UNIVERSITY OF TROMSØ UIT

Faculty of Health Science, Institute of Clinical Medicine

Department of Orthopaedic Surgery

Retro-trochanteric sciatica-like pain

In-depth analyses of clinical symptoms, treatment options, histological and ultra structural findings in tendon biopsies

M. Khaled Meknas

A dissertation for the degree of Philosophiae Doctor

May 2010

UNN – We care – and share responsibility together

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CONTENTS

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LIST OF PAPERS

Paper I

Khaled Meknas, Anders Christensen, Oddmund Johansen (2003). The internal obturator muscle may cause sciatic pain; Pain 104: 375–380

Paper II

Khaled Meknas, Jüri Kartus, Jan Inge Letto, Magne Flaten, Oddmund Johansen (2009). A 5-year prospective study of non-surgical treatment of retro-trochanteric pain. Knee Surg Sports Traumatol Arthrosc; 17:996-1002

Paper III

Khaled Meknas, Jüri Kartus, Jan Inge Letto, Anders Christensen, Oddmund Johansen (2009). Surgical release of the internal obturator tendon for the treatment of retro-trochanteric pain syndrome: a prospective randomised study, with long-term follow-up. Knee Surg Sports Traumatol Arthrosc; 17:1249-56

Paper IV

Khaled Meknas, Oddmund Johansen, Sonja E. Steigen, Randi Olsen, Leif Jørgensen, Jüri Kartus (2010). Ultrastructural and histological characteristics of the internal obturator tendon in hip osteoarthritis and fracture of the collum femoris. Could tendinosis be involved in osteoarthritis*?* Submitted

The papers will be referred to in the text according to their roman numbers.

ABBREVIATIONS

AB/PAS	**A**lcian **B**lue/**P**eriodic **A**cid **S**chiff
CT	**C**omputerised **T**omography
ECM	**E**xtra-**C**ellular **M**atrix
ESWL	**E**xtracorporeal **S**hock **W**ave **T**herapy
FAI	**F**emuro-**A**cetabular **I**mpingement
FCF	**F**racture of the **C**ollum **F**emoris
GAGs	**G**lycos-**A**mino-**G**lycan**s**
H&E	**H**aematoxylin and **E**osin
MMP	**M**atrix **M**etallo**p**roteinase
MRI	**M**agnetic **R**esonance **I**maging
OA	**O**ste**o**arthritis
PRP	**P**latelet-**R**ich **P**lasma
TEM	**T**ransmission **E**lectron **M**icroscopy
VAS	**V**isual **A**nalogue **S**cale

INTRODUCTION

Pain localised in the hip region may be part of a symptom pattern pointing towards well-known diseases. Additional complaints, clinical findings and supplementary examinations such as standard radiographs and MRI might point towards treatable pathology in the back, hip and even the knee. In some cases, the pain may have serious consequences for a patient; however, it may be diffuse and with a pattern that is not readily understood and treatment attempts may not be successful. For many years, our institution has continuously encountered a patient group of this kind which complains of pain in the hip region of a diffuse yet serious character, without a clear diagnosis and often with a very long history of unsuccessful treatment attempts. These patients have often undergone radiographic examinations of the hip, to verify or exclude osteoarthritis (OA); they may have been examined for pathology in the back using MRI or CT; and some of them may have been operated on because of pathology indicating a spinal cause diagnosed by well-established diagnostic procedures. As reported in Paper I in the present thesis [1], a surgical study was performed, as we expected the so-called "piriformis syndrome" in a number of patients with unclear pathology after performing multiple radiographic assessments. During the surgical procedure, no pathology was found around the piriformis muscle and tendon. Exploration, however, revealed a clear pathology in all cases, consisting of a very tense internal obturator tendon, which had an impact on the sciatic nerve. The observation in Paper I justified a study with a conservative approach. The described technique for treating a supposed tense piriformis muscle conservatively is often based on the assumption that it changes from an outward to an internal rotating muscle when the hip is in flexion [2]. This may not apply to the internal obturator muscle. Future exploration of the influence of the internal obturator muscle and tendon on the motion pattern of the hip joint is indicated in order better to understand what in fact constitutes the "piriformis syndrome" and how our findings are related to that syndrome.

Disc herniation

Low back pain is very common and the number of cases with additional sciatic pain is low in comparison. Compression of a nerve root is one of the most common causes of sciatica; a herniated disc is compressing the root in 90% of cases [3]. Other possible causes of sciatica include lumbar spinal stenosis and, more rarely, tumours or cysts. Typical dermatomal distribution of pain which worsens on coughing, sneezing or straining, increased finger-floor

distance and sensory symptoms, such as numbness or paresthesia, are significant predictors of nerve root compression in patients with low back pain radiating distally into the leg [4].

Medical history and physical examination are the mainstays of sciatica diagnosis. The straight leg raising test or Lasegue's test is a commonly used test in patients with suspected sciatica. In addition, changes in the Achilles and patellar tendon reflexes, reduced strength in the big toe, ankle and knee are typical signs in patients with nerve root compression. The distribution of pain radiating in the lower limb, a characteristic and definitive feature of the condition, can be evaluated using pain drawings [3]. Disc herniation is reported in 20-36% of individuals without symptoms of sciatica or low back pain and, furthermore, many patients with clinical symptoms of sciatica do not display lumbar disc herniation on imaging [3]. Conservative treatment strategies for disc herniation are primarily aimed at pain reduction, either by using analgesics or by the non-surgical reduction of pressure on the nerve root using traction, spinal manipulation or physiotherapy, for example. Conservative treatment regimens are currently the first-line option for patients with sciatica. The adequate management of pain and an active approach, with patients being reassured and advised to continue their daily activities as much as possible, is the preferred treatment strategy [5].

If the patient has not improved after 6-8 weeks of treatment, imaging should be considered to determine whether a herniated disc with nerve root compression is present. Surgery may be needed to relieve the pressure on the nerve root. There are several surgical methods to treat disc herniation; they include discectomy, microdiscectomy, microendoscopic discectomy, transforaminal endoscopic discectomy and chemonucleolysis. The cauda equine syndrome is an absolute indication for immediate surgery, but elective surgery is the treatment of choice for unilateral sciatica [3].

Lumbar spinal stenosis

Lumbar spinal stenosis is defined as a narrowing of the spinal canal. In some patients, this condition becomes symptomatic. The classic presentation is that of bilateral neurogenic claudication, defined as intermittent pain radiating at varying degrees to the buttocks, thigh and leg, which gets worse with prolonged standing, walking, or lumbar extension [6].

However, many individuals remain asymptomatic and radiographic findings do not necessarily correlate with clinical symptoms. Lumbar spinal stenosis occurs with normal vertebral alignment, while some patients also suffer from concomitant degenerative "spondylolisthesis", which is defined as the forward slipping of one lumbar vertebra in relation to another with an intact neural arch. In most cases, "spondylolisthesis" affects the

L4-L5 level. It commonly occurs in patients over the age of 50 and affects females six times more frequently than males. Degenerative spondylolisthesis is generally asymptomatic, but it can be associated with symptomatic lumbar spinal stenosis and radiculopathy [6].

Treatment options are either non- surgical methods or surgical intervention depending on the severity of the stenosis and the number of levels involved. Surgical fusion and laminectomy are the methods most commonly used to treat spinal stenosis [6].

The management of degenerative lumbar disease is demanding. Conservative treatment consisting of oral pain medication, epidural corticosteroid injections, traction and spinal manipulation has been described with varying results. Surgery may be necessary when the patient has symptoms due to either instability or neurological compression [5].

Tendinitis/tendinosis/tendinopathy

Tendons function to transmit muscular force across joints, resulting in body movement and joint stabilisation. Tendons are primarily composed of collagen, proteoglycans, water and cells. The predominant constituent is collagen, which makes the tendon ideally suited to withstand and transfer tensile loads. Ninety-five per cent of the collagen content is type I, while the remaining 5% is type III and IV. The predominant cell type is the tenocyte, which synthesises and supports the tendon matrix. Vascularity within the tendon is relatively sparse and corresponds to the low metabolic turnover rate of these tissues [7].

Tendinitis is an inflammation in a partially torn tendon. The tendon damage occurs through acute and chronic injury. An acute injury disrupts vascular tissues within the tendon and results in a well-studied healing process involving three phases: inflammation, repair and remodelling. The first phase, inflammation, occurs as a haematoma forms from erythrocytes and activated platelets. This is followed by the infiltration of inflammatory cells, including neutrophils, monocytes and macrophages that migrate to the injury site to remove debris. Shortly afterwards, chemotactic signals induce fibroblasts to start synthesising collagen. The second phase, repair, is highly vascular and cellular and involves the deposition of collagen and tendon matrix components. During the final phase, remodelling, the vascularity and cellularity of the injury site decrease and the collagen becomes more structured and organised. The injured site never achieves the original histological or mechanical features of a healthy uninjured tendon. Tendinitis develops within a short time frame, as a result of a single traumatic episode. After the initial traumatic episode, the term “tendinitis” wrongly continues to be used clinically to describe any painful condition of the tendon. Instead, accurate histological and pathophysiological terminology should be used [7].

The term “tendinosis” is used in histological descriptions to indicate degenerative changes without inflammatory cells but with changes such as collagen fibril disorientation, rounding of tenocyte nuclei, increased ground substance, hypervascularity and increases in proteoglycan content in the histological specimen [8-10]. Tendinosis refers to the intratendinous degeneration that is thought to be a result of chronic overuse and it requires a more prolonged time frame than tendinitis to develop.

“Tendinopathy” is a term that is commonly used in chronic tendon disorders and is a broad, overarching term referring to any abnormal condition of the tendon when the patient seeks help as a result of pain.

The terminology when discussing tendon pathology is fairly confusing. It is, however, generally accepted that an inflammation plays a role only in the initiation, but not in the propagation and progression, of common tendon disorders [8].

In particular, tendons are more elastic at low strain rates and stiffer at higher rates of tensile loading. Accordingly, the rate of tissue loading can influence the injury pattern of a tendon. Total tendon strains (percentage deformity) of 1% to 2% result in the straightening of the crimp pattern of unloaded tendon collagen. Strains of 2% to 6% are well tolerated by most healthy tendons. With a strain higher than 6%, incomplete tears start to occur within the tendon. Complete structural failure typically occurs in the range of 8% to 10% [7].

Tendon microtrauma can also result from non-uniform stress occurring within a tendon, producing abnormal loading concentrations and localised fibre degeneration. There is empirical evidence that a repeated load associated with athletic activity leads to tendinopathy.

The common injury sites include the Achilles, patellar, rotator cuff and thigh adductor tendons [8]. An impingement theory of tendinopathy has also been suggested, in addition to the vascular theory that suggests that tendons generally have a poor blood supply [8].

