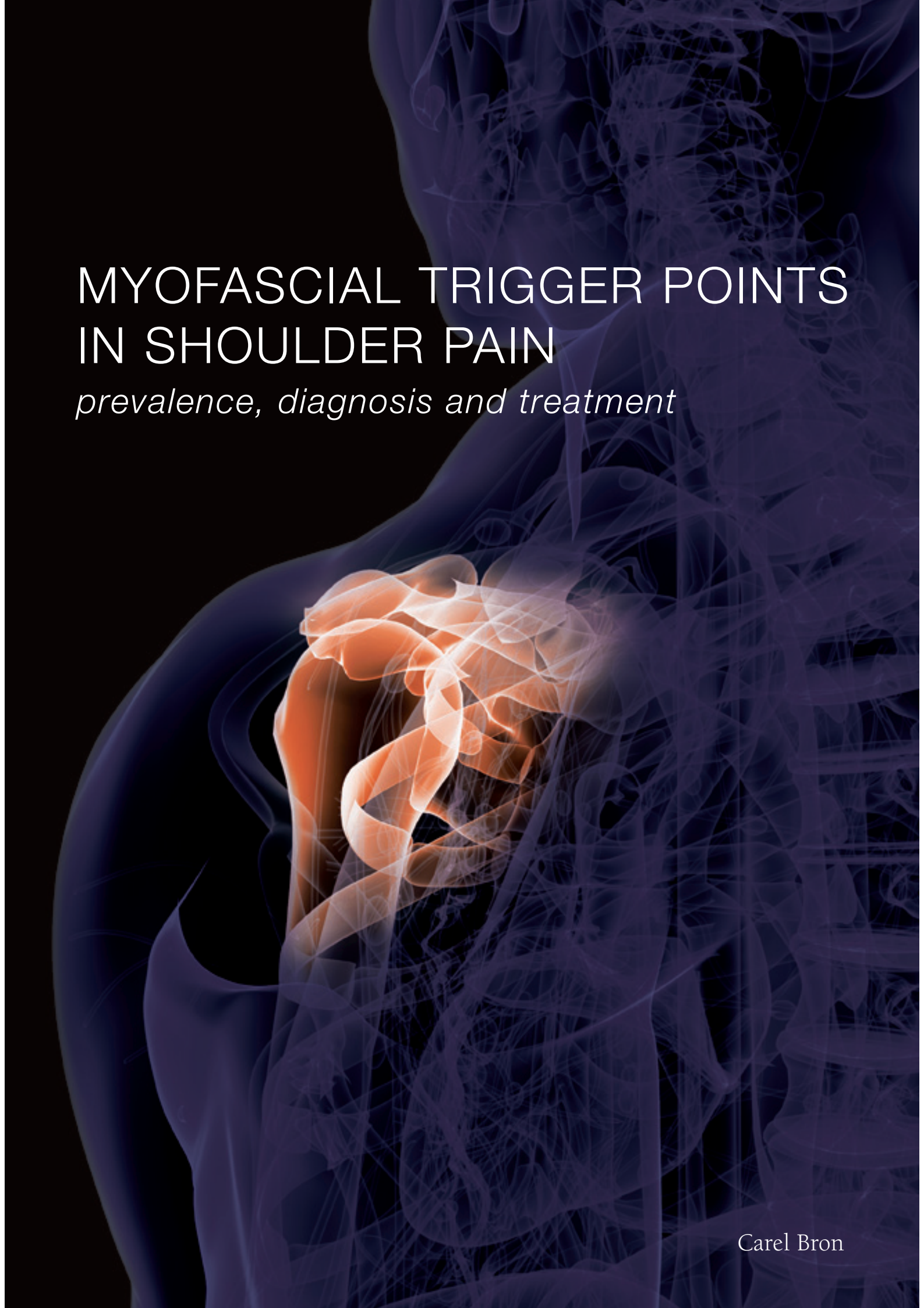
MYOFASCIAL TRIGGER POINTS IN SHOULDER PAIN

prevalence, diagnosis and treatment



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MYOFASCIAL TRIGGER POINTS IN SHOULDER PAIN
PREVALENCE, DIAGNOSIS AND TREATMENT

