Epidural Fat: Considerations for Minimally Invasive Spinal Injection and Surgical Therapies

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Abstract: A large number of patients that come to Hospital for radicular pain are treated with minimally invasive spinal injection or minimally invasive procedures that embody a growing number of surgical techniques. In both techniques, the knowledge of the epidural fat and other surrounding anatomic structures may be of interest as the epidural fat has its role in the distribution of the medication and in surgical procedures. There are areas in the epidural space consisting of a genuine space filled with adipose tissue, veins and nerves and other areas where the dural sac rests on the vertebral bodies, vertebral pedicles, vertebral laminae and the ligamentum flavum. Nerve roots cuffs are lateral prolongations of dura mater, arachnoid lamina and pia mater that enclose nerve roots in their way across the epidural space towards the intervertebral foramen and dorsal root ganglion located within the intervertebral foramen. There is adipose tissue surrounding all mentioned structures and fibrous ligaments attaching nerve root cuffs to bones. Lumbar epidural fat has a metameric and discontinuous topography, it varies along the spinal canal and also in pathology of the spine, altering the amount and distribution of fat around the affected area. Transforaminal or translaminar injection approaches to dorsal root ganglion and dorsal nerve root are both, valid alternatives to treat radiculopathy. The transforaminal technique, in general offers greater selectivity than the translaminar approach. However, depending on the area affected, it is important to asses which way may be more suitable for delivering a solution in the affected level. The transforaminal offers an easier approach to the preganglionic and ganglion areas, whereas the translaminar technique reaches the epidural, preganglionar space and less frequently the ganglionic area. The distribution of epidural fat tissue may influence the surgical strategy aiming at protecting neural structures.

Keywords: Epidural lipomatosis, epidural fat, spinal injection, minimally invasive

INTRODUCTION

A large number of patients that come to the Pain Clinics for radicular pain are treated with minimally invasive spinal injection. The purpose of these injections is to deposit corticosteroids and local anaesthetics next to the inflammation site, using either a translaminar or transforaminal, approach in order to decrease or preferably eliminate the pain.

In addition to injections, minimally invasive spinal surgery limits damage of soft tissue around the spine, thereby diminishing postoperative pain and allowing earlier return of patients to their regular activities. Advantages of this procedure include reduced blood loss, shorter hospitalization and quicker rehabilitation. Minimally invasive spine surgery approaches have been described for most surgical procedures of the spine over the past few decades including spinal fusion, deformity corrections, and repair of herniated discs.

MINIMALLY INVASIVE SPINAL INJECTION

The target of minimally invasive spinal injection is the dorsal root ganglion and sensorial nerve roots within nerve root cuffs affected by degenerated discs or foraminal stenosis. Ultrastructural anatomical features of the

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spine may help explain their influence on the spread of substances injected in the epidural space and in transforaminal blockade.

Epidural steroid injection (ESI) by translaminar approach is a minimally invasive procedure providing pain relief around the neck, arms, back, and legs caused by inflamed spinal nerves. The main causes of back pain include: spinal stenosis; spondylosis; and disc herniation [1]. The effects of translaminar ESI tend to be transitory and its duration shorter, compared to using a transforaminal approach [1].

The transforaminal approach is useful for both diagnostic and therapeutic means in patients with radicular pain frequently caused by disc herniation and foraminal stenosis. It is performed also when more than one disc is involved, or when findings on the electromyogram (EMG) show alteration of two or more nerve roots. In this case, clinicians can differentiate which disc is causing the symptoms, providing valuable information prior to surgical procedures.

Minimally invasive surgical therapies

Minimally invasive spine surgeries embody a growing number of surgical techniques that allow surgeons to perform spinal procedures through smaller incisions. Although certain less invasive surgical techniques have been described by spine surgeons for many years, it is only recently that advancement in technology has stimulated broad interest in the spinal community for minimally invasive approaches. In 1955, Malis started using a binocular microscope intraoperatively in conjunction with bipolar coagulation, to facilitate his surgical approach [2-4]. Once intraoperative surgical microscopes were established in surgery for discectomies, Yasargil and Caspar independently introduced the concept of minimally invasive microdiscectomy [5,6]. In 1975, Hijikata described the first percutaneous discectomy [7]. Since then, automated discectomies have replaced percutaneous discectomies. Current concepts include the use of adjuvant therapy in addition to automated techniques involving lasers and thermal heating probes. The concept of minimally invasive spine surgery is advancing rapidly, as new technologies and new applications are being developed.