Recently, some interest has focused on the role of the nervous system in the tendinopathy process. Neurally mediated mast cell degranulation could release mediators such as substance P and calcitonin gene-related peptide. Substance P, a pro-inflammatory mediator, is definitely increased in rotator cuff tendinopathy [8]. Larger amounts of the neurotransmitter glutamate have been identified in the ultradialysate in Achilles tendinopathy compared with normal tendons [11]. However, the neural theory does not explain why morphologically pathological tendons are not always painful [8].

When tendinopathic specimens were histologically analysed in one study, no inflammatory cells were found. However, it is presumed that a chemical inflammatory response as

cytokines and prostaglandins and an angina-like effect in the tissue, can be pain producers in different ways in tendinopatically changed tendon [12].

Tendon degeneration and retro-trochantric pain

The examination of the histological and ultrastructural characteristics of the peri-articular tendons in the hip region could be one way of better understanding the patho-physiological process in this area.

Degenerative tendon disorders and overuse injuries in sports and repetitive occupational activities are major problems in the general population, as well as being difficult to treat [8;13]. A better understanding of the cellular interaction during tendon injury and degeneration may help to increase the opportunity to treat the condition.

Magra et al. [14] stated that the interaction between the various intrinsic and extrinsic factors and the genetic "make-up" of an individual may increase the likelihood of one individual developing tendinopathy compared with another. They speculated that gene therapy might prove to be an effective method to aid tendon healing. The morphological changes in tendinopathy have been analysed in several studies [15-19] including the shoulder [19-22], elbow [10], patellar and Achilles tendons [23-28]. However, there is limited information in the literature in terms of the ultrastructural and histological changes in the tendons in the hip and gluteal region. Lempainen et al. [29] confirmed tendinosis using histological analysis in 103 cases of proximal hamstring tendinopathy in athletes. Grimaldi et al. [30] used magnetic resonance imaging (MRI) and showed a significantly smaller piriformis muscle in patients with hip OA compared with patients with non-osteoarthritic hips, while Broadhurst et al. [31] found an abnormal piriformis morphology in a significant number of patients with chronic buttock pain using ultrasonography. Lequesne et al. [32] studied the correlation between MRI findings and clinical and surgical findings in "refractory greater trochanteric pain syndrome". They found tears in the gluteus medius and minimus tendons and they introduced the term "hip rotator cuff syndrome" [33]. Pathology in the short rotators of the hip is regarded as a possible source of retro-trochanterically located sciatica-like pain [34] and it was suggested that the overuse of the piriformis muscle contributed to the ''piriformis syndrome" [35]. Recently, the approach to symptoms from the hip joint has become more active. The opportunity to perform hip arthroscopies and address pathology such as labral lesions and FAI syndrome has increased the potential for treating symptoms from the hip joint before it is subjected to joint replacement surgery [36-38].

Some authors suggest that pain in the osteoarthritic joint may be caused by the spasm and pressure in the surrounding muscles and tendons towards the joint capsule, which is richly innervated [39;40].

Theoretically, the pathology in the short rotator muscle tendons could contribute to the symptoms experienced by patients with osteoarthritic hips or degenerative lumbar disease. Treatment of the tendinosis in patients with mild and moderate OA might therefore be an option in order to reduce the symptoms. The overall incidence of retro-trochanteric pain is unknown, as it is often an exclusion diagnosis.

Osteoarthritis

Osteoarthritis (OA) is the most common form of arthritis and a leading cause of chronic disability. OA characterised by joint pain, tenderness, limitation of movement and a varying degree of inflammation is most common in the hip, knee and hand joints.

Synovitis is an intrinsic component of OA, which becomes more extensive as the disease progresses. It may not be apparent clinically, but it can be detected by arthroscopy, MRI and ultrasound. Synovitis may contribute to the progression of cartilage degradation [41].

The conservative treatment for hip and knee OA includes physiotherapy with an exercise and muscle strengthening programme, cryotherapy, or orthotic management such as footwear or bracing. Furthermore, pharmacotherapy with NSAIDs and analgesics is extensively used in clinical settings, as are intra-articular injections with corticosteroids.

However, the treatment of choice for advanced hip and knee OA in elderly patients is still arthroplasty [42].

Piriformis syndrome

The piriformis muscle originates from the anterior surface of the sacrum and inserts into the upper part of the greater trochanter, passing out of the pelvis through the greater sciatic notch. Contracture of the piriformis muscle has been thought to cause the “piriformis syndrome”, with a well-known clinical picture with sciatica-like symptoms [35].

Back in 1928, Yoeman [43] reported that sciatica might be caused by a periarthritis involving the anterior sacroiliac ligament, the piriformis muscle and the adjacent branches of the sciatic nerve. In 1947 [44], Robinson introduced the term “piriformis syndrome”. The incidence of ‘‘piriformis syndrome’’ among patients with low back pain has been reported to be 5-36% [45;46]. One MRI imaging paper has shown a lack of nerve root compression in the lumbar

spine in spite of symptoms of sciatica in 16.4% of the patients in a cohort paper and 4.9% of them were found to have the “piriformis syndrome” [47].

It has been argued that the piriformis muscle may irritate the sciatic nerve due to an anatomical abnormality such as a hypertrophic muscle. The entrapment and irritation of the sciatic nerve in the hip region has been largely thought to be influenced by the piriformis muscle. Anatomical variations such as a bipartite piriformis muscle [48;49] and the piriformis muscle lying anterior to the nerve [50] have been described as irritating the sciatic nerve.

The etiology of “piriformis syndrome” is not clearly known, although it has been argued that the pain syndrome may be caused by trauma to the pelvis or buttock [35;51], in addition to anatomical abnormalities of the piriformis muscle, as mentioned above [48;49], or as a recurrent problem after spinal surgery [52]. Adhesions between the piriformis muscle and the sciatic nerve have been reported by Benson et al. [51]. Cox et al. [34] argued that the gemelli-obturator internus muscles and the associated bursa should be regarded as possible sources of retro-trochanterically located sciatica-like pain. Overuse of the piriformis muscle was suggested to contribute to the ‘‘piriformis syndrome’’ by Mayrand et al. [35]. The ‘‘piriformis syndrome’’ has also been reported as a complication following hip replacement surgery [53;54].

There are no laboratory or radiographic methods for diagnosing the syndrome [55-60], and there are a few reports in the literature regarding electrophysiological analysis [61;62].

A number of methods exist for the treatment of the ‘‘piriformis syndrome’’ in the hip region. They include physiotherapy [2;34;35], extracorporeal shock wave therapy (ESWT) [63;64], injections with platelet-rich plasma (PRP) as used in other tendinopathies [65;66], injections of anaesthetic agents with or without steroids [52;67-69] and the surgical release of the tendon [1;51;70]. A surgical tenotomy to relieve the nerve from the pressure of the tense muscle has resulted in immediate pain relief [48;50;52]. Dezawa et al. [71] even described an arthroscopic technique for the release of the piriformis tendon.

Obturatorius internus syndrome

The obturator internus muscle is located inferior to the piriformis and arises within the pelvis. It originates at the medial surface of the pubis, covers the obturator foramen and passes through the lesser sciatic notch to insert onto the greater trochanter laterally.

There are 6 external rotator muscles of the hip: the piriformis, superior gemellus, obturator internus, inferior gemellus, obturator externus and quadratus femoris. They are in close

anatomical proximity to one another and they work as a functional unit as a triceps muscle [57].

The tendon of the piriformis muscle was found to have fused with the internal obturator tendon in 48 of 112 cases in an anatomical study [72], which can indicate a strong interaction between the piriformis and internal obturator muscles and the sciatic nerve, and it also runs parallel to the piriformis muscle in its attachment to the trochanter major. Pathology in the internal obturator muscle may be obscured by the complex anatomy in the region. Because of its proximity and similarity in both structure and function, most treatment for the “piriformis syndrome” also affects the internal obturator [46].

AIMS OF THE STUDY

The initial aim of this work was to clarify the role of the so-called ”piriformis syndrome” in patients with retro-trochanteric pain. Observations in Paper I provided a broader perspective, with the internal obturator muscle and tendon possibly playing a role in the syndrome. Additionally, modifications of treatment of the “retro-trochanteric pain syndrome” evolved as equally important aims.

The specific aims of the four individual studies included in this thesis were as follows:

- To evaluate the short-term results after surgical treatment in patients with the so-called “piriformis syndrome”

- To evaluate the medium-term results of conservative treatment of patients with retro-trochanteric pain syndrome using a specific stretching programme

- To evaluate the long-term results for the patients included in Paper I

- To evaluate the ultrastructural and histological characteristics of the internal obturator tendon in patients with hip OA and in patients with a fracture of the collum femoris (FCF)

DESIGN AND DEMOGRAPHICS OF THE STUDIES

Table 1. Patient allocation

	Number of included patients	Comments
Paper I	6 surgically treated patients and 6 controls	All 9/12 patients were also included in Paper III
Paper II	13 patients	
Paper III	4 surgically treated patients and 5 controls	All 9 patients were also included in Paper I
Paper IV	10 patients with OA and 10 patients with FCF	

Paper I

Twelve patients (three males and nine females), mean age 47 (25-66) years, with retro-trochanteric pain in the buttock, radiating distally to the knee and intolerance to sitting more than 40 min, were included in a prospective, randomised study with either surgical or no treatment. Sealed envelopes were used during the randomisation procedure. The median duration of symptoms was 7.5 (2-20) years and all the patients had undergone various conservative treatments before inclusion in the study. The patients were followed for six months and they were repeatedly questioned about pain and examined during the follow-up period.

Paper II

Thirteen patients (one male and twelve females), mean age 49 (36-61) years, who had localised retro-trochanteric pain in the hip region, which spread diffusely down the lower extremity, were included in this conservative treatment study. The median duration of the symptoms was 8 (1-20) years. The patients had made previous attempts at conservative treatment such as physiotherapy, non-steroidal anti-inflammatory drugs and injections of local anaesthetic agents in combination with corticosteroids. None of the patients had previously undergone an extended period of physiotherapy aimed at stretching and relaxing the internal obturator muscle. All the patients had to wait for a minimum of six months between inclusion in the study and the start of the treatment. During that time period, no patient improved spontaneously and their symptoms remained unchanged.

Paper III

This is a long-term report on the twelve patients included in Paper I. Nine of twelve of the initial patients from Paper I could be followed up in Paper III.

Paper IV

The material in Paper IV consisted of tendon samples from the short external rotators of the hip, e.g. the internal obturator muscle, obtained during open surgery at the time of total hip replacement in 10 consecutive patients with OA of the hip; median age 60 (48-75) years. Samples from 10 consecutive patients with FCF (Garden III or more), median age 82.5 years (60-85), who also underwent a total hip replacement, served as controls. A minimum of two samples were obtained from each patient.

