proximally to the inferior border of each LuV's dorsal lamina. Each muscle band consists of one or several series of bundles, clustered with each other, these bundles originate from the laminae and SP of LuV, to form singular attachments distally (Bogduk, 2005; Gilchrist et al., 2003).

(Garfin et al., 2018; Rickenbacher et al., 2013) described, the multifidus is segmented into 3-6 muscle bands. Each of these bands formed by several fascicles emerges from the tip of the SP and the lateral surface of the vertebral lamina. Each group's bundles extend distally to form separate attachments to the mamillary processes (MP), the iliac crest, and the sacrum. The multifidus' shortest bundles are the 'laminar fibers,' which emerge from the distal end of each vertebral lamina's dorsal surface and insert into the vertebra's MP (Kanga, 2013).

In this manner (Bogduk, 2005) pointed out Even as several multifidus bundles attach to the MPs, some of the deeper bundles fibers attach to the facet joints capsules

that adjacent to the MPs. This binding enables the multifidus to prevent the joint capsule from being entangled within the joint through the multifidus' movements.

(Garfin et al., 2018; Rickenbacher et al., 2013) stated that, the multifidus arising from the fourth sacral vertebrae all the way up to the fourth or fifth cervical vertebrae. It is located lateral to the interspinales and coats the transversospinal system's short muscles as well as the uncovered portions of the vertebral arches and SPs between them. The semispinalis cover it, as well as the belly and the large aponeurosis of the longissimus in the lumbar and sacral regions.

(Garfin et al., 2018) also, add the lumbar multifidus has a rather complicated anatomy. It has a broad physiologic cross-sectional area, but their fibers are short, unlike the other paraspinal muscles (PSM) which have specified origin and insertions. This one-of-a-kind architectural anatomy is intended to generate massive forces over short distances. Moreover, the length of the multifidus sarcomere is located on the ascending part of the length-tension curve.

Most notably, (Bogduk, 2005) mentioned that there is a secondary effect of multifidus on the lumbar lordosis (LL) by increasing the compressive and bendable pressures on every vertebra and IDs that interposing between its attachments. Because the line of motion of every long multifidus bundle lies posterior to the LS's lordotic curve, so the bundles will behave like bowstrings on those parts of the curve which lie between the bundle's attachments. The bowstring impact will appear to amplify the LL, resulting in posterior ID compression, anterior disk tension and longitudinal ligament strain. The medial branches of the dorsal rami of SNs C3-L5, and S1 occasionally, innervate the multifidus (Rickenbacher et al., 2013).

2.3.4. Lumbar Erector Spinae Muscles

Lateral to the multifidus, the ERS is presented; it is bounding the shape of the lumbar back muscles in the LR. The longissimus thoracis (LT) and the iliocostalis lumborum (IL) are the two muscles that make up this muscle group. Moreover, each of these muscles is made up of two parts: a lumbar part made up of bundles originating from the LuV, and a thoracic part made up of bundles arising from the thoracic vertebrae or ribs (Bogduk, 1980; Macintosh and Bogduk, 1987).

These four parts respectively are known as the LT pars thoracis, LT pars lumborum, IL pars thoracis, and IL, pars lumborum (Macintosh and Bogduk, 1987).

(Bogduk, 1980) also stated the entire LS and a major component of the thoracic region are covered with these muscles, as well these muscles group forms a common muscle mass in the LS and their divisions are separated by lumbar intermuscular aponeurosis. The lumbar intermuscular aponeurosis, it's an anteroposterior prolongation of the erector spine aponeurosis. It looks like a flat sheet of collagen fibers that extend inferiorly for 6–8 cm from the medial margin of the posterior superior iliac spine. The posterior tendons of the anterior four bundles of the lumbar part of the LT are most reasonable for its formation (Kanga, 2013).

The trunk's main extensor is the ERS. It is also important for regulating the flexion of the trunk. When standing on one knee, the lower portion of the ERS on the non-weight-bearing limb works hard to keep the pelvis from falling. The primary muscle mass is located in the LR and is in charge of preserving the secondary lumbar lordotic curvature when sitting and standing (Palastanga and Soames, 2011).

2.3.4.1. Longissimus Thoracis

In the middle of VC, the LT is considered the longest and thickest of the ERS group, due to their superior attachment, the LT fascicles can be split up into three sections: **Longissimus capitis**, **Longissimus cervicis** and **Longissimus thoracis**, that extends in different areas of TPs alongside the VC (Drake et al., 2019) .

As per (Keith, 2014) The most distal and visible part of the ERS group is the LT. Hence the LT is carving up into two portions: lumbar and thoracic. According to (Bogduk, 2005), the lumbar section of the LT is an isolated fourth portion of the longissimus muscle, known as the longissimus lumborum (pars lumborum), anyway, it is more often recognized as a part of the LT. (Rickenbacher et al., 2013) added there is deep fleshy origin of the LT, with fibers terminating on the LS, while the bundles originating from the broad superficial tendon of origin spread to the ribs and thoracic vertebrae.

As indicated by (Bogduk, 2005; Macintosh and Bogduk, 1987) In the lumbar region, the LT pars lumborum consist of five bundles, all arise from the accessory process and the neighboring medial end of the posterior surface of the TP of a LuV. The insertion site of the L5 bundle is through the posterior superior iliac spine and ilium, and bundles from L1 to L4 cover it. Bundles from L1 to L4 become tendinous on their lateral surfaces.

The lumbar longissimus bundles are posteroanterior and superoinferior in direction. As a result, each bundle's action can be deduced to perpendicular and horizontal directions, the relative sizes of which vary from L1 to L5. Hence the longissimus's relative action varies at each segmental stage. Moreover overall action of the LT differs depending on whether the muscle contracts unilaterally or bilaterally.

LT is innervated by the anterior branches of the dorsal rami of the spinal nerves; L5 supplies only the lowest medial protuberance, while L4 supplies the lowest lateral protuberance (Rickenbacher et al., 2013).

2.3.4.2. Iliocostalis Lumborum

IL is the most lateral of the ERS muscles, and it connects to the costal components. The Iliocostalis is divided into three regions depending on their origin: iliocostalis cervicis, iliocostalis thoracis, and IL (Drake et al., 2019).

Due to the multiplicity of sections of the iliocostalis, specifics will be focused on the IL; hence reviewing this region is related to the topic of this research.

As per (Keith, 2014) The IL muscle is split into lumbar and thoracic parts. The lumbar portion of the IL is made up of muscle mass that emerges from the sacrum's lateral crest, the iliac crest's anterior edge, and the thoracolumbar fascia. It normally attaches to the L1-L4 vertebral TPs and the neighboring portion of the middle layer of the thoracolumbar fascia (Bustami, 1986; Drake et al., 2019).

(Bogduk, 2005) described, the muscle bundles from L4 is the deepest, and caudally it is attached directly to the iliac crest. The most medial fibers of IL contribute to the lumbar intermuscular aponeurosis but only to a minor extent. The muscle bundles from L2 covers L3 and L1 cover L2, with insertions on the iliac crest becoming more

dorsal and lateral. (Luk, Ho, and Leong, 1986) added, the ILL represents the L5 bundle of IL. This ligament is said to be totally muscular in neonates and infants. The muscle fibers are completely replaced by collagen by the third decade of life, resulting to formation the ILL.

The lateral branches of the posterior rami of the SNs T 9 L1 innervate the IL. Which emerge from between the longissimus bundles and go through each origin and slip from its ventral surface (Rickenbacher et al., 2013).

2.4. Lumbar Lordosis

There are four curvatures that present in an adult's VC, these curvatures respectively are in the following regions; cervical, thoracic, lumbar, and sacral. The thoracic and sacral curvatures termed "kyphoses" (singular as kyphosis) they are concave forwardly, whilst the term "lordoses" (singular as lordosis) is used for cervical and lumbar curvatures, they are concave backwardly (Keith, 2014). The term lordosis is likewise derived from the Greek word "lordos," which means "forward curving." The term "lordosis" was originally used as a medical term by "Galen of Pergamon" (Boos and Aebi, 2008).

From the same perspective, The wedging of lumbar VBs and IDs forms LL, which is an inward (ventral) curvature of the LS (Vaz et al., 2002; Vialle et al., 2005). As indicated by (Been, Barash, Pessah, and Peleg, 2010) and (Cheng et al., 1998) The geometry of the VBs and the form of the IDs both have an impact on LL, with each accounting for almost half of the variation in lumbar lordotic angles (LLA) found in adults. The LLA is increased when the anterior part of the VBs and IDs (Dorsal wedging) is longer than the posterior part, but the LLA is reduced when the anterior part is shorter than the posterior part (more ventral wedging). (Been et al., 2010) added All the five LuV contribute to the formation of LL, but it's worth noting that nearly 40% of total lordosis is attributed to the L5. The L1 barely makes about 5% of the total.

As indicated by(Roussouly and Nnadi, 2010) and (Schwab et al., 2010) The LLA and pelvic and thoracic orientation in space have a close correlation. A more horizontally inclined sacrum (higher sacral slope, more vertical sacral endplate),

increased pelvic incidence, and increased pelvic tilt are all associated with greater LLAs. Also in the same context (Schwab et al., 2010) agreed with (Ostrowska et al., 2003) that more lordosis is associated with higher thoracic kyphosis, although there have also been occurrences of increased lordosis associated with lower thoracic kyphosis. Small LLAs are frequently associated with a more vertical sacrum, a small pelvic tilt, pelvic incidence, and less thoracic kyphosis; however, examples of reduced LL with higher thoracic kyphosis have been documented as well.