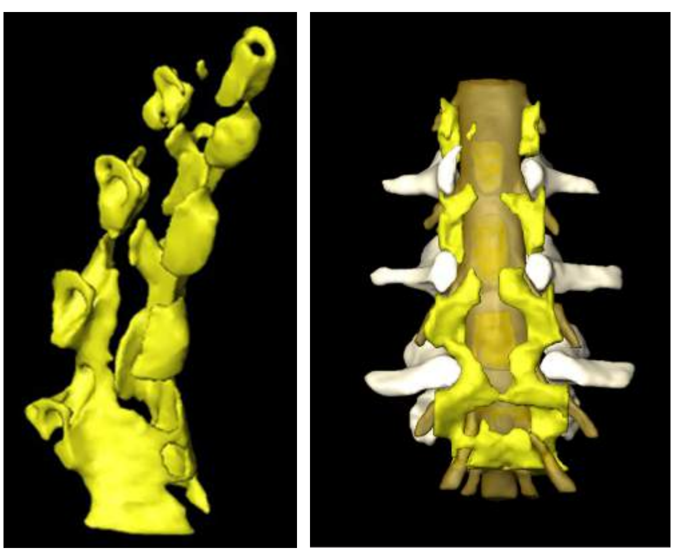

Figure 1. 3D MR images reconstructed with Amira® software. **A.** Human epidural fat. **B.** Human dural sac and epidural fat. Perspective from anterior position.

Advantages of Minimally Invasive Surgery over Classical Surgical Techniques

Classical surgical approaches produce more severe postoperative pain and delay the return of patients to full activity. Dissection of the paraspinal muscles from their normal anatomic points of attachment results in healing by scarring of these muscles. The multiple layers of each individual muscle adhere to one another at the scar site, losing their independent function. This type of dissection results in loss of nerve endings to muscles affected, with subsequent wasting, resulting in permanent muscle weakness of the back [8-10].

Epidural Fat and related Structures

There are areas in the epidural space consisting of a genuine void filled with adipose tissue, veins, and nerves (Fig. 1) and other areas where the dural sac rests on the vertebral bodies, pedicles, laminae and the ligamentum flavum [17].

Nerve roots cuffs are lateral prolongations of dura mater, arachnoid lamina, and pia mater that enclose nerve roots in their way across the epidural space towards the intervertebral foramen and dorsal root ganglion, located within the intervertebral foramen. The thickness of nerve root cuffs is formed by internal cellular and external fibrillar components (Fig. 2).

At the cervical levels, the intervertebral foramina are similar to neural canals:4 to 6 mm in length, 10 mm in the craniocaudal diameter, and 5 mm in the anteroposterior diameter [18]. Structures that pass through the foramina include: the mixed spinal nerve, with their respective nerve root cuffs; lymphatic vessels, the spinal branch of the segmental artery; and the communicating (intervertebral) veins between the internal and external vertebral venous plexuses. There is also adipose tissue surrounding all previously mentioned structures and fibrous ligaments attaching nerve root cuffs to bones. The spinal nerve occupies only one fifth of the intervertebral foramen in the cervical region. Dorsal nerve roots and ganglia are in contact with the superior facet. Ventral nerve roots contact the uncinate process and the floor of the neural foramen [18].

