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Timing of surgery for sciatica

Peul, W.C.

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THE SCIATICA TRIAL

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INTRODUCTION & OUTLINE OF THE THESIS

“L’art de la médecine consiste à amuser alors que le patient guérit de la nature.”

-Voltaire-

**“.....Thou cold sciatica,
Cripple out senators, that their limbs may halt
As lamely as their manners.....”**

William Shakespeare 1564 Timon of Athens, Act IV. Scene I

Shakespeare permitted Timon of Athens to rage against false friends in high places and wish them to suffer from sciatica. Although the natural course of sciatica is said to be favorable, classical literature, myths and even the Bible refer to sciatica as a punishment or demon curse, which disables people by means of excruciating lower leg pain.

The literal translation of the Greek word ‘sciatica’ is hip pain¹, which leaves room for dispute about today’s use of the word ‘sciatica’ in scientific communications. Undoubtedly “lumbosacral radicular syndrome” (LSRS) or sciatic neuralgia is a better description of the disease but it is not often used in peer reviewed manuscripts and thus in this thesis. Sciatica is defined as pain radiating from the low back or buttock into a lumbar or sacral dermatome. In addition to radiating leg pain patients may present with motor and sensory deficits and decreased tendon jerks or reflexes as a result of malfunction of the compressed spinal nerve, near its exit from the dural sac. Generally this area of the nerve is misnamed as the nerve root. Strictly speaking, the roots or radices have their origin proximal to the spinal cord or conus medullaris. Although literally incorrect, this thesis makes use of the term ‘nerve root’ to describe the former anatomical area of the nerve, to avoid inconsistencies with existing scientific publications. Compression of the spinal nerve root generates pain directly or indirectly by an inflammatory response. The most frequently cited cause of impingement of lumbar nerve roots is extruded or herniated disk material, which occupies the natural space under and beside the nerve root and displaces the nerve within the bony margins of the nerve root, which extends from the lateral recess to the intervertebral foramen. Through a weak spot in the annulus fibrosis, the fibrous outer ring of the intervertebral disk, the centrally located soft nucleus pulposus tissue leaks outward, which results in three successive degrees of disk herniation: local disk protrusion, disk extrusion and sequestered nuclear fragments in the epidural space. A herniated disk most commonly occurs at one of the two lower disk levels of the lumbar spine. The intensity of pain and severity of neurological deficit vary and are not correlated with either site or size of the herniated disk. Sciatica results in loss of the ability to move freely and function normally at home and work or during leisure activities. In the vast majority of cases sciatica decreases in the course of two months^{2,3}.



Figure 1. “Just before crossing into the land, Jacob wrestles with an angel and defeats him. Jacob refuses to release the angel until the angel blesses him. The angel gives Jacob a new name—Yisrael—Israel, “the God fighter,” “one who struggles with God.” But in the struggle, Jacob is also hurt. Torah tells us that the angel wrenches Jacob’s thigh. The Hebrew text says he tears Jacob’s sciatic nerve, which we know runs all the way down the lower back (Genesis 32:25–29). Further, Torah says that Jacob was limping (Genesis 32:32).”

How to intervene in the natural course for the remaining minority of patients with persistent sciatica?

Before the advent of disk surgery in 1934^{4,5}, this problem was of great interest to physicians and scientists for many centuries.

It is generally believed that Hippocrates (460-370 BC) was the first to describe the treatment of sciatica⁶. He advocated traction as a beneficial method to relieve patients of their pain and loss of function (ref). However, when Egyptian, Etruscan, and Arabic manuscripts (1550 BC) were reviewed, earlier descriptions of the clinical phenomena of spinal disorders were encountered⁷. Furthermore the Bible describes Jacob as enduring sciatica after struggling with an angel in the desert (fig.1).

Whereas the emperor’s physician Galen (129-200 A.D.)⁸ is claimed to be the first pioneer of spinal research, Caelius Aurelianus, born in Algeria (400 A.D.), was the first author to describe sciatica⁷. He taught and practiced in Rome and described sciatica as a clinical syndrome with pain radiating to the buttocks and leg. “In advanced stages muscle wasting could occur”. He associated the radiating complaints with lift-



Figure 2.

ing heavy objects and published his hypotheses in “*De Morbis acutis et chronicis*”⁹ (figure 2).