2.4.1. Male and Female Variations in Spinal Curvatures and Lumbar Lordosis

Many researchers have questioned whether male and female spinal curvatures are different. According to (Middleditch and Oliver, 2005) Until middle age, males and females have the same LL. (Vialle et al., 2005) discovered a difference in LL between males and females, as assessed by the Cobb angle, Likewise, curvature angles for the area of the spine between T12-L1 and S2 were calculated using a 3-D electromechanical digitizer. (Norton et al., 2004) noted that the LLA was 13.2° larger for females than for males, computed by depending on the proportion of lordosis depth and length. (Hay et al., 2015; Hegazy and Hegazy, 2014) found three features in the form of the female lumbar curve: larger curvature (the curve is sharper), more dorsally in the high segment (backward inclined), with a more caudal spike (inferiorly). Hence the greater lordosis found in females according to (Hegazy and Hegazy, 2014; Janssen et al., 2009; Norton et al., 2004; Vialle et al., 2005). Moreover During pregnancy, there is an increase in LL, especially in the latter several months (Masharawi et al., 2010; Whitcome et al., 2007). (Letafatkar et al., 2010) added, the degree of LL in women has been demonstrated to be strongly related to the number of pregnancies.

There is more than one reason for this occurrence, increased abdominal weight; a compensating rearward lean is used to enhance balance (Colliton, 1996). (Calguneri et al., 1982; Marnach et al., 2003) added, increased lordosis is seen in women with a large number of pregnancies, and a considerable increase in joint laxity occurs during the last trimester of pregnancy, possibly due to muscular imbalance induced by overstretched weak abdominal muscles and strong back muscles.

2.4.2. Evaluation of Lumbar Lordosis

The Assessment of LL is useful for planning orthopedic surgical treatments, monitoring the course and treatment of spine abnormalities, and defining normal and abnormal reference values (Stokes, 1994).

Various methods have been used to measure the curvature of the LL, despite the fact that they all entail measuring one or more of the lumbar VBs' angles. The angle created by the planes through the apex surface of L1 and the apex surface of the sacrum has been employed. This is referred to as the 'L1-S1 lordosis angle' (LLA) (Epstein et al., 1962; Farfan et al., 1972).

There are other methods of measurement, which have been relied upon such as measuring the angles between the apex of L2 and the apex of the sacrum, and between the apex of L2 and the base of L5, which they dubbed the "lumbosacral lordotic angle" and the "lumbolumbar lordotic angle", respectively (Fernand and Fox, 1985), also the angle between the apex of L3 and the sacrum (Gilad and Nissan, 1985), or the angle produced by planes that cut the L1-L2 disk and the L5-S1 disk (Hansson et al., 1985; Hellems and Keats, 1971).

The angle created by the five lumbar segments (L1–L5) is the most frequent way to assess LL. The top line is drawn at the superior endplate of L1 and the lower line is drawn at the superior endplate of the sacrum when using Cobb's method (Been and Kalichman, 2014). As a result, the measurements obtained in these numerous research varied slightly. Despite this, they all have significant differences.

2.4.3. Measuring Techniques

To assess LL, a variety of techniques are utilized. These techniques or methods are separated into two categories: clinical and Radiologic assessment. The degree of lordosis is assessed directly on the individual's body during a clinical examination. Each technique of assessment has its own set of benefits and drawbacks, but the most significant issue is that it is impossible to compare measurements taken using different approaches (Been and Kalichman, 2014). Various 3D posture analysis technologies and surface topography technologies are used in clinical settings to evaluate LLA (Pazos et

al., 2007; Zabjek et al., 2005). (Been and Kalichman, 2014) added The fundamental benefit of these measurements is that they do not emit radiation, allowing for more frequent assessment of spinal curves and better monitoring of LLA changes. Surface anatomy is used in clinical procedures to assess the LLA, although only minor correlations with radiologic data have been identified. Because of differences in PSM development, subcutaneous fat thickness, and anatomic variances in SP length and direction, comparisons across individuals are difficult.

From that, it was concluded that using clinical techniques to assess LLA might be a valuable tool for tracking patients' improvement. But when absolute LA parameters need to be determined, clinical procedures in their current form are inadequate for research or clinical assessment.

Many radiologic methods like Two-dimensional radiography, three-dimensional (3D) computed tomography (CT), and magnetic resonance imaging (MRI) have all been used to assess LL. For example, (Ferguson, 1930) proposed one of the first approaches. The angle formed by two straight lines connecting the centers of the end vertebrae and the center of the apical vertebra is used to assess the deformity.

The Cobb method or modified Cobb method (Figure 2.5), which is performed by using vertebral endplate lines to estimate angles on sagittal radiographs, is relatively simple to use and has been demonstrated to be quite accurate. The Cobb method's most significant flaw is that two spinal curvatures of different magnitudes might potentially result in the same Cobb angle; as a result, additional methods have been devised to address this issue. The LLA is measured using several anatomic markers on the VBs (Been and Kalichman, 2014; Vrtovec et al., 2009). Likewise, The anterior and posterior tangent methods (Figure 2.5) identify the LLA by examining the anterior or posterior VB wall (Been and Kalichman, 2014).

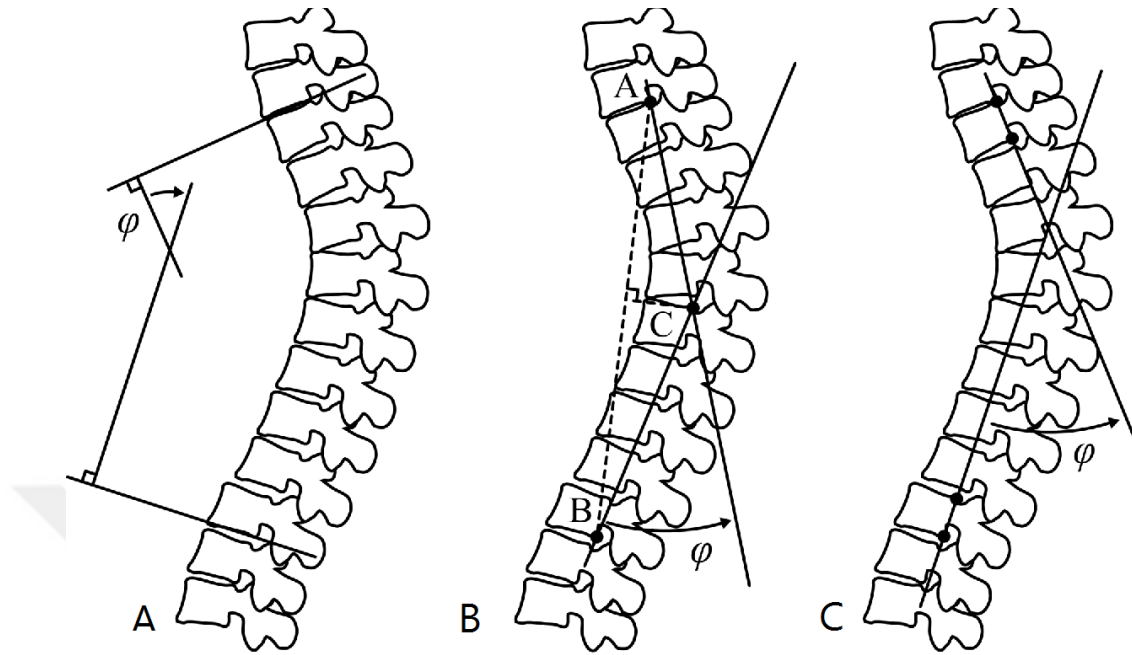


Figure 2. 5. Methods for evaluating spinal curvature examples. (A) Modified Cobb method, (B) Tangents method, (C) Posterior tangents modified from (Hay et al., 2015)

Also, a centroid method is quite similar to the posterior tangent method; however, this method is suggested since it is determined by the slope of the spine curve (Schuler et al., 2004). Notably, some approaches, such as the best-fit ellipse, create a LS geometrical model in the form of a circle. All of these approaches were shown to be accurate in determining LL.

2.4.4. Measurement of Lumbar Lordosis Using the PAL Method

A novel and straightforward methodology that may yield more representative findings than those provided in the previous methods, by using direct lateral roentgenograms to assess lumbar lordosis. Discovered by (Kuru et al., 2008), he described This approach gives a measurable criterion for determining flat back syndrome or an increase in LL by measuring the degree of lumbar spinal curvature utilizing the upper and lower borders of certain vertebrae. In this study, the planimetric method was utilized as the gold standard. The PAL was also estimated using the point-counting approach. Hence, pal technique provides simple way to evaluate LL on regular roentgenograms without needing to alter the process. Because point counting can be

done in a few minutes per subject, this approach is quick and affordable, but it also has the potential to be alternate criteria for diagnosing and assessing LL owing to the benefits outlined above (Kuru et al., 2008).