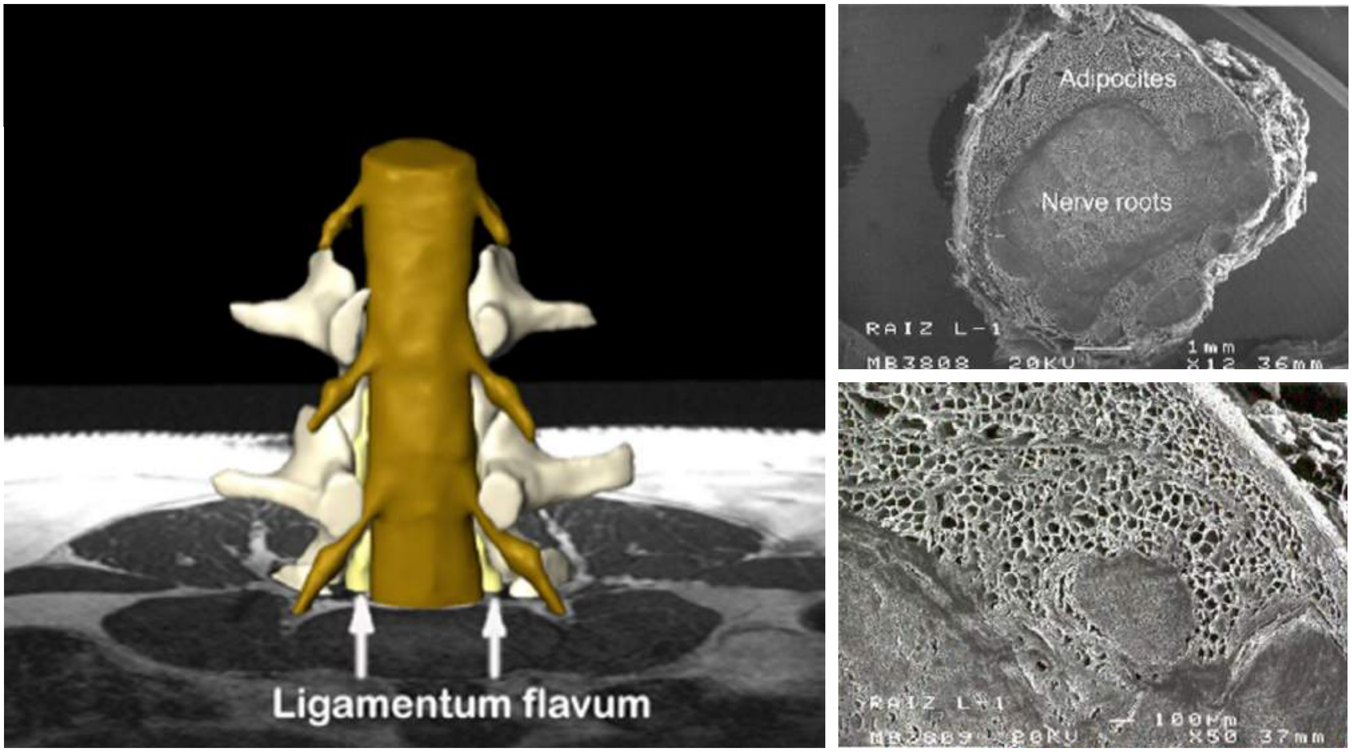

Figure 2. A. Human dural sac with its dural root cuffs and ligamentum flavum. 3D MR images reconstructed with Amira® software. Perspective from anterior position. **B** and **C.** Human dural root cuffs. Transversal cut. Scanning electron microscopy. Magnification: B: x12, C: x50. Figure C is a detail of figure B. Figures used with permission from Reina MA, et. al., 2007 [26] and Reina M.A., et al., 2008 [27].

Epidural fat and blood vessels are found in the superior aspect of the intervertebral foramen. The dorsal nerve root and dorsal root ganglion are located posterior and slightly superior to the ventral root [19-21].

At the lumbar levels, the craniocaudal diameter of intervertebral foramen is between 19-21 mm and the anteroposterior diameter varies from 9-11 mm, superiorly, to 7.4-9.3 mm, inferiorly [22, 23]. Nerve root cuffs surround neural elements and their accompanying radicular arteries and veins until they exit the foramen [24, 25] (Fig. 3). The size of the nerve root within the nerve root cuffs has a diameter of 5-6 mm and can increase up to 10-12 mm around the ganglion (Fig. 2) Adipocytes could be seen inside the thickness of nerve root cuffs [26, 27].

At lumbar levels, the spinal nerve is located in the upper third of the foramen. As it enters the intervertebral foramen, the spinal nerve progresses very close to the medial and inferior aspect of the superior pedicle, which forms the upper boundary of the intervertebral foramen. Here the nerve is accompanied by branches of the lum-