Een wetenschappelijke proeve op het gebied van de medische wetenschappen

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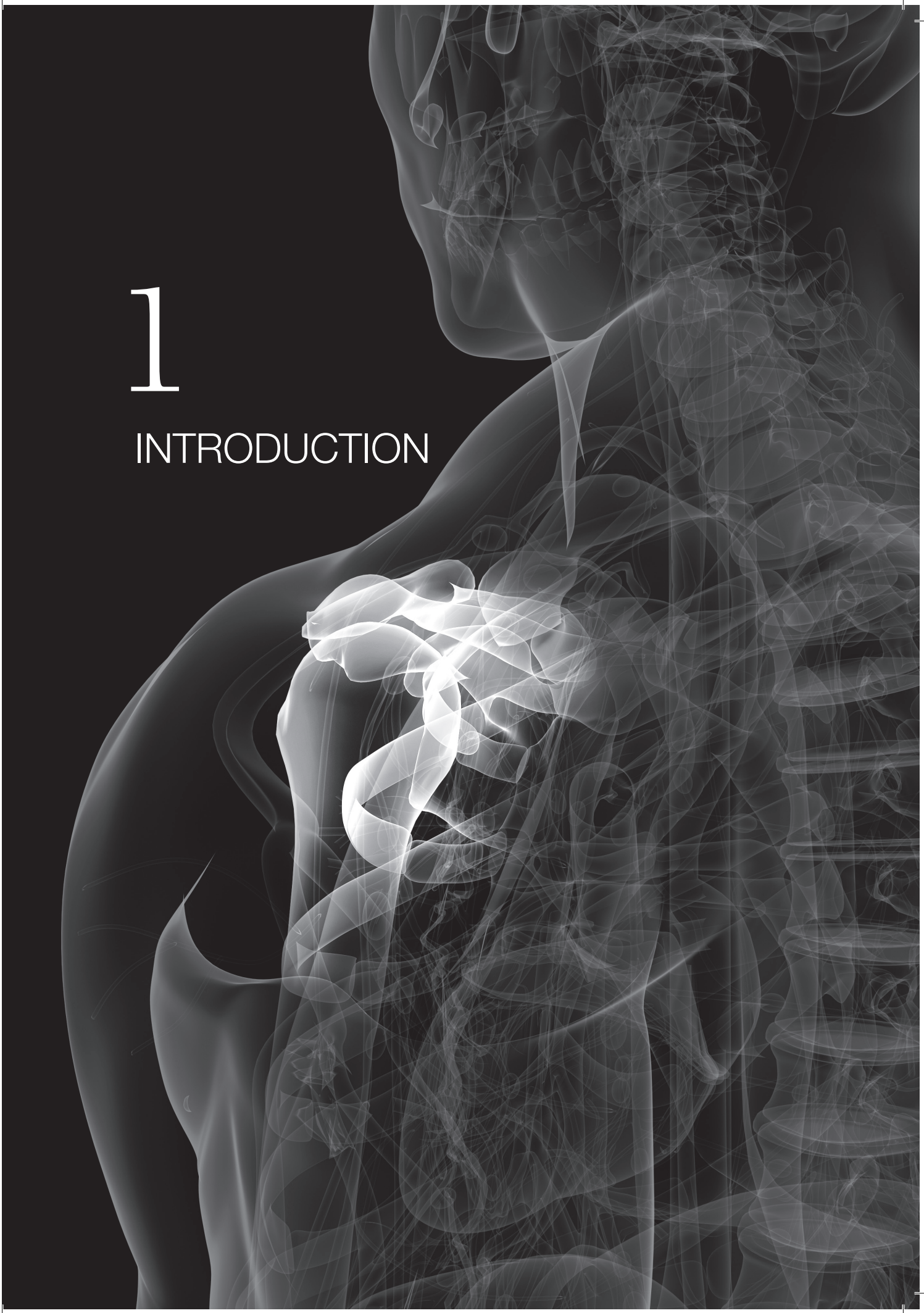
CONTENTS

Many patients have suffered grievously and needlessly because a series of clinicians unacquainted with myofascial trigger points erroneously applied the psychogenic label to them covertly if not overtly.