2.4.5. The Muscles and Its Relations with Lumbar Lordosis

While in a static, upright position, the abdominal and back musculatures are thought to influence pelvic inclination and LL (Jull, 1987; Walker et al., 1987). It's conceivable that the balance between flexors and extensors muscles of the trunk, rather than the strength of the individual muscle group, impacted LL in the static posture (Been and Kalichman, 2014). (Kim et al., 2005) investigated the link between trunk muscular strength (PSM, PM and multifidus) and LL, the lordotic angle was determined to be related to the ratio of extensor torque to flexor torque.

Furthermore, a high LL was related with strong spinal extensors and weak spinal flexors and vice versa. It was found that the trunk muscular strength imbalance can have a substantial impact on the lordotic curvature of the LS and it may result in LBP (Been and Kalichman, 2014). As per (Hamilton, 1982; Woodburne, 1957), the PM muscle has an effects lordotic curvature by flexing the LS and therefore decreasing the LLA. (Bogduk et al., 1992) has a different opinion about the PM by increasing the LLA, while (Nachemson, 1968) and (Penning, 2000) argue that the PM function is to keep the lordotic curvature of LS in an erect position by adjusting its contraction to the instantaneous degree of lordosis imposed by external forces like weight-bearing. (Copaver et al., 2012) stated that there is relation between the morphology of PM and the spinal curve, the muscle morphology determines its surface and the fact that LL has an impact on muscle architecture. But he found there are no correlations between the LL and the size of the cross sectional area of the PM muscle.

Extensor muscles (PSM) are also important for maintaining movement stability (Aspden, 1989; Hammerberg and Wood, 2003). According to (Meakin and Aspden, 2012) a spine with significant lordosis necessitates a higher load in the standing position than one with minor lordosis. Due to the fact that muscular force is related to muscle volume (Akagi et al., 2009; Blazeovich et al., 2009), greater LL necessitates a bigger extensor musculature to provide adequate loads and sagittal stability (Folland and

Williams, 2007). The degree of LL was shown to be related to extensor muscles volume and strength (Meakin et al., 2013; Sinaki et al., 1996). While LBP was associated with reduced extensor muscles volume (Danneels et al., 2000).

It's unclear if the relation between LL and extensor muscle size is causal or correlative, nevertheless, (Been et al., 2010) and (Meakin et al., 2009) found a link between spine form and vertebral morphology and posterior element orientation. Differences in these parameters impact the forces necessary to maintain the spine, which may show as variations in extensor muscles volume. Variations in muscles size, on the other hand, may be the driving factor in lumbar curvature. Several investigations have found a decrease in LL, which is thought to be accompanied by age-related muscle mass loss (Hammerberg and Wood, 2003; Takeda et al., 2009).

3. MATERIAL AND METHODS

3.1. Ethics Committee Decision

In this research, Ondokuz Mayıs University Medical Research Ethics Committee was applied and the medical research ethics committee approval was obtained with the official document numbered 14.09.2018, B.30.2.ODM.0.20.08 / 1873 (APPENDIX 1). As a result of the ethics committee approval of 31 women and 31 men aged 19-84 years were (mean age 45.5years) used from the radiological imaging center of the Radiology Department of Ondokuz Mayıs University and kept for our image bank.

3.2. Image Preparation

The samples for this study were from Ondokuz Mays University Hospital's radiology department. CT scan images of the spine, in particular, were retrieved from the Radiological Department's archive system with ethical approval. A total of 70 pictures were gathered, however eight were discarded due to low resolution and hence could not be processed by ImageJ. As a result, the final sample size was 62 (n = 62), including 31 female and 31 male aged 19 to 84 years (mean 45.5). The pictures stored on a computer disk (CD) were initially accessed with OsiriX, a DICOM medical image viewer (Figure 3.1).

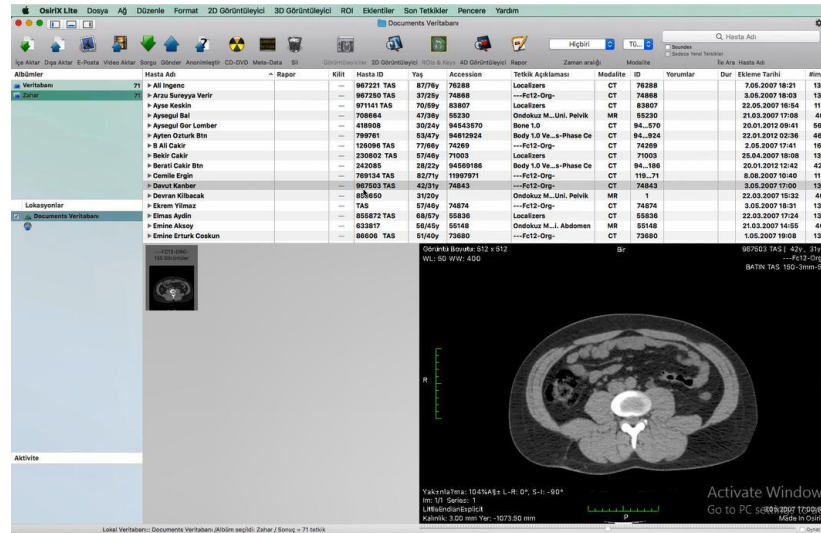


Figure 3. 1. 3D Medical Images by OsiriX Software

For explaining, this method was used for processing the image by picking one image from an already prepared file, copying it into database folder of the OsiriX, and then selecting 3DMPR from the 3D Viewer tab. In the sagittal, coronal, and transverse planes, the images in the files were shown in a single window using the 3D MPR tool. The CT image was then transferred to the orthogonal plan. The midline was moved up and down substantially to find the umbilicus; the sternum and spinal column were in the same plane, known as the sagittal plane. One image had been prepared and was ready for usage (Figure 3.2).

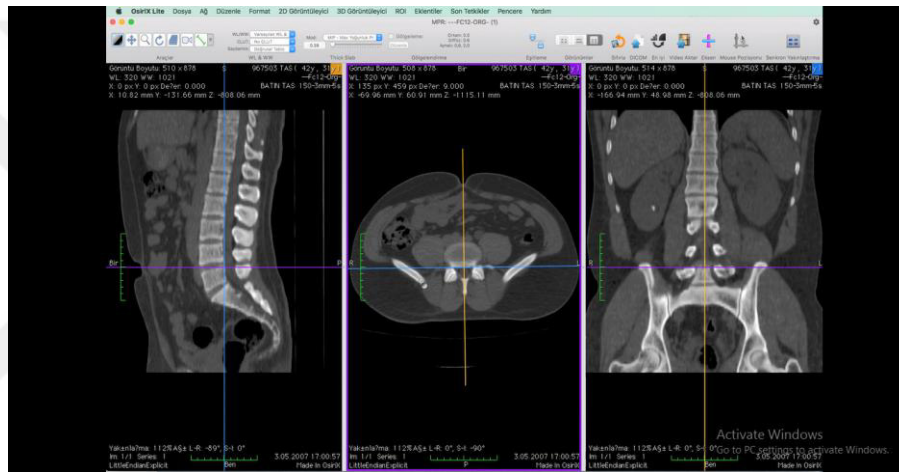


Figure 3. 2. OsiriX Program Calibrated Images

The OsiriX software was used to export the axial sections of the images brought to the orthogonal plane corresponding to the region between the upper edge of the first lumbar vertebra and the lower edge of the fifth lumbar vertebra (Figure 3.3).

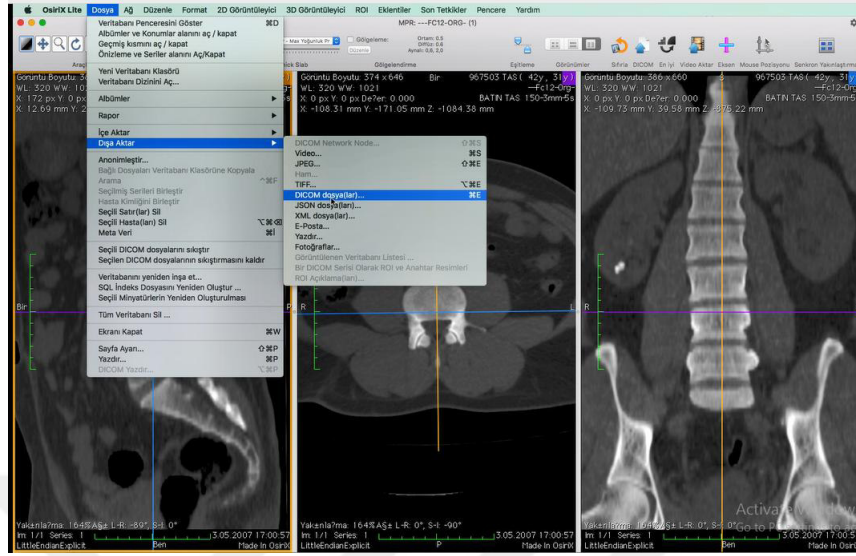


Figure 3. 3. Exported Images by OsiriX Software

To calculate PAL, a line was drawn from the upper corner of L1 to the lower corner of L5 in the back of the spine. The length of those landmarks was measured by the software. Then, the semilunar area in front of this straight line and behind of spine was delineated in the software and the sectional area of this region was measured in the software. The measured length and sectional area were used to estimate the PAL using the following formula:

$$PAL = \frac{\alpha}{l^2} \times 100$$

Where, α is the semilunar sectional area, l is the length of the line between the posterior ends of L1-L5 (Figure 3.4).