Paulus of Aegina (625-690 A.D.) seems to be the first one to perform laminectomies when the posterior elements were fractured and pushed into the spinal cord or cauda equina¹⁰. The next known successful laminectomy was performed almost 12 centuries later! After the fall of Rome, during the Dark Ages, knowledge and many of the skills of this ancient era were lost or not described.

Just before the 16th century Sabuncuöglü (Turkish scientist and physician), who treated patients with medicine and heat cauterization, and described this therapy for non-refractory sciatica in “*The Imperial Surgery*”¹¹; Turgut, 2007 2713 /id}. In the same century Andreas Vesalius (1514-1564) wrote and depicted his findings about human intervertebral disk spaces and the spinal column in “*De humani Corporis Fabrica*” (1543)¹² ¹³. The second person, after Caelius Aurelianus, who discussed sciatica in depth as a clinical entity was Domenico Cotugno (1736-1822). His monograph “*De ischiade nervosa commentarius*”¹⁴ described this radiating pain as a disease of the sciatic nerve. For at least a century sciatica was known as “*Cotugno’s disease*”¹⁵. He (figure 3) did not relate the disease of the sciatic nerve to compression of the root in the spinal canal or to the plate drawings of disks by Vesalius. In the belief that the pain arose from the nerve itself, Cotugno probably was not aware of a possible relationship.



Figure 3.

“For it seems to be an acrid and irritating matter, which lying on the nerve, preys on the stamina, and gives rise to pain”.

Domenico Cotugno 1764

Localization of neurological complaints or deficit and their anatomical correlation with the spinal cord and cauda equine was of no concern to scientists after Hippocrates. In the 18th century this problem was a primary concern for the first time when Giovanni Morgagni (1682-1771) described neural tissue compression caused by “tumors”, which in fact were probably cases of Pott’s disease¹⁶. Spinal surgery for this reason was not performed until 1829 when Alban G. Smith performed a laminectomy in the United States¹⁷. An anatomical relationship between sciatica and compression of nerve roots in the spinal canal was still not suspected by the scientific community, not even after the earliest report of posterior displacement of intervertebral disk material in 1806 by Kocher¹⁸. During post mortem investigations the latter scientist suspected the correlation between disk displacement at the spinal cord level and loss of function below this level.

Rudolf Virchow (1821-1902) described the traumatic rupture of an intervertebral disk in 1857¹⁹ which was known thereafter as “Virchow’s Tumor”²⁰. A few year later in 1864 Ernest Lasègue (1816-1883) recognized the association between sciatica and low back pain and wrote about the physical signs of patients’ neuritis²¹⁻²³. However, while living in the same time period and scientifically interested in closely correlated pathology, the completely different scopes of the works of Ernest Lasègue and Rudolf Virchow prevented the recognition of one disease. It was at least a half a century later before this relationship was described.

In 1909 Fedor Krause described (figure 4) the surgical relief of sciatic pain²⁴. Together with Oppenheim, he reported on the removal of an “enchondroma”, which in retrospect can be regarded with certainty as a ruptured disk.