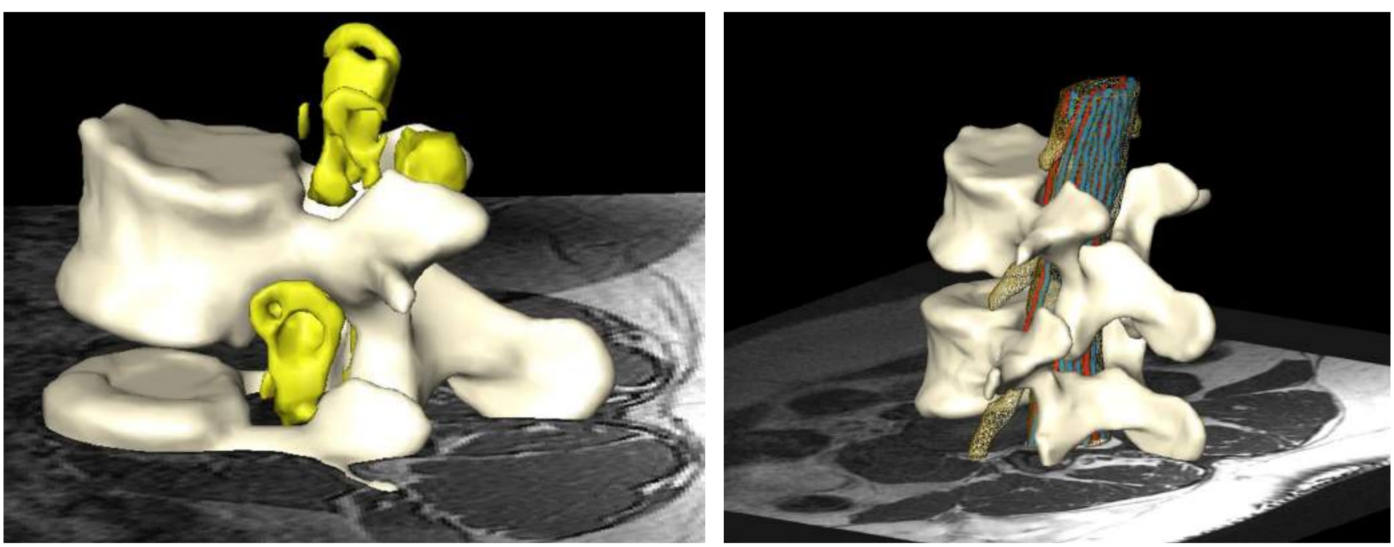

Figure 3. 3D MR images reconstructed with Amira® software. **A.** Distribution of fat into intervertebral foramen. **B.** Distribution of nerve roots into human dural sac and its dural root cuffs. Figures used with permission from Reina MA, et. al., 2010 [52].

bar segmental artery, superior segmental (pedicle) veins connecting external and internal vertebral venous plexuses, and by the sinuvertebral nerve. In the lumbar region, small vascular pedicles travel towards pockets of epidural fat located in the posterior epidural space.

The ligamentum flavum is perpendiculary disposed and connects the adjacent laminae. Its superior portion attaches to the anterior surface of the lamina above while its inferior portion attaches to the posterior surface of the subadjacent lamina. It also projects an anterolateral extension which provides reinforcement to articular facets. The ligamentum flavum has a thickness of about 3-5.5 mm in healthy individuals. Embryologically, the ligament originates from right and left segments that fuse in the midline [28, 29]. The fibrous posterior longitudinal ligament extends along the posterior surfaces of the vertebral bodies from the base of the skull to the sacrum.

The posterior longitudinal ligament adheres to the dural sac at upper lumbar levels and separates from the sac at lower lumbar levels due to the presence of epidural fat. Laterally, the posterior longitudinal ligament projects fibers attaching to the medial edges of the intervertebral foramina. The spinal epidural space is filled with epidural venous vessels placed anterolaterally and posterolaterally. There are also spinal nerve roots crossing the epidural space and their respective dural cuffs.

Figure 4. Epidural fat observed during surgery. Figure used with permission from Reina M.A., et al., 2006 [31].

Epidural fat

Fat is ubiquitous in the epidural space, indeed it is the main component [30]. It fills the dural sac and protects its contents against the effects of lashing, deceleration, and rotational forces inflicted on the vertebral column. Thermal and mechanical protection is offered by the epidural fat.

Fat cells, or adipocytes, are unilocular with color varying from white to yellow; according to the amount of carotenes in the diet [31]. These large cells (up to 120 µm in diameter) are shaped spherically and become polyhedral when large amounts of cells aggregate to become fat tissue. Every fat cell has a single large lipid vacuole in the center and a peripheral oval nucleus. Fat tissue is held together in packs inside the epidural space by pedicles containing vessels [31].

Epidural fat does not have a semifluid nature and contributes to the shape of the epidural space in the spinal canal (Fig. 4). Lumbar epidural fat has a metameric and discontinuous topography. It is mainly located in the posterior aspect of the epidural space. In the axial plane, the morphology of fat deposits is similar to a tetrahedron, with a blunt posterior apex in contact with the ligamentum flavum, an anterior base oriented towards the posterior surface of the dural sac, and lateral aspects determined by the vertebral arches. The distribution of the epidural fat in the spinal canal, especially in areas of higher mobility, suggests a protective function.

The epidural fat extends craniocaudally from the inferior aspect of one vertebral lamina to the superior aspect of the lamina of subadjacent vertebra and in the lateral direction towards the point where articular facets and ligamentum flavum intersect. It also fills the space between vertebral arches and intervertebral foramina, wrapping the nerve root cuffs [32-35]. The epidural fat does not usually adhere to these structures, allowing mobility of the dura within the vertebral canal. However, small amounts of epidural fat covered by a thin connective membrane do adhere to the posterior midline by a vascular pedicle entering the epidural fat at the plane where the right and left portions of the ligamentum flavum meet.