Dr. Janet Travell (1901 – 1997) and dr. David Simons (1922 - 2010)



1

INTRODUCTION

1

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Incidence and prevalence of shoulder pain

Shoulder pain is a very common musculoskeletal disorder. In primary care, the yearly incidence is estimated to be 14.2 per 1000 people. The one-year prevalence in the general population is estimated to be 20 to 50%. The estimates are strongly influenced, for example, by the definition of shoulder disorders, including or excluding limited motion, age, gender, and anatomic area. Thus, shoulder pain is widespread and imposes a considerable burden on the affected person and on society. Women are slightly more affected than men and the frequency of shoulder pain peaks between 46 and 64 years of age [1]. People at high risk of shoulder pain include those working as cashiers, garment workers, welders and bricklayers as well as those who work with pneumatic tools or in the meat industry. Hairdressers, plasterers, assembly workers, packers and people who work for long hours at computers, such as secretaries and programmers, are also at high risk [2]. Shoulder pain tends to be persistent or recurrent [3]. Between 22 and 46% of patients who visit a medical practitioner because of shoulder pain report a history of a previous pain episode [1, 4]. Six months after initial medical consultation and despite medical treatment, persistent shoulder symptoms have been reported in up to 79% of patients. Of those with persistent symptoms, more than half typically do not seek any additional treatment [4, 5].

Definition of shoulder pain, shoulder complaints and shoulder disorder(s)

Shoulder pain, shoulder complaints and shoulder disorders are frequently used terms and appear synonymous. According to the online version of the Oxford dictionary, a disorder is defined as a disruption of normal physical or mental function, a complaint as an illness or medical condition (especially a relatively minor one) and pain as physical suffering or discomfort caused by illness or injury (*http://oxforddictionaries.com* accessed October 2010). It is clear from these definitions that there is certain overlap between the terms. In this thesis, we will use the term shoulder pain.

Most shoulder pains are caused by a small number of relatively common conditions. One of the most common causes of shoulder pain is thought to be the subacromial impingement syndrome (SIS). This syndrome includes tendonitis or tendinopathy of the rotator cuff and the long head of the biceps brachii muscle, or subacromial or subdeltoid bursitis. Other less common causes of shoulder pain are tumors, infections and nerve related injuries [6-11].

The clinical picture

The main clinical feature of SIS is pain, which is mostly localized at the front and lateral side of the shoulder and halfway up the upper arm, sometimes radiating past the elbow to the radial side of the hand. Pain may already be present at rest but will definitely occur or

increase in severity during or shortly after movement. It is especially painful when reaching forward, sideways or above the head or when putting the hand behind the back. The patient may wake up frequently during the night because of the pain caused by lying on the affected shoulder but also while sleeping on the unaffected side. The patient may display a so-called painful arc. During abduction [12], the first part (0 to 60º) often progresses without pain, the middle part (60 to120º) is painful and the last part (120 to 180º) is again without pain or at least much less painful. Due to these impairments, patients are often limited in their daily activities, including work, leisure and sports.

Inflammation

Steinfeld et al. proposed that up to 90% of all shoulder pain is related to local inflammation of the subacromial soft tissue [13]. However, Khan et al. found that there is a lack of evidence that pain is related to the inflammation of tendons [14]. Light microscopy in patients operated on for tendon pain revealed collagen separation with thin, frayed and fragile tendon fibrils separated from each other lengthwise and disrupted in cross section. Although there was an apparent increase in tenocytes with myofibroblastic differentiation (tendon repair cells), the classic inflammatory cells were usually absent. Therefore, they proposed to abandon the term tendinitis and replace it by tendinopathy [14, 15].