METHODS

Clinical examination

The pain was classified using a visual analogue scale (VAS) graded from 0-10, where 0 indicated no pain and 10 indicated the worst possible pain. The patients were tested for pain and weakness on resisted abduction and external rotation of the thigh in a sitting position; the Pace sign, which was categorically classified by the patient as positive (pain) or negative (no pain) (Figure 1). Correspondingly, the Freiberg sign for pain and weakness on forced passive internal rotation of the extended thigh was used and it was also categorically classified by the patient as positive (pain) or negative (no pain) (Figure 2).

All these tests are poorly validated despite they are frequently used in the clinical setting.

Buttock and leg pain during passive straight leg raising performed by the examiner (Lasegue's sign) was classified as positive if the patient reported that radiating pain occurred before 60° of hip flexion.

Limping and tenderness at palpation were performed and categorically classified by the examiner and the patient respectively as either positive or negative. The patients' sitting and walking ability was classified by the patients according to five-grade scales.

The use of analgesic and anti-inflammatory drugs for each patient was classified using a five-grade scale. Zero points represented no drugs, one point represented paracetamol irregularly, two points paracetamol/codeine or NSAID regularly, three points paracetamol/codeine and NSAID regularly and four points paracetamol/codeine and additionally buprenorphin, tramadol or morphine. These evaluations were made at the start of the study, at 6 months and at 8 years in both the surgical and the control group.

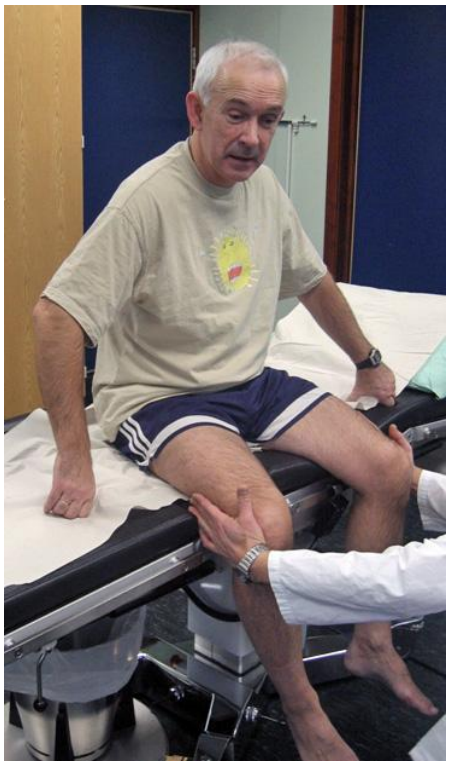

Figure 1. Pace's sign. The patient is in the sitting position. During resisted abduction and external rotation of the thigh, the small rotators of the hip are stretched. The test is classified as positive if pain is registered (illustration photograph).

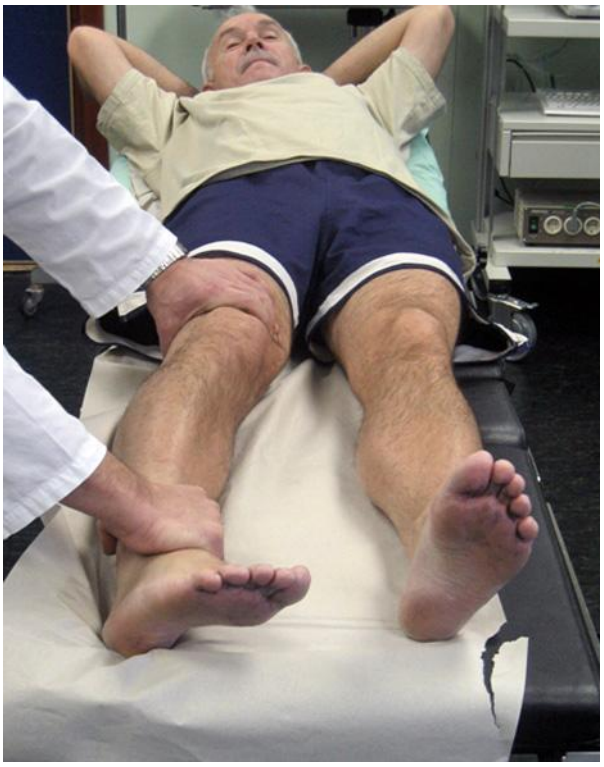

Figure 2. Freiberg's sign. The patient is in the supine position with the thigh extended. The leg and thigh are passively internally rotated by the examiner. The test is classified as positive if pain is registered (illustration photograph).

Radiographic assessments

The patients in Papers I, II and III underwent standard antero-posterior radiographs of the pelvis and hips, a lateral view of the hips (bilaterally) and either CT using a Siemens Somatom Sensation (Siemens AG, Erlangen Germany) or MRI using a Philips Intera 1.5 Tesla (Royal Philips Electronics, Amsterdam, Netherlands) of the lumbar spine. The examinations were performed to rule out the possibility that the symptoms experienced by the patients in Papers I, II, and III originated from the spine or the hip joint.

All the radiographic assessments were performed by an experienced radiologist following standard evaluation protocols for the examinations. However there were no specific intra- or inter-observer classifications were performed.

Non-surgical rehabilitation programme

In Paper II, all the patients were hospitalised at the Rehabilitation Centre of North Norway for a four-week supervised rehabilitation programme. They participated in two daily treatment

sessions of approximately 30 minutes each. The exercise programme in the present paper aimed at reducing the tension in the internal obturator muscle. The exercise programme was designed to be simple to teach, remember and perform both at the clinic and subsequently at home without supervision. It aimed to stretch the muscles around the hip by separate active and passive abduction, flexion and extension exercises (Figure 3 A-D). During abduction and flexion of the hip, the knee was kept extended (Figure 3A and C). During extension of the hip, the patient grasped his/her ankle and helped force the knee into flexion, while keeping the body in an upright position (Figure 3B). Two additional exercises were also included for the treatment of the small external rotators. One was a combined forced passive internal rotation with additional pressure towards hip flexion and adduction (Figure 3D). The other was direct massage of the insertion of the small external rotators by a therapist. All these exercises were performed for 15-30 seconds at a time and repeated 5-15 times, depending on the ability of the patient to tolerate the stretching. If the pain was intolerable, that specific exercise was discontinued and the patient moved on to the next exercise. During the next session, a new attempt to tolerate that specific exercise was made. The patients were not denied access to other training activities, as they were accommodated at the rehabilitation centre, but they were only formally instructed and motivated for the specific programme.

Figure 3. The stretching exercises in flexion (a), extension (b), abduction (c) and a combined flexion, adduction and internal rotation position (d), copyright Ninni Sernert.

Surgical technique and postoperative management

In Papers I and III, an exploratory operation was performed using a postero-lateral approach in the hip region. The fascia lata was split and the external rotators and the sciatic nerve were identified. Examinations of the anatomy, as well as the relationships between structures during passive flexion and internal rotation, plus the Lasegue test, were made during the operation. The internal obturator muscle was found to be tense, hyperaemic and in close contact with the sciatic nerve (Figure 4A and B). The nerve was flattened and slightly hyperaemic. During the Lasegue manoeuvre performed on the operating table, the internal

obturator and not the piriformis muscle impinged on the sciatic nerve at an early stage during the hip flexion movement. To relieve the tension towards the sciatic nerve from the internal obturator muscle, a sectioning of the tendon was performed at its insertion to the greater trochanter. An immediate release of the tension towards the sciatic nerve during the Lasegue manoeuvre was observed after sectioning the tendon (Figures 5A and B). Prophylaxis against infection was administered intravenously using 2 grams of Cefalotin (ACS Dobfar Generics, Luxembourg) just before the operation. Weight-bearing supported by crutches was allowed immediately after surgery. A gradual increase in activity as tolerated by the patients was allowed. The patients underwent no formal sessions of physiotherapy.

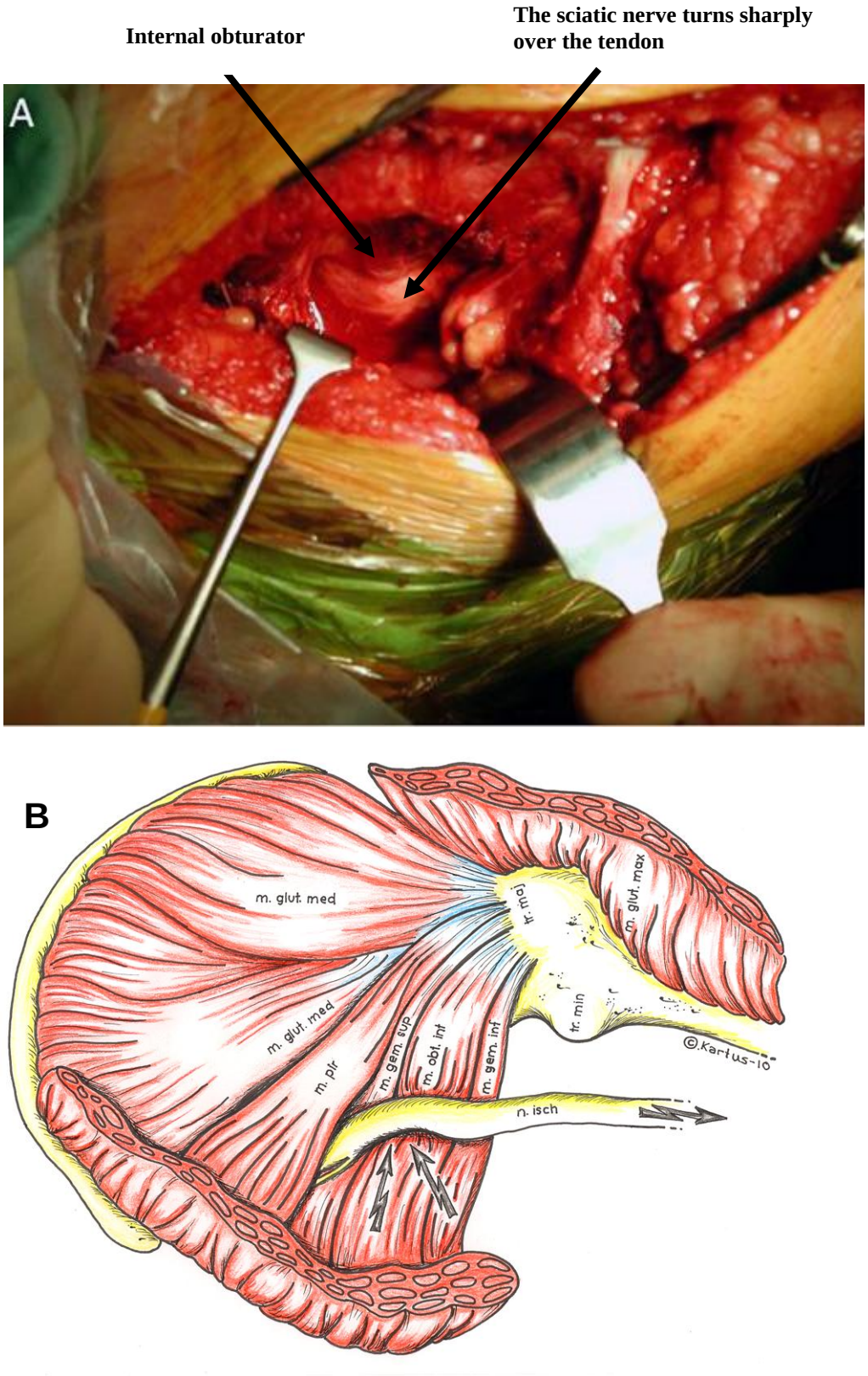

Figure 4. The sciatic nerve and the internal obturator tendon as found during an operation for retro-trochanteric pain syndrome. The internal obturator tendon is tense and hypertrophic, lying in close contact with the sciatic nerve, which turns sharply over the tendon. Figure 4 A is used and modified with permission from the IASP® (International Association for the Study of Pain®), originally published in Meknas et al [1]. Figure 4 B, copyright Catarina Kartus.