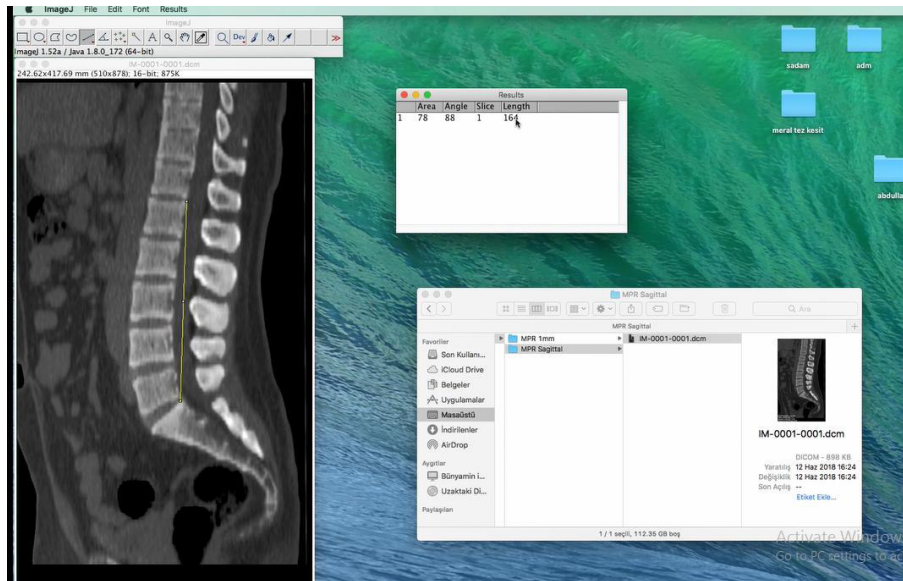


Figure 3. 4. ImageJ Software's First Calculation in Sagittal View

The second computation is carried out with the assistance of polygons (feature in image J) The pointer was moved over the bodies (in the middle of the VBs) after drawing a line between the first and fifth lumbar VBs (Figure 3.5). The results of these two measurements were copied and pasted into a Microsoft Excel spreadsheet.

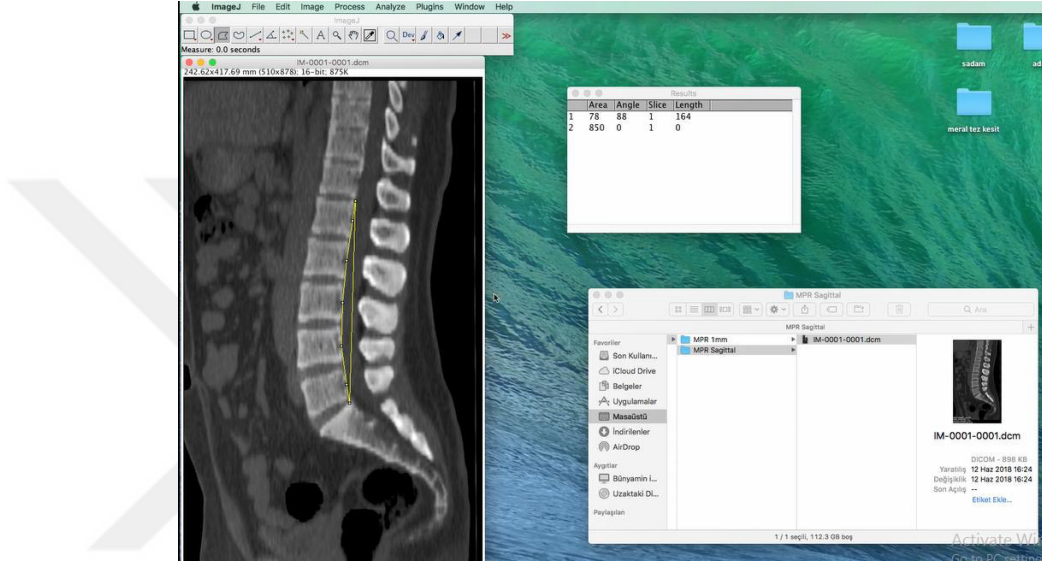
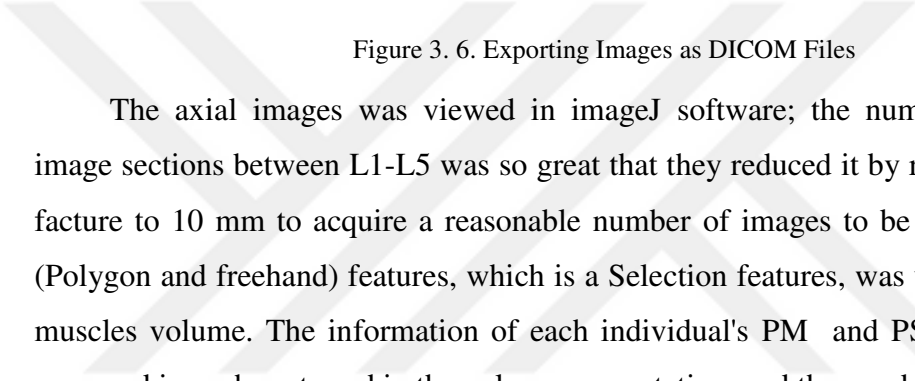


Figure 3. 5. The Second Calculation Process in Sagittal View in the imageJ Software

The same image series were processed for the steological volume estimation of the pre/postvertebral muscles. The images in the axial plane was exported as a new file named (MPR 1mm),and fixed to the orthogonal plan, the section thickness was already set to 1mm, and there was also an option to determine the thickness of the area (FROM – TARGET), FROM L1 to L5, which is the TARGET, within folder (MPR 1mm). After that, the images were exported and stored as DICOM files (Figure 3.6).



$$V = t \times \sum a,$$

Where "v" is the volume of midbrain, pons or medulla oblongata, "t" is the section thickness and " $\sum a$ " is the total sectional area of the consecutive sections millimeter square (m^2) of the midbrain, pons or medulla oblongata

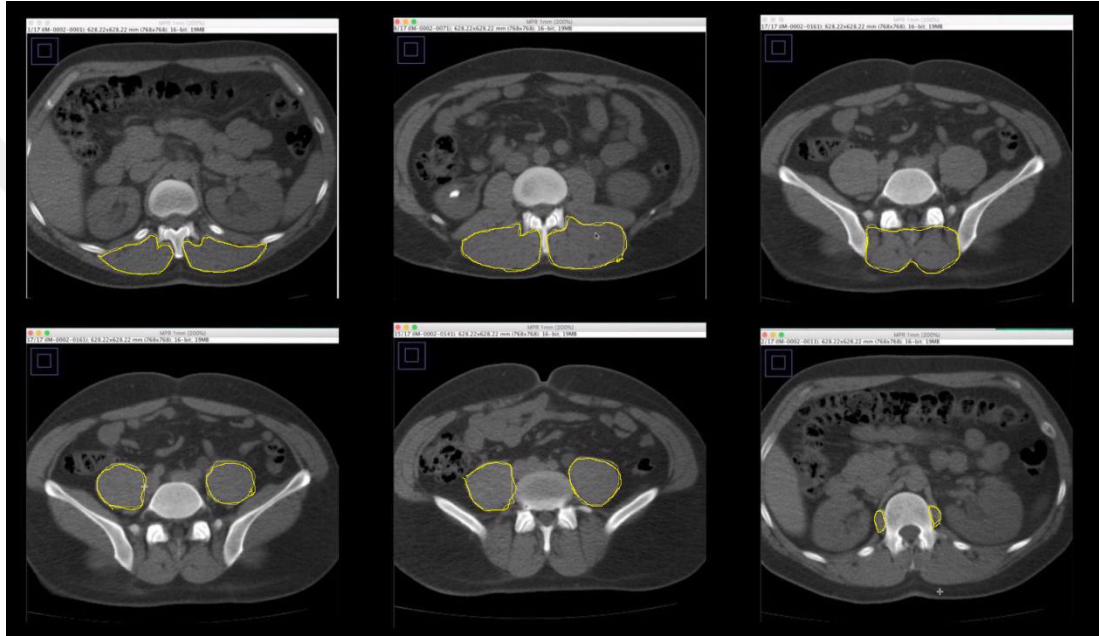


Figure 3. 7. ImageJ Software Measurement Stages of Anterior and Posterior Muscle Volumes

Every patient went through the same procedure. The results were then entered into an excel spreadsheet (Figure 3.8)

Name Surname	Sex	Age	PAL	Anterior Volume cm ³	Posterior Volume cm ³	Ant/Post Fraction %	Anterior CE	Posterior CE %
Temel Sankaya	male	41	4.15	267.0	672.1	28.4306	0.587	0.417
L		159			68	84	1	159
A		1048		2	1048	0	1	0
Section thickness		10						
Section	Post Area	Section	Ant Area	Posterior			Anterior	
1	3525		2346		3923		1	2346
2	4286	2	2349	2	4286	2	2	2349
3	4847	3	2505	3	4847	3	3	2505
4	4483	4	2552	4	4483	4	4	2552
5	4213	5	2577	5	4213	5	5	2577
6	4778	6	2345	6	4778	6	6	2345
7	4784	7	2435	7	4784	7	7	2435
8	4477	8	2167	8	4477	8	8	2167
9	4760	9	1711	9	4760	9	9	1711
10	4543	10	1609	10	4543	10	10	1609
11	3980	11	1332	11	3980	11	11	1332
12	3904	12	932	12	3904	12	12	932
13	4241	13	821	13	4241	13	13	821
14	3467	14	471	14	3467	14	14	471
15	2461	15	211	15	2461	15	15	211
16	2351	16	178	16	2351	16	16	178
17	1735	17	159	17	1735	17	17	159
18	0	18	0					
19	0	19	0					
20	0	20	0					
Total		672.12		26700				

Figure 3. 8. Patient name, sex, age, PAL, Length, Area, Anterior Volume, Posterior Volume, Ant_Post_Fruction, Anterior CE, Posterior CE, On an excel sheet, they were documented

3.3. Statistical Analysis

Data Analysis was performed using SPSS 22 (IBM SPSS Statistics 22, SPSS inc., an IBM Co., Somers, NY). A total of 62 CT scan images (n = 62) fulfilled the inclusion criteria for this study. From the 62 CT scans, 31 of them belonged to females and the rest (31) were males. Groups will be based on gender. Non-numerical variables, such as sex, must be transformed into analyzable forms before being used in SPSS data analysis. As a result, males were classified as "1" and females as "2." Data are expressed as mean±standard deviation or frequency and percent. Categorical variables (Gender) were presented as a count and percentage as shown in the (Table 3.1) below.