The volume of the posterior epidural fat deposits increases caudally, from L1-2 to L4-5. The average height of these deposits is 21 mm (range 16-25 mm) and the width increases craniocaudally from 6 to 13 mm [34] (Fig.1A).

Epidural fat in the posterior aspect of the epidural space is uniformly distributed while in the lateral areas, fat is compartmentalized into groups of cells by a web of connective tissue that extends from the intervertebral foramen to the posterior longitudinal ligament. Adjacent to each vertebral disc, connective tissue fills the space left between the posterior longitudinal ligament and the disc. In the anterior aspect of the epidural space, epidural veins are often found with dura mater attaching to vertebral discs.

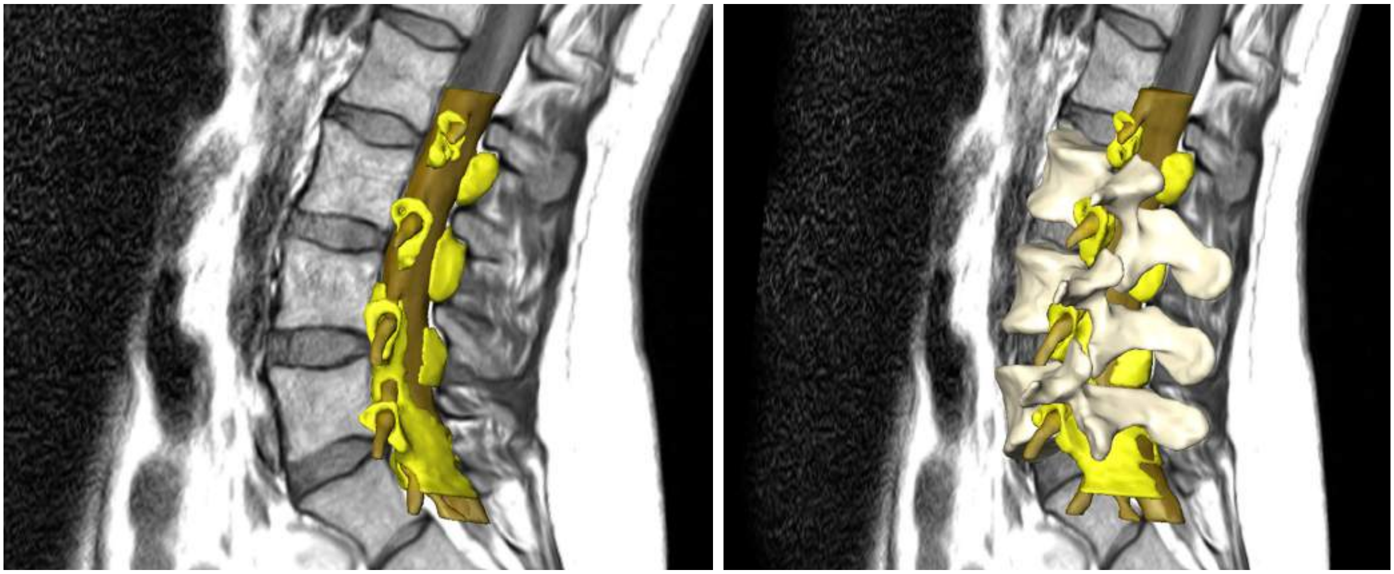

Figure 5. 3D MR images reconstructed with Amira® software. **A** and **B**: Distribution of epidural fat and foraminal fat in lumbar vertebral column.

Althougth epidural fat is distributed differently in the cervical, thoracic, and lumbar regions, within each region the distribution remains consistent. In the cervical region, fat is absent, or almost nonexistent, in the anterior and lateral aspects of the epidural space. A small deposit is sometimes seen in the posterior aspect. At thoracic levels, the epidural fat forms a broad posterior band with "indentations". It is thicker near the intervertebral disc and less prominent around the middle section of the vertebral bodies and close to the base of the spinous processes. In the upper to middle thoracic levels (T1-7), epidural fat is continuous and the indentations are more evident. In the lower thoracic region, [T8-12] the distribution of epidural fat becomes patchy.

In the lumbar region, the fat in the anterior, and posterior, aspects of the epidural space forms two isolated structures (Fig. 5). The posterior epidural fat acquires its greatest volume in the caudal lumbar levels.