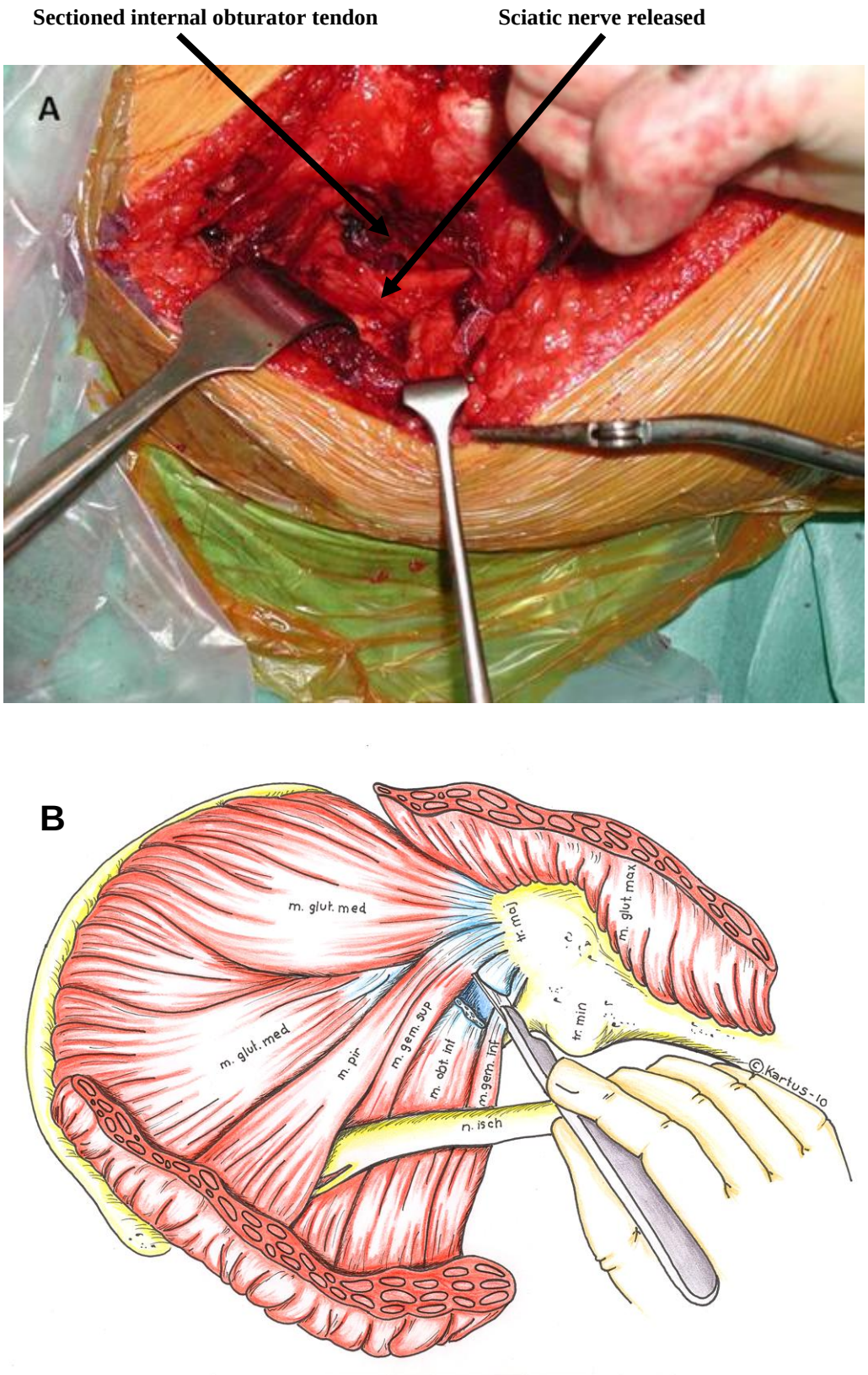

Figure 5. After sectioning the internal obturator tendon, the sciatic nerve is released from the tendon.
Figure 5 A is used and modified with permission from the IASP® (International Association for the Study of Pain®), originally published in Meknas et al. [1]. Figure 5B, copyright Catarina Kartus.

Biopsy procedure

In Paper IV, the biopsies were obtained in an open fashion during total hip replacement using a postero-lateral approach in the hip region. The fascia lata was split and the external rotators and the sciatic nerve were identified. Before entering the intra-articular area, macroscopic biopsies from the short rotator (internal obturator tendon) were taken using a standard surgical knife.

Histological analysis

The samples destined for light microscopy were fixed in 4% formalin, embedded in paraffin blocks and sectioned at 4-5μm. The sections were stained with haematoxylin-eosin (HE), to evaluate the fibre structure, cellularity and vascularity, and with Alcian Blue/Periodic Acid Schiff (AB/PAS), to detect sour/neutral mucins for glycosaminoglycans (GAGs). Furthermore, the Perl, van Gieson and van Kossa stains were performed to identify hemosiderin, collagen and calcium deposits respectively. The fibre structure, cellularity, vascularity and the presence of GAGs were classified according to a semi-quantitative scoring system (Table 2) [73]. The staining for hemosiderin and calcium deposits was dichotomously classified as positive/negative. All biopsies were evaluated by two independent, experienced pathologists.

Table 2. Evaluation of biopsy samples with a semi-quantitative 4-point scoring system

	Grade 0	**Grade 1**	**Grade 2**	**Grade 3**
Fibre structure	Straight, parallel, packed fibres, with slight waviness	Slight separation of fibres, increased waviness	Separation of fibres, deterioration of fibres	Complete loss of fibre structure and hyalinisation
Cellularity	< 100 cells/high power field (HPF)	100-199 cells/HPF	200-299 cells/HPF	> 200 cells/HPF
Vascularity	Vessels running parallel to the collagen fibre bundles in the septa	Slight increase in vessels, including transverse vessels in the tendon tissue	Moderate increase in vessels within the tendon tissue	Markedly increased vascularity with clusters of vessels
Glycosaminoglycans	No alcianophilia	Slight alcianophilia between the collagen fibres	Moderate increase in alcianophilia	Markedly increased alcianophilia forming blue lakes

Ultrastructural analysis

For the transmission electron microscopy (TEM) analysis, the specimens were fixed in 8% formaldehyde in Hepes buffer. The biopsies were cut into small cubes and half the material was immersion-fixed in McDowell's fixative for electron microscopic studies [74]. Ultrathin sections were mounted on formvar-coated 100 mesh copper grids and stained with 5% uranyl acetate and Reynold's lead citrate [75]. Micrographs were obtained using a Jeol JEM 1010 (Tokyo, Japan) with a Morada camera system (Olympus Soft Imaging Systems, Münster, Germany).

For sampling, two blocks from each patient were sectioned and mounted on carbon-coated formvar films on copper grids.

Micrographs for measuring the fibril diameters were obtained at random, from one to three groups of cross-sections from each block. At a magnification of x 50,000, a minimum of 100 fibril diameters were measured using the Soft Imaging System (Olympus, Münster, Germany). The relative fibril diameter distribution was calculated in percent. The morphology of the extracellular matrix (ECM) was evaluated and dichotomously classified as homogeneous or irregular at a magnification of x 3000. One experienced technician evaluated all the micrographs.

Statistical Methods

Paper I

Wilcoxon's paired samples rank sum test was used to test the outcome of the treatment of pain. A p-value of $p < 0.05$ was considered statistically significant. Median values are reported, apart from age, where the mean value is used.

Paper II

All values are reported as median values unless otherwise indicated. Wilcoxon's paired samples rank sum test was used for the longitudinal comparisons. A p-value of $p < 0.05$ was considered statistically significant.

Paper III

The power analysis was performed before the start of the long-term follow-up using the data collected from the short-term Paper I. The decrease in pain in the treatment group as measured with the VAS was the primary variable.

It was hypothesised that there would be a mean long-term decrease in the pain score of 3 on the VAS, with a standard deviation of 1.5, compared with the preoperative values. With the alpha value set at 0.05 and the power at 80%, the required sample size would be four patients in the treatment group. Based on these calculations, it was decided that the six patients enrolled in each study group in Paper I were sufficient to justify the long-term paper.

Mean standard deviation (SD) values are reported for the VAS and median (range) values for the other variables. The repeated measures ANOVA test and Fisher's post-hoc test were used to analyse the change over time in terms of the VAS for pain within the study groups. For all other ordered variables, within-group comparisons were made using the Wilcoxon's paired samples rank sum test. Dichotomous variables were analysed using Fisher's exact test.

Paper IV

Median (range) values are presented. The Mann-Whitney U test was used for comparisons between the OA and FCF groups. The within-group comparisons were made using the Wilcoxon's paired samples rank sum test and the dichotomous comparisons were made using Fisher's exact test. A p-value of < 0.05 was regarded as statistically significant. The comparison of the fibril diameter distribution was performed at group level and involved 1,145 fibrils in the OA group and 1,215 fibrils in the FCF group.

Ethics

All the studies were approved by the regional ethics committee of northern Norway.

SUMMARY OF PAPERS

Paper I

Twelve patients, three male and nine female, mean age 47 (25-66) years, with pain in the buttock, radiating pain distal to the knee, were included in a prospective, randomised study for either surgical or conservative treatment. The median duration of symptoms was 7.5 (2-20 years. Six patients were operated on in the hip region in an attempt to relieve pressure on the sciatic nerve. The piriformis muscle and tendon, as well as their relationship to the sciatic nerve, were found to be normal. However, the internal obturator tendon was found to be very tense, slightly hyperaemic and compressing the sciatic nerve; the nerve was slightly flattened where the obturator muscle was lying against it (Figure 4 A and B). To relieve the tension on the sciatic nerve from the obturator muscle, a sectioning of the tendon to the internal obturator muscle was performed at its insertion on the greater trochanter in all surgical cases. An immediate release of the tension in the sciatic nerve during Lasegue's test was observed after sectioning the tendon (Figure. 5 A and B).