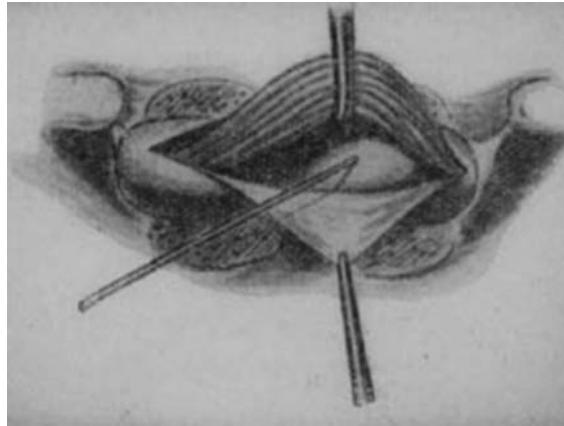


Figure 4. Surgical transdural approach of 'disk enchondroma' by Dr. Oppenheim as described by Fedor Krause, 1909. "He made a low lumbar midline incision and reflected the paravertebral muscles far laterally exposing the laminae with their spinous processes. The laminar arches were removed in one piece, after which the dura was opened longitudinally, nerve roots separated and again opening the dura but now the posterior dural sac covering the space-occupying lesion. This so-called enchondroma, a tumor of cartilaginous tissue had a close relationship with the lumbar disc and seemed to originate from it".

In the same year Taylor described an unilateral approach performed on a cadaver²⁵. Joel Goldthwait (1911)²⁶ reported on a patient with recurrent sciatica who had been operated on by Harvey Cushing²⁷. No lesion was found but they concluded that the pain originated from recurrent disk dislocation into the spinal canal, explaining the negative surgical exploration by assuming that the disk had slipped back into place. Goldthwait, who hypothesized that this condition could produce sciatica, was with far in advance of his time but failed to arouse much interest. Looking at his manuscript today, his honest description of the negative exploration by Cushing resembles the experience of many surgeons today, despite the help of sophisticated imagery. Four years later Charles Elsberg (1915) surgically removed a piece of ruptured ligament of "subflavum" which was compressing the fourth lumbar nerve root; the sciatica then disappeared^{28;29}.

Walter Dandy introduced air myelography in 1918 for the diagnosis of space-occupying brain lesions. It never worked well for spinal pathology but it was a big step forward in neuro-imaging after the discovery of the X-ray in 1895 by William Conrad Roentgen³⁰. In 1920 an assistant of the French neurosurgeon Sicard injected Lipiodol into the subarachnoid spaces by mistake. After this "mistake" they observed the patient in the vertical position under the fluoroscope and to their surprise saw the first myelogram; they described lesions compressing lesions the dural sac³¹.

In 1927 Putti suggested that sciatica was caused by an inflammation of the lumbar nerve roots in the spinal neuroforamina^{32;33}. He thought that the pain was second-



Figure 5. Dr. William Jason Mixter, neurosurgeon

ary to irritation caused by arthritis of the posterior intervertebral articulations. In addition to the fact that his conclusions were far ahead of his time, he was the first to conclude that sciatica could be explained by degenerative low back disorders and not by a tumor.

In the same period Walter Dandy 1929 found cartilaginous fragments (extruded and sequestered disk material) lying loose in the spinal canal. He discovered that these nodules were of disk origin and could produce sciatica³⁰. He thought that the “lumbar disk syndrome” was related to trauma and that the disk was affected by a process he called osteochondritis desiccans with fragments acting as a sequester. His drawings are beautiful examples of a herniated disk. In his opinion the lumbar spine had a predisposition toward such pathology because of a deficiency of the posterior longitudinal ligament in this area. At that time neurosurgical and orthopedic societies were still convinced that nerve root compression was caused by a benign tumor, whereas neurological and rheumatological literature did focus on an inflammation of the sciatic nerve.

However Dandy stated that removal of these masses would cure the pain and improved function. Unfortunately he still called these masses “tumors”, which in a strict sense they are, but this did not result in a scientific breakthrough. In the same year this observation was also reported in Paris by the neurologist, Alajouanine, who successfully guided a famous general surgeon, Petit Dutailis, who used a transdural approach for a “disk tumor” at the level L3-L4³⁴⁻³⁶.

Shortly thereafter the German pathologist Schmorl (1931) described his findings on the anatomy and pathology of disks investigated by radiological examination of post-mortem dissection of spines³⁷. These descriptions established modern understanding of degenerative changes and disk herniations.