Rotator cuff degeneration and other structural abnormalities

Partial or full thickness ruptures of the rotator cuff tendons are very common and their prevalence increases with age [16, 17]. Rotator cuff tears are seen as often in symptomatic as in asymptomatic subjects [18]. The size of the tear does not correlate with pain intensity or level of disability [19]. Therefore, it is uncertain to what extent rotator cuff ruptures cause shoulder pain. Other abnormalities seen in magnetic resonance imaging (MRI) and ultrasonography (US), including osteophytes, subacromial and joint fluid, are often seen in asymptomatic high level athletes and does not predict shoulder pain or disability [20-23].

Etiology

In 1972, Neer [24] described SIS as a distinct clinical entity although Jarjavay first recognized subacromial disorders in 1867 when he described a few cases of subacromial bursitis [25]. Neer hypothesized that the anterior third of the acromion, the coracoacromial ligament and the acromioclavicular joint impinges upon the insertion of the supraspinatus tendon into the greater tubercle. He also postulated that osteophytes within the coracoacromial ligament lead to tearing of the rotator cuff tendons. This is referred to as outlet stenosis or external impingement (see below for internal impingement).

Table 1: Neer's classification of SIS

Stage	age (years)	Findings
1	< 25	Shoulder pain is experienced that corresponds to the explanation originally provided by Neer but no abnormalities can be found by modern imaging techniques. These complaints are often explained as acute inflammation of the subacromial structures.
2	25 to 40	It is assumed that the pain is caused by a chronic inflammation of the subacromial structures. This is associated with edema formation and minor hemorrhage.
3 and 4	> 40	It is possible to detect abnormalities through medical imaging techniques, namely partial (stage 3) or full thickness (stage 4) ruptures and the formation of osteophytes, especially on the undersurface of the anterior portion of the acromion.

It is apparent from *Table 1* that there is a chronological order between the four stages. Several studies have shown that there is a strong association between age and rotator cuff rupture, indicating that ruptures of the rotator cuff tendons become more prevalent with increasing age, while the association between rotator cuff ruptures and pain intensity and dysfunction seems to be absent [16, 17, 19, 26-28].

A further distinction is made between primary SIS and secondary SIS. Imaging reveals abnormalities comparable to stage 3 according to Neer only in primary SIS, whilst secondary SIS is defined by the same symptoms but without demonstrable abnormalities, which is comparable to Neer's stages 1 and 2.

Secondary SIS can be defined as a relative decrease in subacromial space as a result of instability of the shoulder [29]. This instability is described as being subtle, mild, minor, occult or functional [30-33]. It is believed that this level of instability cannot be identified by clinical tests or medical imaging techniques [29]. This kind of SIS is mostly seen in younger patients (< 40 years), who are often active in sports. The theory behind this concept comes from Jobe et al. [30, 34] who hypothesized that a combination of shortening of the posterior capsule and instability of the anterior capsuloligamentous complex could lead to compression of subacromial tendons and bursae. This hypothesis has never been confirmed. Recently, Poitras et al. found that experimental shortening of the posterior capsule in cadavers did not lead to an increase of subacromial pressure [35].

A third distinction is made with external and internal impingement. Walch et al. first identified internal impingement during shoulder arthroscopy [36]. Individuals presenting with posterior shoulder pain brought on by positioning of the arm at 90° of abduction and

90° or more of external rotation, typically from overhead positions in sport or industrial situations, may be considered as potential candidates. Mcfarland et al. have argued against this and consider the contact between the undersurface of the rotator cuff tendons and the glenoid rim as purely physiological and not pathological [37]. It is worth mentioning that in the position of the arm at 90° of abduction and 90° or more of external rotation, the subscapularis muscle is under stretch and may contribute to pain in the shoulder during this maneuver. Referred pain from the subscapularis muscle is located at the back of the shoulder according to Simons et al. [38].