The median pain score was reduced from the preoperative value of 8.5 (7-10) to 3.5 (0-9) at 6 weeks ($p < 0.05$), 3.5 (0-10) ($p < 0.05$) at 3 months and 5.5 (0-10) at 6 months (n.s.) postoperatively (Table 3). No significant reduction in pain was found in a control group. There was a tendency towards a lower consumption of drugs in the surgical group at 6 months. This tendency towards lower drug consumption was not found in the control group.

Conclusion

A syndrome clinically similar to the "piriformis syndrome" has been described. It was observed during the operation that the internal obturator tendon was lying against the sciatic nerve and impinged it. Sectioning the internal obturator tendon reduced the pain significantly at six weeks and three months. The reduction seen at six months was no longer significant.

Table 3. Pain as expressed on a VAS for patients in the surgical and control groups

Patient no	Pain Score			
	At inclusion	At 6 weeks	At 3 months	At 6 months
Surgical group				
1	9	9	10	10
2	9	5	5	8
3	10	1	2	8
4	7	5	5	5
5	8	2	2	2
6	7	0	0	0
Control				
7	8	1	1	9
8	4	1	1	7
9	9	6	6	7
10	7	7	7	7
11	8	8	8	5
12	5	5	5	4

Paper II

Thirteen patients (one male and twelve females), mean age 49 (36-61) years, who suffered from pain in the hip region, which spread diffusely down the lower extremity, were included in this conservative treatment study.

The median duration of the symptoms was 8 (1–20) years. The patients were treated using a specific supervised stretching programme with special emphasis on the internal obturator muscle. The duration of the stretching programme was four weeks. At inclusion, the median pain on the VAS was 6.0 (3-7). The VAS for pain decreased to 4.0 (0-7) ($p = 0.01$) at 12 weeks. Five years after treatment, the VAS for pain was still significantly lower than at inclusion, 4.0 (0-7) ($p = 0.018$). A significant reduction in the number of patients limping was also observed, both at 3 months and at 5 years after the treatment (Table 4).

Six of thirteen patients had a positive Lasegue test at inclusion, while at 12 weeks the test was negative in all thirteen patients and three patients had a positive Lasegue test at five years ($p = 0.014$, $p = 0.016$ respectively). Significantly fewer patients had a positive Freiberg sign at three months and five years ($p = 0.025$, $p = 0.018$ respectively) than at inclusion.

There was no significant reduction in pain on palpation of the external rotator muscles neither in positive Pace sign at 5 years compared with before the treatment (Table 4).

Conclusion

It appears that a specific stretching programme results in both a short- and long-term decrease in symptoms in patients with suspected internal obturator muscle syndrome.

Table 4. The median VAS for pain and the clinical examination tests at inclusion, three months and five years after treatment; p-values indicate comparisons with inclusion values

	At inclusion	Three months	Five years
VAS for pain **Median (range)** **p-values**	6.0 (3-7)	4.0 (0-7) **0.01**	4.0 (0-7) **0.018**
Lasegue's test (positive) **p-values**	6/13	0/13 0.014	3/11 0.16 (n.s.)
Tenderness on palpation **p-values**	13/13	9/13 **0.046**	11/11 1.0 (n.s.)
Freiberg's sign positive **p-values**	7/13	0/13 **0.025**	0/11 **0.018**
Pace's sign **p-values**	9/13	6/13 0.16 (n.s.)	5/11 0.32 (n.s.)
Walking **Median (range)** **p-values**	3 (2-5)	2 (1-4) **0.011**	2 (1-3) **0.023**
Limp **p-values**	10/13	3/13 **0.014**	3/11 **0.014**
Sitting **Median (range)** **p-values**	3 (2-4)	2 (2-3) **0.034**	2 (1-3) **0.034**

Paper III

Twelve patients suspected to have piriformis syndrome were randomised to either operative treatment or a control group as previously reported in Paper I. At inclusion all patients underwent both clinical and radiographic examinations of the hips and either CT or MRI of the lumbar spine. At six months all patients underwent clinical examinations (Table 5). Six patients were operated on with sectioning of the tendon to the internal obturator near its insertion to the trochanter major. There was no significant pain decrease in either group at 6 months (Table 6). At 8 year 9/12 patients were reexamined, four patients in the surgical groups and five in control group. One patient had died in each group and one patient in the surgical group refused to attend the long-term follow-up examination. At 8 years, the decrease in pain was significant in the surgical group ($p = 0.03$) but not in the control group (Table 6). Three patients who needed opioids preoperatively managed without such drugs at 8 years after the operation. Two patients in the operated group were working half time at the 8-year follow up after having been out of work for 3 and 10 years preoperatively. At inclusion 4/12 patients had minor degenerative changes at the L3–L5 level as seen on CT or MRI. At 8 years, the corresponding change was found in 7/9 patients ($p = 0.025$). No per- or postoperative complications or re-operations were registered during the period of the study. The level of pain medication decreased significantly in the whole study cohort at six months ($p = 0.03$) and at eight years ($p = 0.02$) compared with the levels at inclusion. If the study groups were analyzed separately the decrease was only significant in the surgical group at six months ($p = 0.04$).

Conclusion

Surgical release of the internal obturator muscle decreases the pain significantly in patients with obturatorius internus syndrome up to eight years after the surgical procedure.

Table 5. The clinical examination tests at inclusion, after six months and eight years

	At inclusion		At six months		At eight years	
	Surgical group (n = 6)	**Control group (n = 6)**	**Surgical group (n = 6)**	**Control group (n = 6)**	**Surgical group (n = 4)**	**Control group (n = 5)**
Lasegue (positive) p-values versus inclusion	5/6	5/6	1/6 0.08 (n.s.)	5/6 1.0 (n.s.)	1/4 0. 16 (n.s.)	0/5 **0. 046**
Tenderness on palpation	6/6	6/6	6/6	6/6	4/4	5/5
Freiberg's sign positive p-values versus inclusion	6/6	4/6	1/6 **0.03**	4/6 1.0 (n.s.)	1/4 0.08 (n.s.)	1/5 0.16 (n.s.)
Pace's sign positive p-values versus inclusion	4/6	4/6	1/6 0.08 (n.s.)	4/6 1.0 (n.s.)	3/4 0. 56 (n.s.)	2/5 n.s.
Walking problems Yes/No p-values versus inclusion	6/6	6/6	3/6 0.08 (n.s.)	4/6 0.16 (n.s.)	2/4 0. 16 (n.s.)	3/5 0. 16 (n.s.)
Limping Yes/No p-values versus inclusion	5/6	4/6	2/6 0.08 (n.s.)	4/6 1.0 (n.s.)	2/4 n.s.	1/5 0. 32 (n.s.)
Sitting problems Yes/No p-values versus inclusion	6/6	5/6	4/6 0.16 (n.s.)	6/6 n.s.	3/4 n.s.	4/5 1.00 (n.s.)

Table 6. The VAS at inclusion, six months and eight years

	Surgical group			Control group		
	At inclusion	**At six months**	**At eight years**	**At inclusion**	**At six months**	**At eight years**
VAS for pain Median (range)	8.5 (7-10)	6.5 (0-10)	4 (1-7)	7.5 (4-9)	7 (4-9)	6 (0-7)
VAS for pain Mean (SD) p-values versus inclusion	8.3 (1.2)	5.5 (3.9) 0.10 (n.s.)	4.0 (2.6) **0.03**	6.8 (1.9)	6.5 (1.8) 0.81 (n.s.)	4.0 (3.2) 0.06 (n.s.)

Paper IV

Ten patients, median age 60 years (48-75), with OA of the hip, and ten patients, median age years 82.5 (60-90), who had suffered an FCF (Garden III or more), underwent an open biopsy procedure in conjunction with a total hip replacement.

The histological analysis demonstrated significantly more scar tissue ($p = 0.02$), calcium deposits ($p = 0.001$) and GAGs ($p = 0.023$) in the biopsies from the internal obturator in the OA group than in the FCF group (Tables 7 and 8, Figure 6 A, B, C, D). The van Kossa stain revealed that calcium salts had precipitated within the areas of scar tissue in 8 of 9 specimens in the OA group (Figure 6 C). The AB/PAS staining for GAGs was positive in 8/9 specimens in the OA group and in 3/8 specimens in the FCF group (Figure 6 D). There was no evidence of inflammation in either group (Table 8). Furthermore, within the OA group, there was significantly more vascularity ($p=0.04$) and the fibre structure in the scar tissue had deteriorated to a significantly greater degree than in the non-scar tissue ($p = 0.02$) (Tables 7 and 8, Figure 6 A, B). The corresponding finding was not made in the FCF group. All the biopsies from the patients in the OA group had limited areas of scar tissue. The corresponding finding was made in 4/8 patients in the FCF group (Table 8).

The scar tissue was composed of both thin and thick irregular collagen bundles, oriented in a more or less wavy, crosswise fashion. The scar tissue was densely fixed to the tendinous tissue, indicating a previous tendon rupture site (Fig 6 B). In and close to these previous rupture sites, the Perl reaction was negative, indicating that there was no bleeding and no remnants of hemosiderin present.

The ultrastructural evaluation revealed that the distribution of fibril diameter displayed significantly fewer small and medium-sized fibrils in the OA group than in the FCF group ($p = 0.001$) (Figure 7 A, B, C and D).

All the samples from the FCF group displayed a normal or close to normal homogeneous ultrastructural pattern, with collagen fibrils running in the same direction. The samples from the OA group displayed a more irregular pattern in 6/9 specimens, with pathological morphological characteristics – e.g. the collagen fibrils were oriented in different directions and there was an increased amount of non-collagenous ECM; in 3/9 samples, the ultrastructural pattern was more or less homogeneous ($p = 0.003$), as shown in (Figure 8 A, B).

Conclusion

Tissue samples from the internal obturator tendon in the OA group revealed more scar tissue, more GAGs and more precipitated calcium salts in the degenerative tissue, as seen in the light

microscope, as well as a change in fibril diameter distribution and more non-collagenous and irregular ECM, compared with the samples from the internal obturator in the FCF group, as seen in the TEM.