A neurosurgeon, William Jason Mixter (figure 5), and an orthopedic surgeon, Joseph Seaton Barr, working close together presented their surgical and pathology

findings and conclusions at the annual meeting of the New England Surgical Society in September 1933⁴. Barr was assigned to review Schmorl's German book³⁷ and had great interest in the histology of the disk. After treating a sciatic patient conservatively without success, he performed a Lipiodol myelogram and convinced Mixter to perform surgery. During surgery a "disk tumor" was removed. The patient did well and Barr asked the pathologist to review the slides together. He immediately recognized the microscopic pictures as being nucleus pulposus shown by Schmorl in his photographs. They reviewed cases which in recent years had been depicted as chondroma's and related diagnoses. Their publication the next year in 1934⁴ convinced the world that sciatica is not caused by a tumor, but that a simple herniation of the nucleus pulposus gives rise to compression of the nerve root. This publication changed the treatment of sciatica. The message was to relieve sciatica by surgery and that the results obtained were very satisfactory if compression had not lasted for too long a period. Most scientific societies adopted this view. Farfan even stated that the "Dynasty of the Disk" had started⁵. After this breakthrough publication, lumbar discectomy became and remained the most frequently performed neurosurgical intervention worldwide. In the Netherlands the first disk surgeries were performed not earlier than after 1937^{38;39}. From that time until 1983⁴⁰ a major question did not arise.

What is the appropriate conservative treatment strategy and how long should this period of natural cure last before surgery is discussed with the patient?

In retrospect however Ernest Hunt questioned the publication directly in the same journal in 1934⁴, asking whether the extensive transdural approach described by Mixter and Barr could be replaced by displacement of the dura and nerve root medially. Moreover he asked whether most patients really needed to undergo surgery.

"I should think there might be a question as to when we should consider that lesion important enough or large enough to justify the rather severe operation of laminectomy; that is to say, are there instances in which with the passing of time nature would take care of it without the necessity of operation with attendant risk, which was apparently five percent in this group?"

Comment Ernest Hunt (N. Eng. Journal 1934)

As expected his latter comment had little impact on society compared to the fact that surgery was a safe and effective option for sciatica. It was suddenly a curable disease in the hands of surgeons.

The direct comparison between surgery and conservative treatment has only

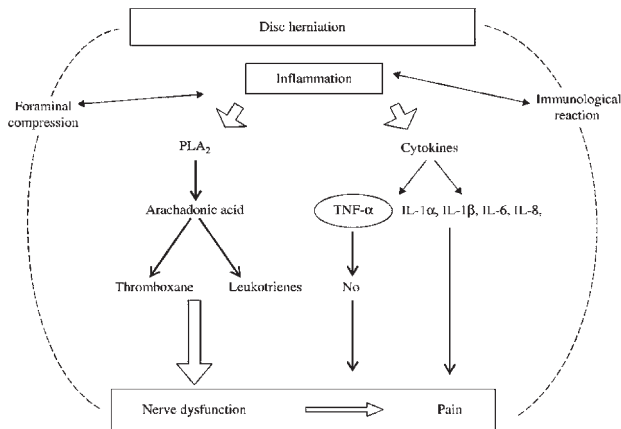


Figure 6. Adapted with permission from Stafford et al. 2007

been described properly once in a randomized trial performed by Henrik Weber⁴⁰. Although the study received considerable methodological criticism, it is still only one of the few trials which tried to directly compare surgery versus conservative treatment. The well known favorable natural course of sciatica and innovative findings with regard to the pathogenesis⁴¹ changed scientific ideas about the treatment of sciatica to a more conservative and medical approach again. In well designed experimental and clinical studies strong evidence was found of an inflammatory response by nuclear disk tissue on lumbar nerve roots, causing sciatic neuralgia by a local release of phospholipase A2 (PLA-2), leukotrienes or cytokines, such as various interleukins (IL) and tumor necrosis factor- α (TNF- α)⁴² (figure 6).

Although apparently very attractive to direct treatment to the chemical or immunological pathogenesis of sciatic neuralgia, randomized controlled trials, investigating treatment by corticosteroids⁴² and anti-TNF- α ⁴³ failed to show beneficial short- and long-term effects of this potential hazardous medical treatment when compared with placebo.

Besides spontaneous cure surgery remains the only proven effective treatment option to directly resolve mechanical compression and hypothetically indirect chemical irritation of compressed nerve roots.