Table 3. 1. Distribution of qualitative Variables

Variables		N	%
Gender	Male	31	50
	Female	31	50

The age of retrospective patients (participants) ranged from 19 to 84 years, with the mean age (M) was 45.58 years, with a standard deviation (SD) of 15.99, meaning that only adult participants were recruited into this study.

4. RESULTS

It is worth noting that this study relied in obtaining its results on the anterior volume and posterior volume variables and compared them with the value of PAL for both sexes, therefore other variables that were measured in this study were excluded; hence, these excluded variables were not involved in obtaining the study results.

The Mean $\pm$ SD of the variables of age, PAL, anterior volume cm³. Posterior volume cm³, anterior CE, Ant post fraction, posterior CE, L (length) and A (Area) providing the assumptions of normal distribution were analyzed. As shown in table 4.1 below.

Table 4. 1. Distribution of quantitative variables of year, PAL, anterior muscular volume (cm³), posterior muscular volume(cm³), anterior CE, posterior CE, Anterior Posterior fraction.

Variables	Mean $\pm$ SD	Minimum	Maximum
Year	45.58 $\pm$ 15.99	19.00	84.00
PAL (%)	4.08 $\pm$ 1.86	0.11	8.89
Anterior Muscular Volume (cm ³)	230.34 $\pm$ 91.45	55.22	415.93
Posterior Muscular Volume (cm ³)	598.03 $\pm$ 154.69	187.93	1033.36
Anterior CE	0.67 $\pm$ 0.20	0.40	1.98
Antior Posterior Fraction	27.06 $\pm$ 5.57	12.26	38.89
Posterior CE	0.47 $\pm$ 0.13	0.37	1.39

The findings shown in Table 4.1. Above were also visualized using a Bar graphs. Figure 4.1; show the Bar graph of anterior, posterior volume variables, figure 4.2 and 4.3 show the Bar graph of the length (L), area (A), anterior CE and posterior CE respectively.

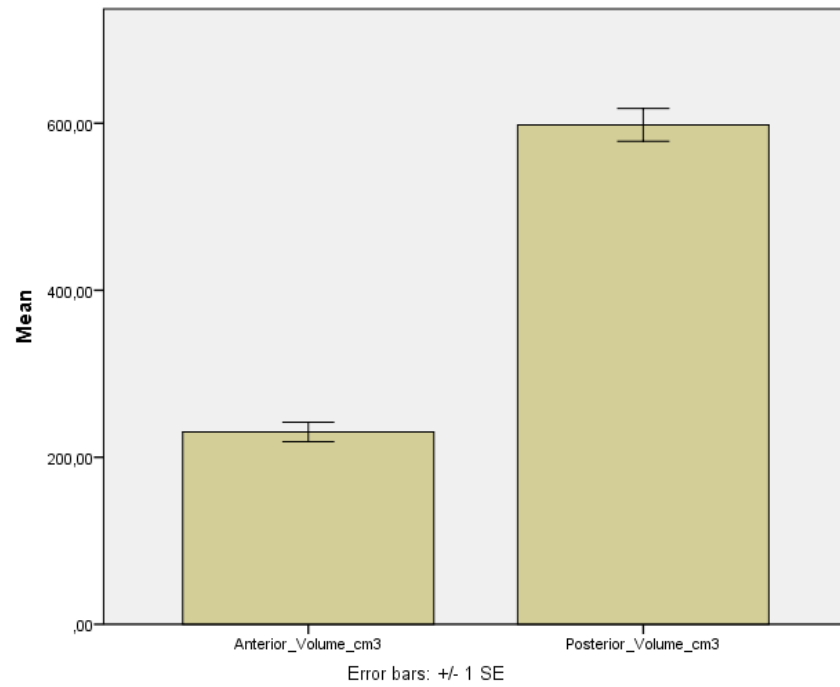


Figure 4. 1. Bar graph with +/-1 standard deviation of the volumes of the anterior and posterior muscles (cm3)

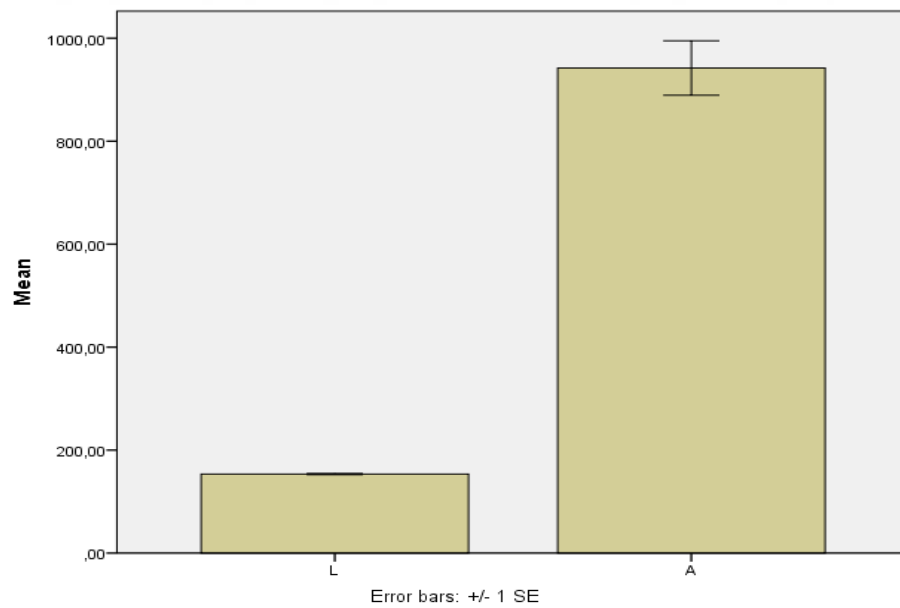


Figure 4. 2. Bar graph with +/-1 standard deviation of the Length and Area variables

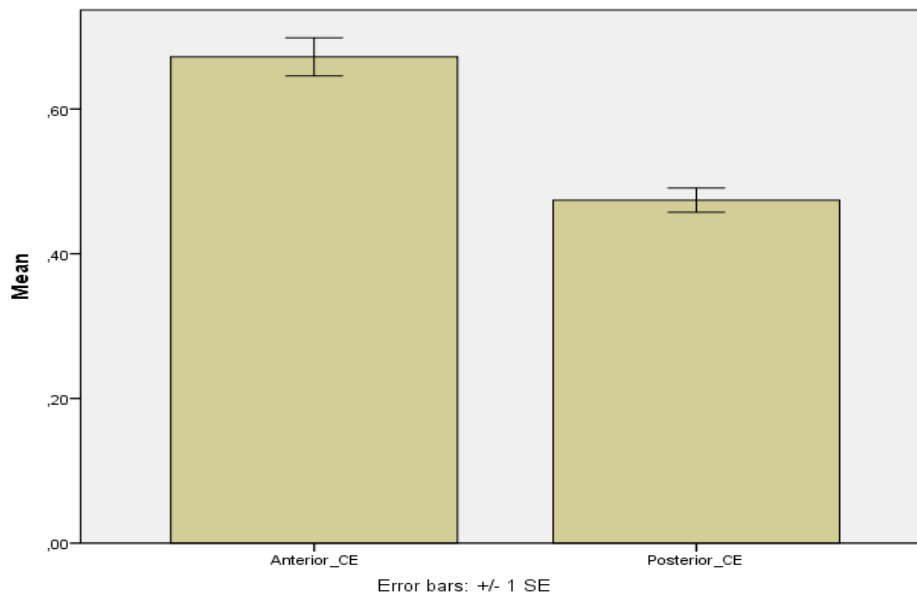


Figure 4. 3. Bar graph with +/-1 standard deviation of the anterior CE and posterior CE variables

4.1. Total Correlation Analysis

Following the confirmation of the test variables' normality, a correlational analysis was performed using Pearson's coefficient.

First of all, the correlation between the total of anterior volume (PM muscle anterior volume) and mean of PAL was counted, and it was discovered that there is no significant correlation between the two variables ($r = -0,055$; $n=62$; $p=0,669$). In this case, a significant correlation was considered at a significance of <0.05 . The mean (M) of the total anterior volume was 230.34 with a SD of 91.45.