Epidural fat in some pathological conditions

The distribution of epidural fat can be altered under certain pathological conditions [36-39]. The following is a brief description of conditions in which the characteristics of the fat of the epidural space are different from the normal arrangement:

Epidural fat and obesity

The idea that there is a correlation between obesity and increased deposits of epidural fat, with subsequent increased risk of spinal canal stenosis, has been challenged by Wu et al [36]. BMI had no correlation with either posterior, or anterior, epidural fat. More importantly, obesity was associated only with subcutaneous fat, not with any specific or computed epidural fat measurement [36]. However, that individual weight is associated with specific, usually posterior, patterns of epidural fat deposition must not be forgotten [36].

Epidural lipomatosis

Epidural lipomatosis is characterized by an increase in epidural fat content [40-43]. In epidural lipomatosis excessive deposits of free fat accumulate in the epidural space in the thoracic region (60% of patients) and the lumbar region (40% of patients) but not in the cervical region. The dural sac of patients with epidural lipomatosis often adopts a star-shape geometric form. This happens due to the position of meningovertebral ligaments inside the anterior and posterior regions of the epidural space [38, 39].

Excessive fat deposits around the dural sac cause spinal cord or nerve root compression, leading to neurological symptoms. Epidural lipomatosis may be idiopathic, but it is also seen in patients on long term steroid therapy or conditions characterized by endogenous steroid hyper-secretion. The observed increase in epidural fat can be up to 72% of the anteroposterior diameter of the spinal canal [40].

MRI of the spinal canal demonstrates increased signal intensity where a high epidural fat content is found, predominantly in the posterior and postero-lateral aspects, displacing and compressing the spinal cord.

Angiolipoma

Spinal angiolipomas are rare benign tumours containing adult fat cells and blood vessels [44-46]. More than 90% of these tumours are found in the epidural space, representing about 0.1-0.5% of all spinal cord tumours in adults [46]. These tumours have a yellowish appearance, a spongy consistency, and frequent hemorrhagic spots. Microscopically, angiolipomas are composed of lobules of adult adipose tissue and blood vessels. MRI of the spinal canal demonstrates areas of reduced signal intensity while characteristic sequences of fat suppression techniques help to identify these tumours.

Kyphoscoliosis

When a patient has a combination of kyphosis and scoliosis of the spine, the epidural fat distributes asymmetrically along the concave portion of the curvature displacing the spinal canal and its contents in the opposite direction [36]. Increasingly thinner vertebral bodies tend to collapse displacing the dura outwards. MRI demonstrates the increased amounts of epidural fat around the scoliotic areas. As scoliosis progresses, compensatory redistribution of epidural fat may be mistaken as lipoma [38].

Spinal stenosis

Spinal stenosis refers to a reduction in the cross-sectional area of the spinal canal leading to chronic pain and neurogenic functional deficits. Characteristically, the cervical and lumbar regions are more commonly affected [47, 48]. Frequently, this condition is accompanied by a reduction in the thickness of the dura mater linked to reduction in the amount of epidural fat around the stenotic area (Fig.6). The spinal cord may become compressed by bone or fatty tissue, with or without involvement of spinal nerve roots.

Epidural Fat and Surgery

Dandy performed cadaveric dissections to describe the components of the epidural space and, more specifically, epidural fat [49]. He described how epidural fat cushions neural structures and its displacement from areas adjacent to intradural tumors. Such observations remain unchallenged at present. During laminectomy, epidural fat is found redistributed around the outer limits of the superior and inferior margins of the stenotic area. Benign intradural tumors cause nerve compression and symptoms have a slow onset. In this case, fat is lacking around the tumor. Epidural fat is believed to protect dura mater and spinal nerve roots [31]. Loss of epidural fat, although not common, may happen in chronic lumbar disc herniation [39]. Surgeons try to avoid unnecessary resection of epidural fat from the surgical area in order to preserve the protective effects of epidural fatincluding: cushioning of the neural structures and reducing friction during back movements. Preservation of epidural fat and vascular integrity are important factors in the prevention of post-surgical complications and epidural fibrosis. Therefore, microsurgery has the advantages of allowing minimal tissue, fat, and vascular damage. It has been advocated that grafts, either form epidural fat deposits, or subcutaneous fat around spinal nerve roots, or over the dural sac may be beneficial; however, this technique is not free from complications and there have been reports of post surgical spinal cord compression after epidural fat grafting procedures [50]. In our experience, during laminectomy, the surgeon removes only the epidural fat that has been displaced at the initial stages of the surgical approach. All efforts are made to keep epidural fat loss around neural structures to a minimum. In cases where large areas of dura mater are exposed and there is significant loss of epidural fat due to the pathological condition, subcutaneous fat grafting has been performed without complications [51].