Still being the most frequent procedure carried out by neurosurgeons worldwide one would expect that lumbar disk surgery would be high on the agenda of scientific meetings as well as orthopedic and neurosurgical journals. This, however, is not the case, probably because lumbar disk surgery is considered to be highly effective, is not

very difficult to perform and most spine surgeons do not doubt the scientific basis of timing disk surgery after 6 weeks of persistent sciatica^{44,45}.

OBJECTIVE AND OUTLINE OF THIS THESIS

After the first description of surgery for sciatica in 1934⁴ and despite the warning about performing surgery too soon by Ernest Hunt, disk surgery increased in popularity with highly variable rates of surgery between countries in the last decade of the twentieth century⁴⁶. The main explanation for this difference rates of surgery rates is the timing of disk surgery per country⁴⁷. The United States and The Netherlands await the natural cure of sciatica for 6 weeks before surgery is considered, while for instance the United Kingdom and Sweden wait at least several months and offer surgery only after a prolonged period of conservative treatment without any result. Which timing strategy is the best is unknown and has not yet been investigated in a randomized trial; only a few observational cohort series have been described. Although the randomized Weber trial and recent SPORT trial^{48,49} compared surgery with conservative treatment, they were not designed to evaluate the current timing of disk surgery for sciatica.

The main objective of this thesis is to compare at random the effectiveness over one year and at two years of the timing of disk surgery after 6 to 12 weeks of sciatica with a strategy of prolonged conservative care for some months.

When a physician meets a patient with sciatica, information is gathered to predict the absence or presence of a disk herniation and to decide what the appropriate treatment strategy should be within the framework of the natural course. In **chapter 2** the actual state of the art of the diagnosis and treatment of sciatica is described.

Data that define the optimal timing strategy for sciatica are not available. Despite ample available epidemiological methods to compare at random surgery after 6 weeks of severe sciatica with conservative care and delayed surgery, such a trial had not yet been designed yet. In **chapter 3** the design is described of the Sciatica Trial, a randomized cost-effectiveness study to answer the question whether the current international guideline which recommends surgical intervention after 6 to 8 weeks of conservatively treated sciatica is supported by high level evidence.

Chapter 4 presents the short-term one year results of this randomized controlled trial, comparing early surgery with prolonged conservative treatment for patients with a clear surgical indication after 6 to 12 weeks of sciatica.

Before implementation of a new treatment algorithm can be considered, the results of epidemiological outcome research should be weighed against the direct and

indirect costs of the different treatment strategies compared. The results of this cost-effectiveness analysis are reported in **chapter 5**.

The presence of a positive straight leg raising test, neurological deficit, MRI appearances of the disk herniation and patient preference guide clinicians in their decision to plan surgery. A subgroup analysis of predictive variables and their interaction with the randomized surgical timing strategy is the main subject of **chapter 6**.

According to the study protocol conservative treatment could be followed by surgery after a delayed period of time following randomization. Persistent complaints of sciatica, despite adequate guidance and analgesics, were of major importance for the decision to perform late surgery. **Chapter 7** might be of great interest to patients and physicians who want to know early in the disease which variables affect the risk of delayed surgery.

Most intervention studies focus on good outcome. The societal impact of unsatisfactory outcome of low back disorders is however high. What is the one year prognosis for patients with sciatica of at least 6 weeks duration, which variables influence the outcome and does gender play a role? To answer these questions in **chapter 8**, all randomized patients of the Sciatica Trial are described as an observational cohort with an unsatisfactory result at one year as outcome of interest.

The goal of this randomized trial was to evaluate the timing of surgery and it's effect on speed of recovery. The high costs of low back disorders are however due to persisting, recurrent or deteriorating sciatica, chronic low back pain and the inability to work or perform daily duties. In **chapter 9** the 2-year results of this trial are described and contemporary scientific study results are compared with other studies on surgical timing.

A synthesis of the results in **chapter 10** includes our future scientific "quest" to define further the optimal timing of disk surgery for sciatica. The dissertation is concluded with a summary in **chapter 11**.