The second Pearson's correlation was between the total of posterior volume (PSMs volume) and mean of PAL; the result indicated that there is no statistically significant correlation between the two variables ($r = 0,046$; $n=62$; $p=0,720$).

Thirdly, a Pearson's correlation was computed between anterior posterior fraction (total) with PAL ($r = -0,160$; $n=62$; $p=0,213$) indicating that there is no significant correlation between these variables (Table 4.2).

Table 4. 2. Bivariate correlation of PAL, Anterior volume, Posterior Volume, and anterior posterior fraction variables in total

	PAL Anterior muscular volume	PAL Posterior muscular volume	PAL Ant Post Fraction
r	-0,055	0,046	-0,160
p	0,669	0,720	0,213

* Correlation is statistically significant at the 0.05 level.

4.2. Disparities in Gender

It was also necessary to identify gender differences before obtaining the Pearson correlation coefficients for the various variables independent of gender. Independent sample t-test was used to compare between groups.

In this instance, the correlation between PAL and anterior volume, posterior volume, and Ant_Post_Fraction, has been established. However, because normalcy is one of the key assumptions of this test, it was necessary to ascertain the gender distribution of the data before running the Pearson correlation test. The broad distribution of variables by gender is shown in (Table 4.3).

Table 4. 3. Distribution of variables of year, PAL, anterior muscular volume (cm3), posterior muscular volume(cm3), anterior CE, posterior CE, Anterior Posterior fraction by sex. Independent samples t test was used

Variables	Sex		t	p
	Male Mean±SD	Female Mean±SD		
Year	45.83±15.33	45.32±16.87	0.12	0.900
PAL (%)	3.78±1.73	4.39±1.96	1.300	0.198
Anterior Muscular Volume (cm3)	303.18±55.64	157.50±54.26	10.43	P<0.0001
Posterior Muscular Volume (cm3)	694.93±139.36	501.13±99.14	6.30	P<0.0001
Anterior Posterior Fraction	30.52±3.54	23.59±5.08	6.23	P<0.0001
Anterior CE	0.61±0.80	0.72±0.27	2.10	0.039
Posterior CE	0.43±0.04	0.50±0.17	2.11	0.039

A box plots was also utilized to display the previously given data. A box plots was created for each variable.

(Figure 4.4), a box plot showing median, minimum and maximum with interquartile distribution of PAL and the gender variables. There are no statistically significant variations in PAL between males and females.

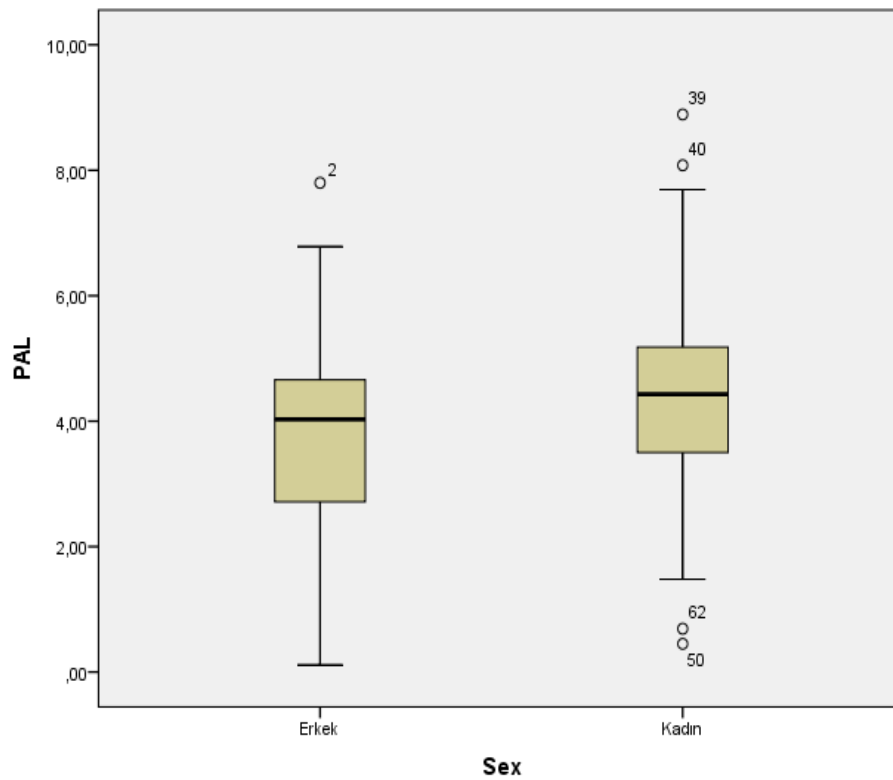


Figure 4. 4. A box plot for PAL and the gender variables

(Figure 4.5), Box plot showing descriptive values of age (median, maximum and minimum) between males and females groups. The minimum age = 19, maximum = 84 this mean only adults participate in this study.

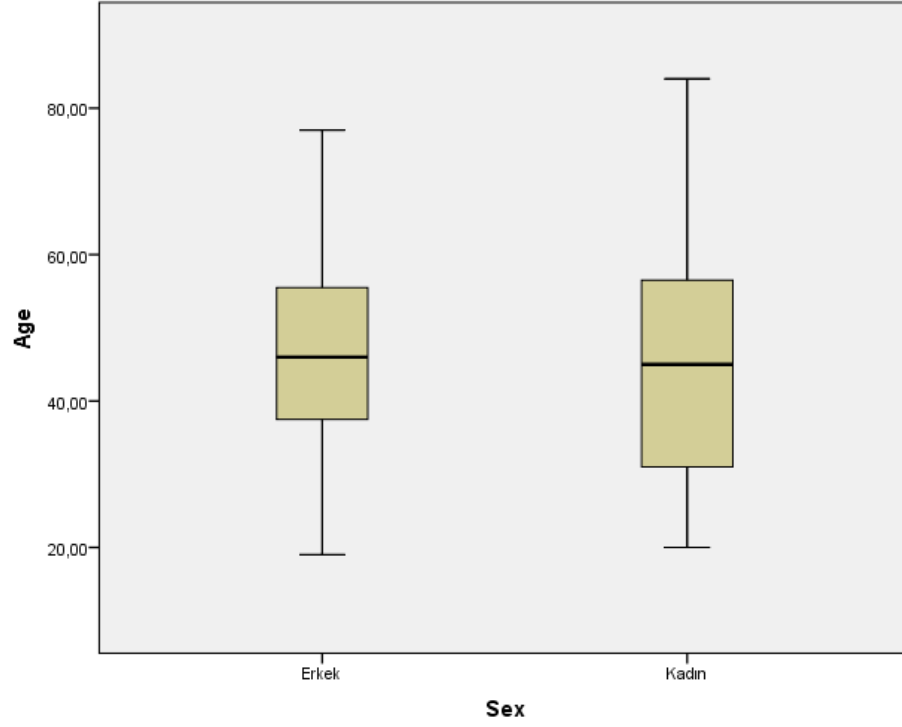


Figure 4. 5. Box plot for the age and gender variables

(Figure 4.6), box plot showing descriptive values of the anterior volume and gender groups. It is noticeable that the anterior volume of males significantly more that of females.

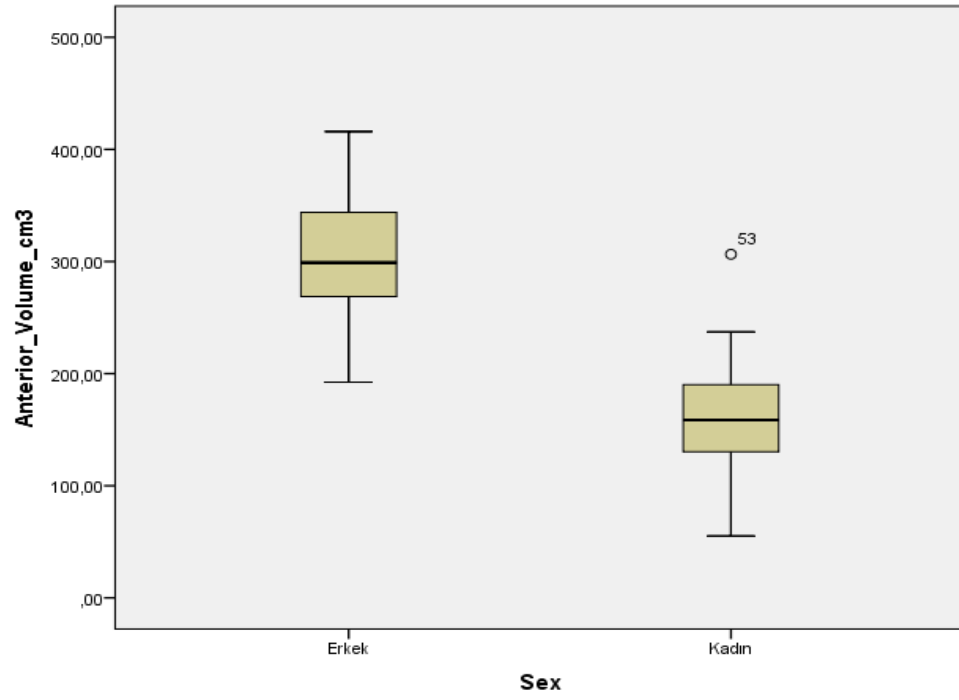


Figure 4. 5. Box plot for the anterior muscular volume and gender variables

(Figure 4.7), a box plot showing the value of posterior volume between genders.