Minimally Invasive Spinal Injection Implications

In the translaminar approach (epidural block), the administered solution will follow a path amid the epidural fat (the real component of the epidural space). Depending upon the pressure exerted on the dura mater, it is possible to separate it from the periostium on the internal surface of the intervertebral laminae [50]. Thus, part of the injection volume will be dispersed among the lateral epidural fat, next to the preganglionar dural cuff, and most of the solution will stay in the posterior epidural space.

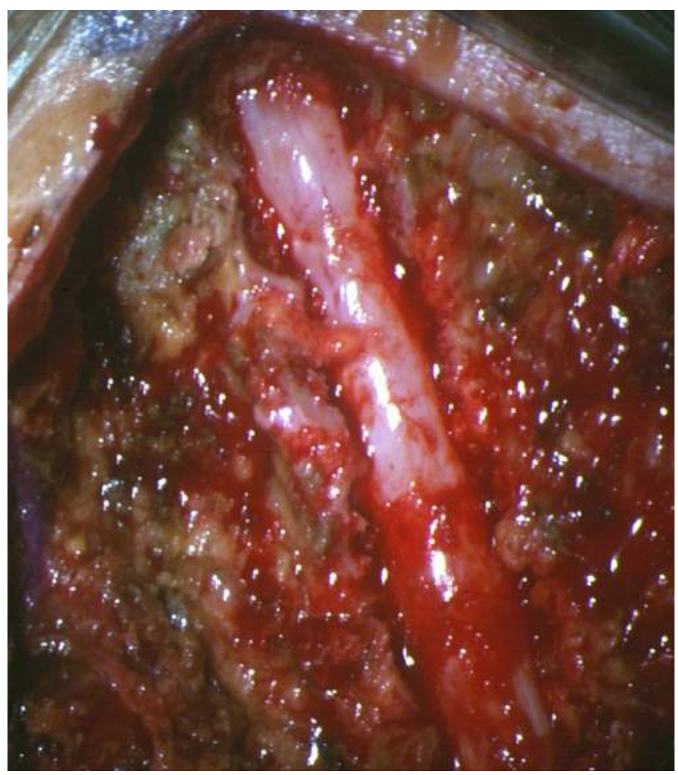

Figure 6. Spinal stenosis. Reduction in the amount of epidural fat around the stenotic area observed during surgery. Figure used with permission from Reina M.A., et al., 2007 [39].

When we use the transforaminal approach, the medication is deposited in the intervertebral foraminal canal, next to the nerve root, and the fat surrounded the nerve [52].

A fraction of drugs injected in the epidural space is absorbed and stored in the epidural fat. The amount of drugs absorbed by epidural fat depends on the lipid solubility of the drug. As such, the epidural fat acts as a drug depot, especially for lipophillic drugs, which upon their release, can move onto neighbouring structures such as the dural sac, nerve roots, and nerve root cuffs. Redistribution of these drugs is in turn affected by tissue permeability, local blood supply, and the surface area involved. Drugs that are more lipid soluble will be released more slowly, potentially leading to prolonged pharmacological effects.

Considerations of Minimally Invasive Surgical Therapies

Anatomical aspects of the structures related to the area of decompression need thorough evaluation prior to surgical procedures. Therefore, it is important to measure both the length and thickness of the ligamentum flavum and how far it extends along adjacent laminae. These data are needed to assess the extent of ligamentum to be resected, in order to produce effective decompression. The other important consideration is the evaluation of damages caused to neural structures by compression, as these are highly vulnerable at the time of decompression. As it has been mentioned above, it is likely that epidural fat helps protect neural structures; therefore, surgeons adapt their surgical technique to preserve it. If there is an extremely narrow canal it is more advisable to enter the spinal canal through a more medial posterior route where more epidural fat protects the thecal sac. Features such as the shape of the spinal canal and consistency of the feature(s) producing compression (i.e. soft tissue [Ligamentum flavum, joint capsule, intervertebral disc] or bone [superior facet, lamina, osteophytes]) are relevant in deciding the most beneficial approach. As compression often tends to be caused by soft tissue, it is advisable to preserve the bony structures as much as possible.