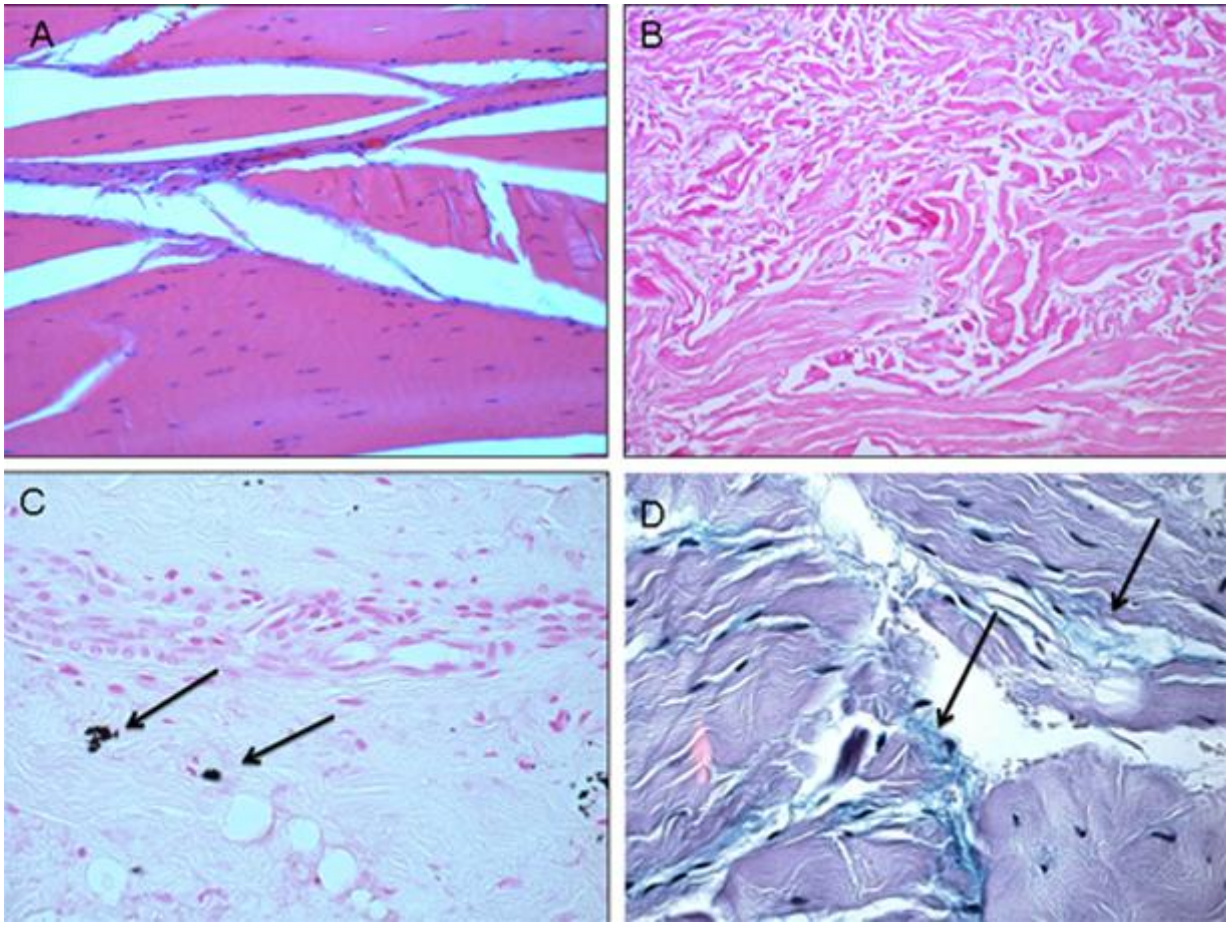

Figure 6. A. Normal tendon from a patient in the FCF group, H&E staining, original magnification x100. **B.** Scar tissue from a patient in the OA group indicating a ruptured tendon. H&E staining. **C.** Calcium deposits (black stain at arrows) in the scar of a previously ruptured tendon in a patient in the OA group. Van Kossa staining. **D.** Moderately increased amount of mucin, indicating GAGs between collagen structures in a patient in the OA group (blue stain at arrows). Alcian Blue/Periodic Acid Schiff staining, Original magnifications x 400.

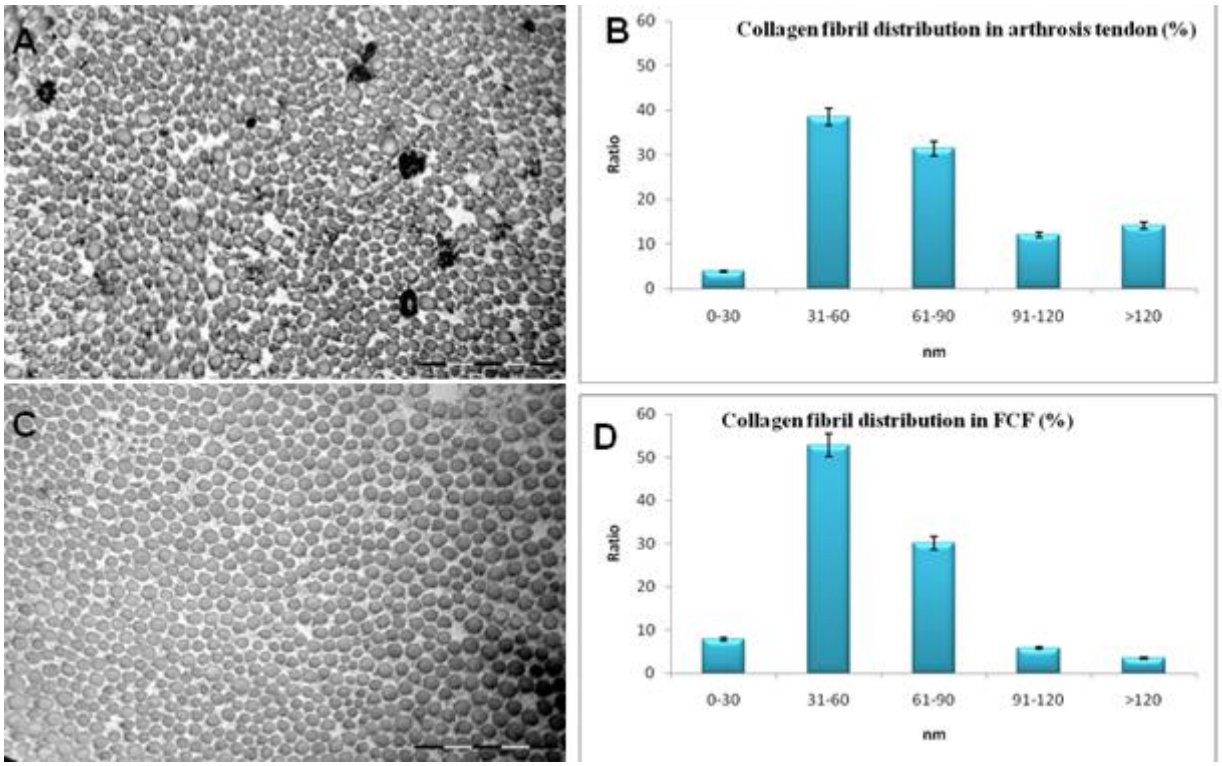

Figure 7. A. Transmission electron micrograph showing fewer small and medium-sized fibrils in the OA group. **B**. Relative distribution of the fibril diameter size in the internal obturator tendon in the OA group. **C**. Transmission electron micrograph showing more small and medium-sized fibrils in the FCF group. **D.** Relative distribution of the fibril diameter size in the internal obturator tendon in the FCF group. Original magnifications x 50,000.

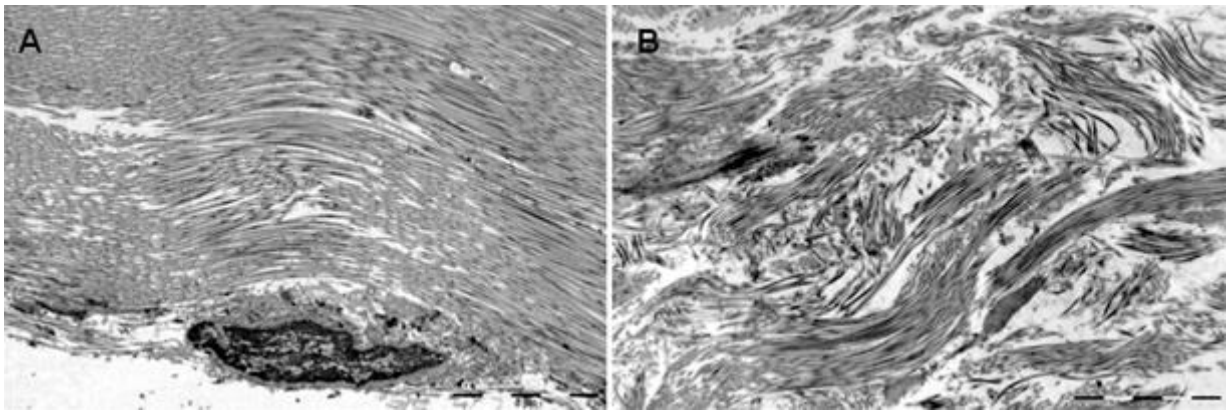

Figure 8. A. TEM micrograph from a patient in the FCF group, showing a homogeneous ECM, where collagen fibrils are running in the same direction. **B.**

Table 7. The histological, semi-quantitative, 4-point scoring system (0-3) for the non-scar tissue (NST) and the scar tissue (ST) in terms of fibre structure (Fibre), cellularity (Cell), vascularity (Vasc) and the presence of GAGs in the OA group and in the FCF group

	OA				FCF			
Patient	**Fibre NST/ST**	**Cell NST/ST**	**Vasc NST/ST**	**GAGs NST/ST**	**Fibre NST/ST**	**Cell NST/ST**	**Vasc NST/ST**	**GAGs NST/ST**
1	1/1	0/0	0/1	0/2	1/-	0/-	0/-	0/-
2	1/1	0/0	0/0	0/1	0/1	0/0	0/0	0/1
3	1/1	0/0	0/0	0/1	X	X	X	X
4	0/2	0/0	0/2	0/2	X	X	X	X
5	0/2	0/0	0/2	0/3	0/1	0/0	0/0	0/0
6	0/1	0/0	0/0	0/0	0/1	0/0	0/0	0/1
7	0/2	0/0	0/0	2/2	2/2	0/0	0/1	0/2
8	1/2	0/0	0/1	0/1	0/-	0/-	0/-	0/-
9	X	X	X	X	0/-	0/-	0/-	0/-
10	0/1	0/0	0/1	0/2	0/-	0/-	0/-	0/-

X indicates that it was not possible to evaluate the sample, as there was too little tissue. Four patients in the FCF group did not have any scar tissue in their samples; this is indicated in the table with -.