The posterior volume of males significantly more than of females.

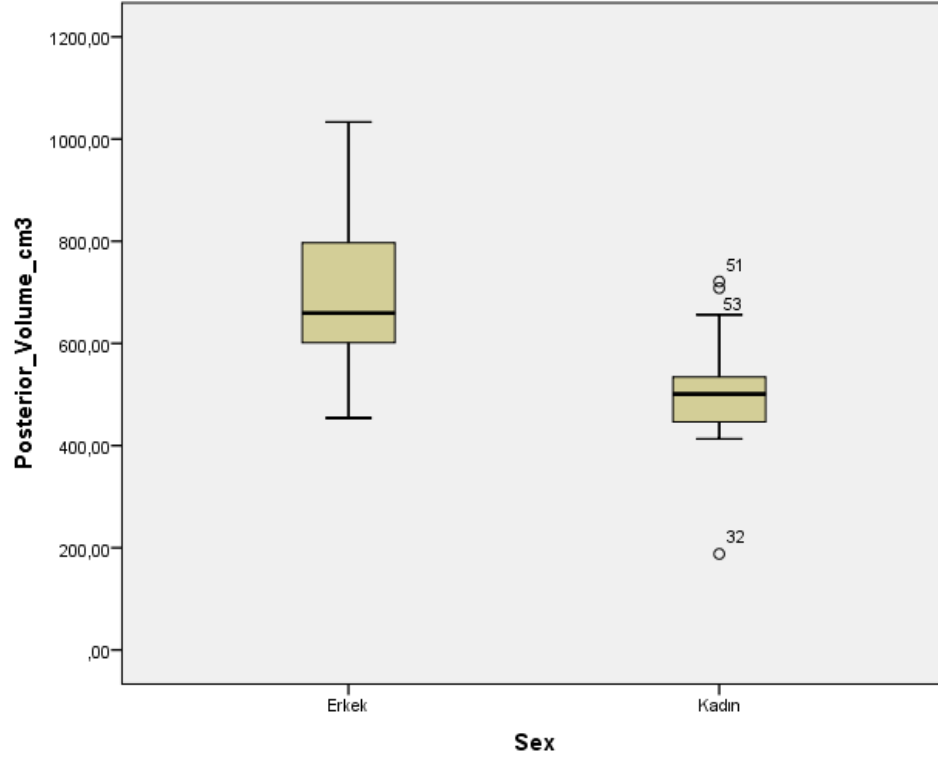


Figure 4. 6. Box plot for the posterior muscular volume and gender variables

(Figure 4.8), a box plot shows the anterior posterior fraction between gender groups. Here, the value of Ant_Post_fraction appears significantly higher in males than in females.

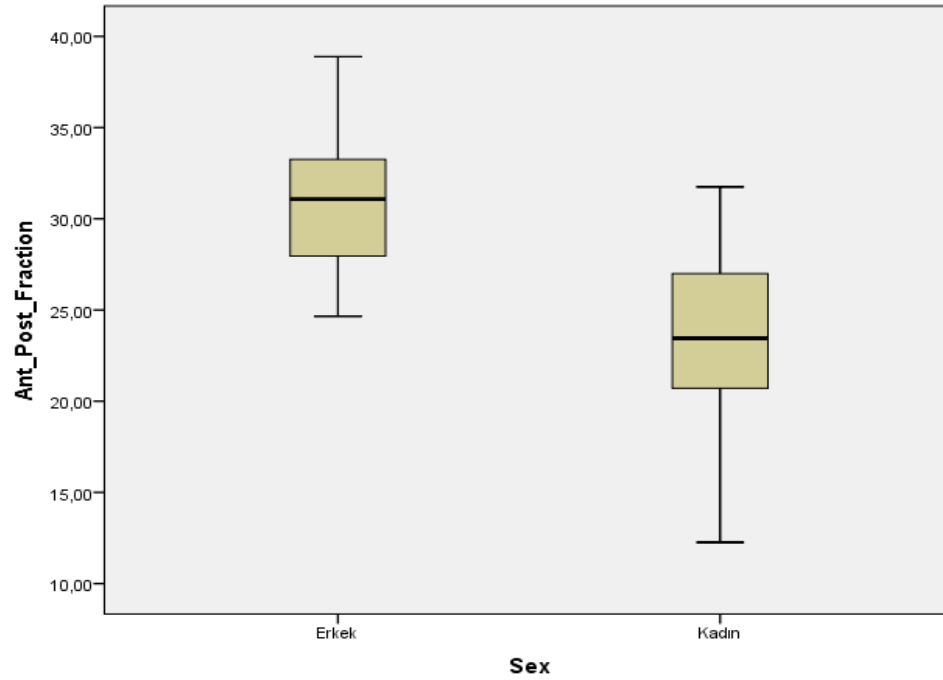


Figure 4. 7. Box plot shows the Ant_Post_Fraction and gender variables

(Figure 4.9), length with gender groups showing the difference in length from L1 to L5. It appears as the length in cm from the first lumbar vertebra to the fifth lumbar vertebra in males is significantly higher than in females.

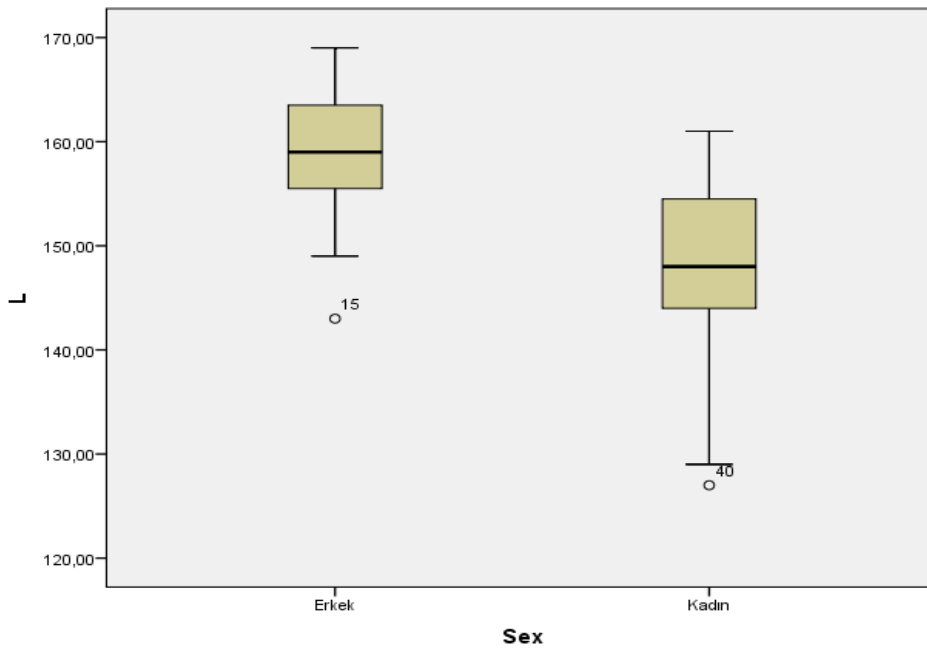


Figure 4. 8. Box plot shows the length with gender variables

It's evident from the data in (Table 4.3), that the PAL value of females ($M=4.39$; $SD= 16.87$) is more than that of males ($M= 3.78$; $SD=1.73$), the T value= 1.300 ; $p=0.198$ (more than 0.05) that indicates there is no significant statistical differences between males and females for PAL. The anterior volume of males ($M=303.18$; $SD=55.64$) is more than that of females ($M=157.50$; $SD=54.26$), $T=10.43$; $p=0.0001$, that show statistically significant variations between males and females for the anterior volume variable, similarly the posterior volume of males ($M=694.93$; $SD=139.36$), considered more than of the females ($M=501.13$; $SD=99.14$) $T=6.30$; $p=0.0001$, it's also indicate that there is strong statistically significant variations between two groups. Likewise, for the Ant_Post_Fraction variable, indicates a considerable statistical difference between males ($M=30.52$; $SD=3.54$) and females ($M=23.59$; $SD=5.08$) $T=6.23$; $p=0.0001$. Also it's noticeable that the length (L) is more in males ($M= 158.90$; $SD=5.96$) than females ($M=148.06$; $SD=8.37$), $T= 5.86$; $p=0.0001$, that showing significant variations.

The first step was to compute Pearson correlation coefficients for the males, According to the findings, the data of PAL/ anterior volume, PAL/ posterior volume and PAL/Ant Post Fraction does not give a strong correlation as shown in (Table 4.4).

Table 4. 4. Bivariate correlation of PAL, Anterior volume, Posterior Volume, and Ant Post Fraction variables of males

	Pal Anterior muscular volume	Pal Posterior muscular volume	Pal Ant Post Fraction
r	0,350	0,288	0,027
p	0,054	0.116	0,887

* Correlation is statistically significant at the 0.05 level.

In contrast, in females the Pearson correlation coefficients between the same variables shows a negative weak non significant correlations between PAL and anterior volume ($r= -0.064$; $n=31$; $p=0.731$), concurrently a positive weak non significant correlations between PAL and posterior volume ($r=0.097$; $n=31$; $p=0.604$) as well PAL and Ant_Post_Fraction ($r= -0.136$; $n=31$; $p=0.464$) (Table 4.5).