Methods for the study of epidural fat

In the study of epidural fat, anatomic dissection with prior epoxy resin fixation of tissue samples is a valuable tool [53, 54]; however, there are limitations to this technique in relation to tissue manipulation and alteration of biological constituents. Other traditional methods used to investigate epidural fat include injection of contrast media and subsequent imaging. More recent improvements on these techniques include, epiduroscopy and cryomicrotomy, and have significantly improved the outcomes of recent studies; tissue manipulation is minimal and original positions and relationships are barely distorted [55]. In some studies, errors have been reported as below 2% for CT and MRI techniques [31] Three dimensional reconstructions of MRI is a new method that enables researchers to evaluate epidural fat distribution with extreme accuracy. Using three dimensional reconstructions of MRI, volume calculations can be made of virtually any structure of interest with the essential advantage of avoiding physiological tissue alteration, other than the pathological condition of the patient [56].

Protocols and Techniques used in the Study of the Spinal Canal

MRI is a particularly useful tool for investigating several pathologies affecting the spinal cord without exposing the patient to radiation. MRI provides graphic tissue slides, in any plane, allowing excellent tissue differentiation due to its high contrast definition. Vertebral bodies, intervertebral discs, ligaments, epidural fat, and neural structures, such as the spinal cord, nerve roots and dural sac, are among the structures that MRI reconstruction is able to reproduce accurately.

Standard hospital MRI equipment (Intera 1.5T MRI - Philips) produces routinely echo spin sequences T1 and T2 weighted in sagital planes and echo spin gradient T2* weighted and echo spin sequences in T1 weighted in the axial plane for the cervical and thoracolumbar spine respectively. In turbo- echo spin sequences in T1 weighted, repetition time (RT) and echo time (ET) are short-lived (10-15 msec) and epidural fat image intensity is high. On the other hand, in potentiated turbo- echo spin in T2 (long RT, ET), epidural fat image intensity is moderate, while in STIR sequences; epidural fat image intensity is low.

In our three dimensional image reconstructions, we used a sequence configuration of T1 Fast Field Echo 3D was: FOV 230 mm., 205 x 256 matrix, 160 contiguous sections per block, thickness per section/distance between sections 1.8/-0.9 mm, nominal voxel size 0.9 mm x 0.9 mm x 0.9 mm, TR 32 msec, TE 4.6 msec, NSA 1, and a sequence configuration of T2 Balance Fast Field Echo 3D was: FOV 230 mm, 246 x 352 matrix, 200 sections per block, thickness per section/ distance between sections 1.3/ -0.65 mm, TR 7.7 msec, TE 3.8 msec, NSA 1. The sequence obtained by T1 Fast Field Echo sequence allowed detailed three-dimensional reconstruction of spinal cord and nerve root structures. The sequence obtained by T2 weighted provides helpful data for cerebrospinal fluid volume determinations, due to its better discrimination of cerebrospinal fluid from spinal cord and spinal nerve roots.

Conclusions

Lumbar epidural fat has a metameric,discontinuous, topography and usually does not adhere to bony structures, allowing mobility of the dura mater within the vertebral canal. The distribution of the epidural fat varies along the spinal canal and also in pathology of the spine, altering the amount and distribution of fat around the affected area. Epidural lipomatosis is characterized by an increase in epidural fat content. In pathological conditions in which there is combination of kyphosis and scoliosis of the spine, the epidural fat distributes asymmetrically. On the other hand, spinal stenosis is frequently accompanied by a reduction in the amount of epidural fat around the stenotic area.

A transforaminal, or translaminar, approach to the dorsal root ganglion and dorsal nerve root are valid alternatives to treat radiculopathy. The transforaminal approach, in general terms, offers greater effectiveness than the translaminar approach. However, depending on the area effected, it is important to asses which way will be easier to deliver the injected solution in the effected level. Transforaminal offers an easier approach to the preganglionar and ganglion areas, whereas translaminar reaches the epidural, preganglionar space, and less frequently the ganglion area. The epidural fat may play a role in the distribution of injected medication.Knowledge of the distribution of epidural fat tissue and its preservation could lead to a modified surgical strategy that helps to protect adjacent neural structures.

Acknowledgement and Authorship Statement

José De Andrés, Miguel Angel Reina and Riánsares Arriazu Navarro participated in the preparation, revision of clinical and anatomical topics, and generation and writing of this paper; Alberto Prats-Galino participated in the preparation, revision of anatomical topics, methods for the study of epidural fat and techniques used in the study of the spinal canal; Rafael García de Sola participated in the preparation and revision of surgical topics; Fabiola Machés and Anna Oliva participated in the preparation, revision of epidural fat in some pathological conditions and generation and writing of this paper; and every authors approving the final edited, reviewed version. No outside funding for this work or other disclosures were reported. Authors report no conflict of interest with material discussed in this article.

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