Table 8. The characterization of calcium deposits, inflammation and scar tissue in both groups

	Calcium deposits		**Inflammatory cells**		**Scar tissue, % of the sample**	
Patient	**OA**	**FCF**	**OA**	**FCF**	**OA**	**FCF**
1	1	0	0	0	90	0
2	0	0	0	0	50	10
3	1	X	0	X	30	X
4	1	X	0	X	95	X
5	1	0	Few	0	95	50
6	1	0	0	0	20	50
7	1	0	Few	0	50	70
8	1	0	0	0	50	0
9	X	0	X	0	X	0
10	1	0	0	0	70	0
	p = 0.001					p = 0.02

X indicates that it was not possible to evaluate the sample, as there was too little tissue.

DISCUSSION

Background considerations before initiating the project

Buttock pain and tenderness extending from the sacrum to the greater trochanter, together with pain radiating to the lower extremity, have been described and the sciatic nerve has been suspected of being irritated [1;50;51;67;76]. In some cases, no clear clinical or radiographic pathology in the spine, hip or knee can be found when patients complain of buttock pain and tenderness extending from the sacrum to the greater trochanter. It has been claimed that soft tissue pathology in the hip may cause the diffuse, sometimes radiating pain [51;55;77] and then the sciatic nerve has been suspected of being irritated [51;70].

This kind of retro-trochanteric pain with radiation has been described as the "piriformis syndrome" [77;78], which may be associated with trauma to the pelvis or buttock [51], anatomical abnormalities like a bipartite piriformis muscle [48;49], the piriformis muscle lying anterior to the nerve [50], or a hypertrophic muscle irritating the sciatic nerve.
Niu et al. [79] suggested that several patients had persistent sciatica, despite lumbar decompression surgery for lumbar disc herniation or stenosis, and the "piriformis syndrome" was subsequently confirmed through a positive response to the injection of a local anaesthetic agent and a positive Freiberg test. The cohort in their study was thus successfully treated for the "pirifomis syndrome" and they therefore suggested excluding the "piriformis syndrome" before diagnosing lumbar radiculopathy.

A number of methods with varying results exist for the treatment of the ''piriformis syndrome''. However, no particular treatment has resulted in long-term improvement. Cox et al. [34] suggested that the distraction and manual stretching of the gemmeli-obturator internus and pirifomis muscles was successful for treating retro-trochanteric pain. Keskula et al. [2] described the importance of stretching exercises for the ''piriformis syndrome'', while Mayrand et al. [35] considered chiropractic care and muscle stretching beneficial. Benzon et al. [52] recommended an injection technique with special placement of the needle to avoid damage to the sciatic nerve, while Mullin et al. [67] reported significant pain relief after the injection of corticosteroids and local anaesthetics in 12 patients with a follow-up period of 9-24 months.

Complete pain relief immediately after the surgical release of the piriformis muscle in two patients with 10 and 11 months of follow-up was reported by Solheim et al. [70]. The

arthroscopic release of the piriformis tendon was performed in six patients with good results [71]. Yoshimoto et al. [47] examined 61 patients with persistent sciatica using MRI and found a lack of nerve root compression in 10 (16.4%) patients, despite exhibiting symptoms of sciatica. Three of these patients had "piriformis syndrome" and two underwent surgery involving piriformis excision, resulting in permanent pain relief.

At the start of the present work, we were unable to find any description in the literature of any syndrome similar to what we found in Paper I, where the internal obturator tendon had an impact on the sciatic nerve. Nor did we find any especially well-described conservative or surgical treatment options for such a condition. It has been established that, when clinical and radiographic examinations exclude other pathologies in the spine, hip and knee, pathology in the remaining structures around the hip must be considered; especially the muscle tendons in the peri-articular area, in line with other joints, e.g. rotator-cuff pathology in the shoulder.

The etiology of retro-trochanteric pain is multifactorial and the clinical diagnosis can be difficult to determine. It has been suggested that the pain in the osteoarthritic hip may be due to spasm and pressure in the surrounding muscles and tendons towards the joint capsule, which is richly innervated [40;80]. However, Tarasvicius et al. [80] found that the radiographic severity of OA of the hip was correlated to decreased elasticity in the joint capsule and decreased intracapsular pressure. Different treatment options for retro-trochanteric pain, including conservative and surgical treatments, are available, but no particular one is recognised as being superior.

Surgical treatment of retro-trochanteric pain syndrome

In Paper I, we suspected ''piriformis syndrome'' in twelve patients and randomised them to either a surgical or a non-surgical group. During the surgical procedure, an unexpected pathology in terms of a tense internal obturator muscle compressing the sciatic nerve was observed, whereas no anatomical abnormality or other pathology affecting the piriformis muscle and its tendon were found (Figure 4 A and B, Figure 5 A and B). We were not able to find any direct entrapment of the sciatic nerve caused by the piriformis muscle. The internal obturator muscle was, however, very tense, slightly hyperaemic and hypertrophic and it was found to be in close contact with the sciatic nerve. The nerve was slightly flattened where the obturator muscle was impinging towards it and the nerve was also slightly hyperaemic. As far as could be observed during the Lasegue manoeuvre performed on the operating table, the internal obturator and not the piriformis muscle impinged on the nerve at an early stage in the

hip flexion movement. These relationships between the internal obturator muscle and the sciatic nerve were defined as pathological. The findings made us consider the presence of the "internal obturator muscle syndrome" and not the "piriformis syndrome" as a cause of retro-trochanteric sciatia-like pain. We were unable to find any previous description in the literature of this pathology. Only anatomical abnormalities of the piriformis muscle supported the term "pirifomis syndrome" [48;49]. Yoshimoto et al. Solheim et al. and Dezawa et al. [47;70;71] also reported immediate and significant pain relief after the surgical release of the piriformis muscle; however, their surgical treatment was based on the clinical diagnosis and there is no description of the small rotator characteristics during the operation. These studies were not randomised and no information was available about drug use before and after the treatment. Furthermore, the activity level and working ability were not reported either. In Paper I, two patients were able to return to work after the operation, after having been out of work because of pain for three and ten years respectively. These patients were still working part time at the eight-year follow-up, as reported in Paper III.

To our knowledge, no other randomised studies of the surgical treatment of retro-trochanteric pain syndrome can be found in the literature, apart from Papers I and III. A significant pain reduction was found after the surgical release of the internal obturator tendon, six and twelve weeks postoperatively. The pain was still significantly reduced eight years after the surgical procedure. There was a tendency towards a reduction in the amount of analgesic drugs consumed in the surgical group but not in the control group.

Six months postoperatively, the decrease in pain was not significant. The reason for this is unknown. The sectioning of the internal obturator muscle and the exploration of the sciatic nerve might have created bleeding and secondary scar formation. Furthermore, at eight years, all the patients initially included in the study could not be found and this naturally created some transfer bias in the conclusion at eight years.

Our findings emphasize that the "internal obturator muscle syndrome" must also be taken into consideration in the clinical setting when the "piriformis syndrome" is suspected.

Conservative approaches towards retro-trochanteric pain syndrome

Many studies have focused on ways of inducing the relaxation of the piriformis muscle. Even though it is an external rotator, the piriformis muscle has been found to rotate the femur internally when the hip is in flexion [2]. In Paper II, we did not choose to perform the stretching exercises by external rotation. Assuming that a tense internal obturator muscle

caused the problems, a different procedure was chosen. To our knowledge, there has been no description of a change in action for the internal obturator muscle from external to internal rotation when the hip is in flexion [2]. The patients in Paper II reported most pain during passive internal rotation and this was therefore regarded as an efficient stretching maneuver for the obturator muscle.

Maximum stretching of the internal obturator muscle was thought to be obtained by passive internal rotation with simultaneous flexion and adduction of the hip. General stretching of the hip muscles was performed in Paper II, supported by the observation that most muscles around the hip appear to be tense in patients with retro-trochanteric pain syndrome. Specific attention was, however, paid to the small rotators, because if "cramping" their proximity to the sciatic nerve could theoretically cause the most problems.

Direct massage by a physiotherapist of the tendons of the small external rotators at their insertion at the trochanter was also part of the treatment programme. The rationale for this procedure is not completely known and it is possible that mechanisms similar to acupuncture could be involved. The six-month observational phase preceding the treatment period in Paper II revealed no improvement in symptoms. Anatomically, the internal obturator muscle is deep to both the piriformis muscle and the sciatic nerve and it runs parallel to the piriformis in its attachment to the trochanter major. Because of its proximity, similar pathway and function, most conservative treatments for patients with ''piriformis syndrome'' would affect the internal obturator muscle as well [46]. Guvencer et al. [78] suggested that the internal obturator, gemelli and quadratus femoris tendons share common insertions with the piriformis tendon and can thereby compensate for the loss of its function. The fusion of the piriformis tendon with the obturator internus tendon was previously confirmed [72]. The clinical improvement was seen only after the treatment programme and not in the period with any other treatment. The decrease in symptoms seen after the stretching programme was therefore probably not only a placebo effect.

One critical point is to get the patients to continue the stretching exercises for an extended period of time. At the rehabilitation centre, the exercises were performed according to the programme managed by physiotherapists associated with the paper. Since the exercises were limited in number, it was our intention that the exercises would be remembered and used by the patients after the initial treatment period. Unfortunately, we have no data on the extent to which the patients actually continued the exercise programme. However, a significant reduction in pain was still found after five years compared with the pre-treatment values. As

in Paper II, we recommend that, in future studies, patients with other pathology in the spinal column and the hip joint should be excluded. Close collaboration between patients, doctors and physiotherapists is also recommended to manage and stick to the specific stretching programme. Retro-trochanteric pain caused by the piriformis or internal obturator syndrome is often underdiagnosed or overlooked in the clinical setting, because the symptoms may be similar to lumbar spine disorders, such as disc herniations or spinal stenosis [46;47].

Reflections on conservative and surgical treatment

From our studies, it seems obvious that a tense internal obturator muscle may contribute significantly to the retro-trochanteric sciatia-like pain syndrome. There is no complete understanding of the aetiology or of the role played by the piriformis muscle. The median duration of symptoms in Papers I and III was 7.5 (2-20) years, while it was 8 (1–20) years in Paper II. This suggests that the patients had suffered for a long time from their symptoms and the disease had already reached a chronic stage. One problem in the clinical setting could be that patients of this type often receive a mixture of treatment algorithms for both back and hip problems. It is therefore important to recognise the problem at an early stage and to start a treatment programme to prevent the disease from progressing to a chronic stage. Larger, controlled studies should be set up thoroughly to evaluate the treatment of this type of pathology.