Table 4. 5. Bivariate correlation of PAL, Anterior volume, Posterior Volume, and Anterior Posterior Fraction variables by female

	Pal Anterior muscular volume	Pal Posterior muscular volume	Pal Ant Post Fraction
r	-0.064	0.097	-0.136
p	0.731	0.604	0.464

* Correlation is statistically significant at the 0.05 level.

Noteworthy, in the discussion part of this study, the causes for discrepancies between independent sample t-tests and Pearson correlation coefficients will be discussed further.



5. DISCUSSION

The goal of this research was to study and evaluate the volume of the prevertebral and postvertebral muscles in lumbar region, and to see if there was a link with LL, which was estimated using the PAL approach. All this is in the interest of finding a new approved method for diagnosis by CT scans for LL, and thus follow-up the stages of development of the problem in the spine, which facilitates the treatment. CT scans were acquired from Ondokuz Mayıs University hospital in Samsun, Turkey, for 62 individuals (31 male and 31 female). Regardless of gender differences, the findings show that there are no statistically significant associations between PAL and anterior muscle volumes, posterior muscle volumes, and Ant Post Fraction $r = (-0,055, 0,046, -0,160)$. Observations of evolutionary changes in spinal musculature, the mechanical role of spinal muscles, and correlations between muscle volume and lumbar spinal curvature changes convincingly demonstrate the involvement of musculature in maintaining LL. There is an undisputed point that confirms the existence of a relationship between the degree of LL and the prevertebral muscle volume (Meakin and Aspden, 2012), (Meakin et al., 2013) found that there is a statistically significant positive association between the LLA and muscle volume. On the other hand, (Copaver et al., 2012) said that there is a relation between the morphology of the PM muscle and the spinal curvature, that muscle morphology impacts its surface, and that LL influences muscle structure. But he observed that there is no relation between LL and the volume of the PM muscle.

In addition, regarding of gender, gender differences in muscle volumes were discovered that may be significant; presence a poor positive but not significant correlations between male's PAL and anterior volume, posterior volume r was (0.350, 0,288), as well the anterior and posterior volume for males is more than in females.

Similarly, it was once additionally found that there are very vulnerable poor correlations between Pal / anterior volume in females $r = -0.064$ and pal/ posterior volume $r = 0.097$. In this case, it can additionally be argued that the reason for the lack of significant correlations between muscle volumes for each gender with PAL is to the presence of numerous individuals and environmental factors that may influence the anterior and posterior volumes of the muscles related to the LL this includes age

(Mannion et al., 2000) and gender (Hides, Gilmore, Stanton, and Bohlscheid, 2008) This has already been taken into account in our study.

It has been observed that there is a relationship between muscles volume and age. There is more of one investigations have found age-related changes in adult skeletal muscle, including a reduction in size.(Frontera et al., 2000) reported a decreasing and changes in muscle strength, volume and also the arrangement of muscle fibers in elderly volunteers. (McLoughlin et al., 1994) added that the PSM volumes on CT scans are related with the age of the patient. In summary, the multifidus and ERS lumbar muscles exhibit comparable morphological alterations, including a loss in size and the mass, as well as an increase in muscle fatty infiltration and asymmetry, which was more pronounced in older people (Fortin et al., 2014).

The Participants in our study varied in age from 19 to 84. The mean was 45.58, while the standard deviation was 15.99. Given the wide age range and the wide standard deviation, It is not excluded from this the influence of the age factor on the results of the sample, also it was predicted that there would be fat changes in the muscle tissues as a result of aging. (Sions et al., 2017) noted that in an older population, females had smaller volume of multifidi, ERS, PM, In addition, the fat component of the ERS in females was greater than in males (Menezes-Reis et al., 2018). Furthermore, there is a link between gender and age and PM fat infiltration and volume change (Urrutia et al., 2018). Males lose more muscle as they age, but females have better functional implications (Doherty, 2003).

Other factors that were not taken into consideration, which are regarded as one of the study's weaknesses, had a direct or indirect impact on the volume of the muscles in question. The factors consist of height, weight, and body mass index (BMI) (Gibbons et al., 1998), training and sports (Bruce et al., 1997), and (LBP) situation (Weber et al., 1997).

Muscle volumes were shown to have a minor relationship with anthropometric parameters (height, weight, and BMI) (Urrutia et al., 2018). (Chaffin et al., 1990) added Height and weight have a substantial impact on the volume of the ERS muscles. A larger cross sectional volume of the PM muscles was associated with taller height, heavier

weight, BMI, and lean body mass, as well as more years of sport and exercise participation (age adjusted) (Gibbons et al., 1998). (Parkkola and Kormano, 1992) found that People with a higher fat content (obesity) are also more likely to have more intramuscular fat in the ERS mass than in the other muscles, according to their research.

In the same context of factors that affecting muscles volume, and because the volume is a primary predictor of a muscle's capacity to generate force, regular strength training is normally expected to result in an increase in LS muscle volume in cross-sectional area (Bruce et al., 1997). So, from the aforementioned study, we conclude that Greater trunk force was related with larger muscles volume. Finally, two studies found that individuals with chronic LBP had reduced PSM volume (Hultman et al., 1993; Parkkola and Kormano, 1992). In addition, decreased muscle volume has been associated higher degree of disk degradation (Parkkola and Kormano, 1992). The effect of spinal pathology on PM size, on the other hand, is contradictory; there is no change in PM volume in patients with LBP compared to controls, but there is a significant drop in multifidus volume (Danneels et al., 2000). However In individuals with acute and chronic LBP, as well as LBP following surgery, there may be a decrease in spinal muscle volumes on MRI and CT scan, with or without a decrease in muscle density on CT scan (Mattila et al., 1986; Storheim et al., 2003) .

It is clear from the above, and Because of the importance of these characteristics mentioned, and their direct correlation with muscles volume, they will be taken into account in the next study and included in the data.

It is noteworthy; there is another limitation in this study. The CT scans were all done in a supine position. Images acquired in this position may not properly demonstrate the relations of the muscles contributing to LL and may not reflect the actual tissue interactions. As a result, it is also suggested that future research duplicate this study, but utilizing CT scans collected in standing posture, to see whether there are any changes in muscles volume.

Furthermore, while repeated measures testing revealed that the method of measuring muscle volumes was repeatable, there was a chance of mistake in creating the polygons in imageJ software around the boundaries of each muscle. Finally, Muscle

degeneration is characterized by decreased muscle volume and an increase in fatty deposits inside the muscle. The method we used only gave a gross measurement of muscle volumes and did not allow for the estimation of muscle replacement by adipose or connective tissues, therefore, the goal in the future study will be to utilizing a very dependable approach based on the difference in signal intensity between muscle and fat tissue.



6. CONCLUSIONS AND RECOMONDATIONS

This anthropometric study was planned to correlate between pre-vertebral and postvertebral muscle volumes with the degree of lumbar lordosis calculated using PAL technique aiming to discover if there is any significant correlation that we could use to establish a diagnosis or to follow changes throughout the course of the disease CT scan images were collected from the Archival System of the Radiological Department of Ondokuz Mayıs University Hospital in Samsun, Turkey, and used in this investigation.

Correlation analysis was used to calculate the degree of relationship between the variables. The findings revealed that there is no significant correlation between the variables regardless of total anterior volume, total posterior volume and the total of PAL. Moreover, there are no statistically significant correlations between anterior volume, posterior volume, and PAL in both genders, according to the Pearson test.

We think that height, weight, BMI, activity status, physical conditions, low back pain history and age-related fat changes in muscles volume are important factors to be considered in our subsequent studies due to their direct relationship to muscle volume. It is also advised that future research replicating this work, should also consider using CT scans in standing position, to investigate whether there are any differences in muscle volumes in relation to the position of patients.

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ETHICAL DECISION



T.C.
ONDOKUZ MAYIS ÜNİVERSİTESİ
KLİNİK ARAŞTIRMALAR ETİK KURULU

Sayı: B.30.2.ODM.0.20.08/1873

14.09.2018

Sayın Prof. Dr. Bünyamin ŞAHİN

Etik Kurulumuza sunmuş olduğunuz **Omurların Ön ve Arkasındaki Kasların Hacimlerinin Lumbar Lordoz Üzerine Etkilerinin Bilgisayarlı Tomografi Görüntüleri Üzerinden İncelenmesi** başlıklı OMÜ KAEK 2018/412 Karar nolu Veri kaynakları taraması+ Radyoloji çalışması nitelikli araştırma projeniz amaç, gerekçe, yaklaşım ve yöntemle ilgili açıklamaları açısından Klinik Araştırmalar Etik Kurulu yönergesine göre incelenmiş ve etik açıdan bir sakınca olmadığına, çalışmanın süresi 6 ayı geçerse 6 aylık bildirimlerinin yapılmasına, çalışma tamamlandıktan sonra sonucunun tarafımıza en geç üç(3) ay içerisinde bildirilmesine 13.09.2018 tarihli Etik kurulumuzda oy birliği ile karar verilmiştir.

Bilgilerinize arz/rica ederim.

Prof.Dr.Emine ŞENTUNÇ

Klinik Araştırmalar Etik Kurulu Başkan Yrd.

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