The concept of “obturatorius internus syndrome” has attracted more attention during the last few years and our paper has been commented on in subsequent work. After our publications, findings similar to those reported in Papers I and III that the internal obturator muscle and tendon and not the piriformis cause sciatic neuropathy have been published. In a case report involving only one patient, Murata et al. [81] also found that the obturatorius internus compressed the sciatic nerve. In line with the findings in Papers I and III, Carola [82] and Gajraj [83] reported an injection technique to reach the internal obturator muscle for the treatment of sciatica-like pain. The chronic nature of retro-trochanteric pain is probably the reason why the patients in Paper II still had significant yet improved pain after conservative treatment. It is our opinion that, if the conservative approach fails, surgical intervention might be advocated.

Radiographic assessments

The clinical diagnosis of the retro-trochanteric pain syndrome is difficult to confirm by only a clinical examination. Retro-trochanteric pain syndrome is an exclusion diagnosis and radiographic evaluation of the spine and hip is therefore necessary to exclude other pathology, which can be the primary cause of the symptoms experienced by the patients [55;77;84]. Blankenbaker et al. [85] studied patients with " trochanteric pain syndrome" using MRI and found that 88% of asymptomatic hips had abnormal findings, with a hyperintensity sign in the trochanteric area, and they therefore concluded that MRI has a high sensitivity to pathology in conjunction with "trochanteric pain syndrome". The radiographic findings in Papers II and III are also interesting. A significant increase in minor degenerative changes in the lumbar column was found in the whole cohort in Paper III. This finding suggests that retro-trochanteric pain syndrome might be associated with early degenerative changes in the lumbar spine and, for diagnostic reasons; changes in the lumbar spine must be taken into consideration. Another explanation could be that the increase in degenerative changes in the lumbar spine is actually a normal ageing process. It is important to mention that neither at inclusion nor at the eight-year control was any pathology found in the hip joints in Papers I and III.

Before initiating conservative or surgical treatment for the retro-trochanteric pain syndrome, other treatable conditions in the hip joint and lumbar spine must be excluded. We therefore recommend performing standard radiographs of the hips and MRI or CT scans of the lumbar spine as a diagnostic algorithm for these types of patient.

Histological findings in patients with hip OA and patients with FCF

Tendon pathology has been studied in close relation to various joints and correlated to clinical and radiographic findings [32;56;85]. Histological changes in the tendon, especially the Achilles, patellar and rotator cuff tendons, have also been investigated [9;19;24;25;27]. Molloy et al. [19] analysed the supraspinatus tendon using a microarray technique and concluded that glutamate plays an important role in tendon degeneration. Svensson et al. [86] used the light microscope and reported increased amounts of GAGs, together with an increase in vascularity and collagen fibre disorientation in the patellar tendon, six years after harvesting its central third as an autograft during ACL reconstruction.

Lohr and Uhthoff et al. [87] studied the histological section of 18 human supraspinatus tendons with selective vascular injections of silicon-rubber compound enabling the visualisation of the vascular bed of the rotator cuff and concluded that a rotator-cuff tear starts

on the articular side of the tendon, with degenerative changes and insufficient vascularity. Using histochemical analysis, Hashimoto et al. [9] found calcifications in 19% of 80 ruptured rotator-cuff tendons and disorientation of the collagen fibrils in the stump of the torn rotator-cuff tendon without distinct inflammatory changes. They suggested that the pathogenesis of the cuff tear is closely associated with age-related degenerative changes in the tendons, followed by microtrauma. Movin et al. [25] detected increased amounts of GAGs in achillodynia and suggested that this was a reactive cell response to tendon insult. Riley et al. [20;21] stressed the importance of metalloproteinases and other enzymes in tendon healing, as well as the importance of an increased proportion of type III collagen, which reduces the ability of the tendon to resist tension force and thereby predisposes to a rupture of the tendon. Cook et al. [24] demonstrated cellular changes in 18 of 50 biopsies from asymptomatic patellar tendons in athletes, suggesting that the tendinosis process starts with cellular activation and proceeds through phases which increase the ground substance.

The importance of substance P for the tissue changes and/or tissue repair that occur during the development of tendinosis was illustrated using immunohistochemical analysis [88].

All these findings are in line with the findings in Paper IV that degeneration is accompanied by increased amounts of GAGs and a change in tendon morphology.

There are a number of studies of the processes involved in tendon injury and degeneration [9;10;19;21;23;24;73;87;89], but only a few studies have focused on the pathological changes in the tendons around the hip. Lempainen et al. [29] used histological analysis and found typical morphological changes of tendinosis in proximal hamstring tendinopathy in athletes with collagen disorientation, increased vascular proliferation, rounding of tenocyte nuclei and increased amounts of ground substance. To our knowledge, the changes in histological structure in the internal obturator tendon in patients with OA of the hip have not previously been reported in the literature.

The histological analysis in Paper IV demonstrated significantly more tendon ruptures with scar tissue, increased amounts of GAGs and calcium deposits in the OA group. Furthermore, within the OA group, significantly more vascularity and deterioration in fibre structure were found in the scar tissue than in the non-scar tissue. The corresponding finding was not made in the FCF group. These findings and the lack of distinct inflammatory changes as seen in the light microscope therefore indicate that the tendons in the OA group have undergone changes similar to those described in tendons in other locations and referred to as tendinosis. It is likely that the tendon pathology increases the symptoms already experienced by osteoarthritic patients. It is worth considering whether performing a radiofrequency microtenotomy of the

small rotator muscle tendons in the hip region might reduce the symptoms experienced by patients with obturatorius internus syndrome or patients with mild intra-articular degenerative changes.

Ultrastructural findings in patients with OA and patients with FCF

In the OA group in Paper IV, the tendon material was irregular and altered, with collagen fibrils oriented in different directions and an increased amount of cell debris, as seen in the TEM (Figure 8). Furthermore, there were significantly fewer small and medium-sized fibrils compared with the FCF group (Figure 7). The change towards more non-collagenous ECM indicates that OA affects not only the joint itself but also the surrounding tissue. The FCF patients were about 20 years older than the osteoarthritic patients and should therefore theoretically have more degenerative findings, which could not be confirmed histologically or ultrastructurally. It is generally believed that a skewed fibril diameter distribution develops in the ageing tendon, with more small and medium-sized fibrils than the normal tendon of an adult person [90;91]. This could be the reason for the difference found in this respect and the tendon in the FCF group was actually normal for the age group. However, there are animal studies that do not confirm any alteration in collagen fibril diameter in tendons with increasing age [92;93].

To our knowledge, the finding of changes in the ultrastructural appearance in the internal obturator tendon in patients with OA of the hip has not previously been reported. The difference in age between the paper groups is unfortunate. It would have been better to use healthy age-matched controls. However, this was not possible for ethical reasons.

Paper IV can also be regarded as a model for future comparisons of the pathology found in patients with retro-trochanteric pain syndrome where the internal obturator muscle is involved and in other articular and/or peri-articular diseases in the hip region. It also provides some interesting perspectives in relation to future studies of treatment in patients with mild radiographic OA and severe symptoms; similar to what has been reported for the treatment of lateral epicondylitis, [94;95] patellar [94] and rotator-cuff tendinosis [96].

Strengths and limitations of the studies

The major strength of Paper I and Paper III is their randomised design, while the relatively long follow-up period is also strength of Paper III. The strength of Paper II is its relatively long follow-up period, as well as the attempt to exclude intra-articular hip problems and spinal disorders through multiple radiographic assessments. The fact that the clinical

evaluations at inclusion and at five years were performed by an independent physiotherapist is another strength, however no control group was available in this study.

The limitations of Paper I and Paper III are that they were not designed with enough power to compare the surgical group with the non-surgical group and that it was not possible to keep all the patients in the study until the long-term follow-up. The difference in age between the groups is the major weakness of Paper IV, but the strengths of Paper IV are that it was performed on humans and that both histological and ultrastructural evaluations were performed.

Clinical relevance

Patients with retro-trochanteric pain syndrome are often misdiagnosed and difficult to treat. Papers I, II and III show that there are both surgical and conservative options to treat these patients, with promising results in both the short and long term. The important thing, however, is to consider the possibility that these patients could have problems from the spine or from the hip joint. In Papers I, II and III, we tried to exclude these possibilities by performing MRI or CT of the lumbar spine and X-rays of the hip joints. However, in some patients, minor pathology was still found in these locations. Paper IV was an attempt to make an in-depth histological and ultrastructural analysis of the pathology in the short rotator muscle tendons of the hip joint. Paper IV actually generated more questions than answers and it might be that tendinosis in these tendons is a part of the OA disease. Further studies should focus on the possible connection between OA and tendinosis and also on possible treatment options. Might it, for example, be possible to reduce the symptoms of OA and even slow the disease process by treating the tendinosis?

Studies of microtenotomy might be indicated, with knowledge of the treatment of epicondylitis in the elbow region.

Differential diagnoses

Several other diagnoses must be considered for patients with retro-trochanteric pain; they include herniated discs, degenerative changes in the lumbosacral spine, spinal stenosis, OA and minor intra-articular pathology in the hip joint, such as labral tears, FAI and even symptoms of proximal claudication. Furthermore, gynaecological conditions, especially when the right side is affected, should not be forgotten [47]. In Papers I, II and III, serious attempts were made to exclude these diagnoses.

FUTURE PERSPECTIVES

In the future comparisons between histological and ultrastructural findings in the tendons of the short rotator muscles of the hip in patients suffering from retro-trochanteric pain syndrome with age-matched patients without such symptoms, as well as age-matched patients with intra-articular hip problems, appear to be very interesting. However, the most interesting future perspective is to relieve the symptoms of minor intra-articular osteoarthritic changes and manage the internal obturator syndrome by treating the tendinosis through either conservative programmes or tenotomy or microtenotomy of the short rotator muscle tendons of the hip.

Furthermore, it appears to be important thoroughly to analyse and classify whether the patients are suffering from spinal disorders, minor intra-articular hip problems or local nerve entrapment of the sciatic nerve in the hip region, as mentioned above.

A larger number of patients are needed for future studies; therefore there is a need for cooperating partners at other centres. It is attractive to consider the possibility of using the national hip replacement registers to compare the subjective results in terms of postoperative pain and patient satisfaction in patients who underwent the surgery using an anterior rotator tendon sparing approach and patients who underwent the same procedure using a posterior rotator tendon sacrificing approach.

Finally, a question posed by us, but not completely answered, is how much conservative treatment compared to operative approaches can relieve the symptoms related to the described syndrome.

CONCLUSIONS

- A specific stretching programme resulted in both a short- and a long-term decrease in symptoms in patients with retro-trochanteric pain

- Surgical release of the internal obturator muscle resulted in both a short- and a long-term decrease in pain in patients with retro-trochanteric pain syndrome

- Tendon biopsy specimens from the short rotator muscle of the hip from patients with OA reveal both histological and ultrastructural degenerative changes

- Tendon biopsy specimens from the short rotator muscle of the hip in patients with FCF reveal a normal age-related histological and ultrastructural appearance.

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PAPER IV

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