Physical examination and clinical tests

A few orthopedic tests have been described with regard to SIS. The Neer test, Hawkins-Kennedy test, empty can or Jobe test, and the painful arc test are specifically designed to assess subacromial impingement, while external rotation lag sign, drop arm test, supine impingement test, and belly press test are designed to detect rotator cuff tears [39]. In general, the results of these tests should be interpreted with caution. With these tests, it is not sufficiently possible to make a reliable statement about whether subacromial impingement is present in patient groups that have not been selected in advance. The most reliable tests are the painful arc test, the empty can test (Jobe), and the external rotation-against-resistance test for detecting rotator cuff tears, while tests for impingement without rotator cuff tears are worthless for diagnostic purposes. Specifically, the sensitivity of the test increases with the severity of SIS. The highly sensitive tests seem to have low specificity values and the highly specific ones seem to have low sensitivity values [40-55].

Imaging

The options for viewing various tissues in the body have increased significantly in recent decades. Thanks to x-ray photography, diagnostic US and MRI, it is possible to detect the presence of structural abnormalities in the shoulder. However, detecting abnormalities in patients with shoulder pain does not provide a guarantee that the abnormalities are actually responsible for the pain. Research in which groups of volunteers without shoulder pain are examined in a similar fashion can provide insight into the importance of the demonstrated abnormalities in patients with shoulder pain. Using MRI, partial (Stage 3) or full thickness (Stage 4) ruptures were found in 34% of the people in a group of 96 volunteers with no shoulder pain [18]. In another MRI study, 42 patients with shoulder pain and 31 patients without were compared. Rotator cuff ruptures were found in the shoulder of patients with pain as well as in the shoulder of patients without pain in over 50% of cases [26]. The authors came to the conclusion that there was a significant relationship between age and the occurrence of ruptures but no relationship was found between pain and the presence of rotator cuff ruptures. In an MRI study of the shoulder of professional baseball players, specifically pitchers (n=14), without symptoms of shoulder pain, no or hardly any difference was found between the pitching arm and the non-pitching arm [20]. In approximately 80% of the cases, rotator cuff ruptures and labral injuries were found in both shoulders,

and acromional osteophytes were observed in half of the players. One throwing athlete had a so-called SLAP (superior labrum from anterior to posterior) tear in both shoulders. A comparable study with asymptomatic high-level athletes (baseball and tennis) (n=20) also revealed a high incidence of ruptures [21]. In this study, fluid in the subacromial space (19 of the 40 shoulders) and in the glenohumeral joint (36 of the 40 shoulders) was also reported. Based on these data, it seems reasonable to be cautious and not necessarily conclude that abnormalities found during imaging can fully explain the pain in individual patients.

Interventions

While many interventions have been employed for shoulder disorders, including steroid injections, non-steroidal anti-inflammatory drugs (NSAID) and other painkillers, surgery, physical therapy, manual mobilization and manipulation, acupuncture, and low level laser therapy, scientific evidence of their efficacy is limited [56-70]. Physical therapy is often the first choice in the management of shoulder pain in patients and may consist of various treatment modalities, such as exercise therapy, massage therapy, muscle stretching exercises, or ultrasound [71-74]. Although frequently administered, the efficacy of these interventions has not been established.

Myofascial trigger points and shoulder pain

Simons et al. [38] claim that "neither impingement syndrome nor rotator cuff disease, as each term is commonly used, is a specific or satisfactory diagnosis (page 545)". As mentioned before, inflammation of subacromial structures is not very common in shoulder pain, which may explain the limited effect of steroid injections and NSAIDs. Narrowing of the subacromial space may result in degenerative changes of the rotator cuff but not in inflammation. Since these degenerative changes occur as often in asymptomatic as in symptomatic subjects, this might again not explain the pain and disability in patients. Physical examination, including specific tests for subacromial impingement, do not take into account that muscles surrounding the shoulder may be tested as well as other structures, and that these muscles may produce the shoulder pain instead of the tendons or bursae. Although the pain is felt deep in the shoulder and clinicians locate the pain in the subdeltoid or subacromial region, the pain might come from painful muscle tissue that is remote from the place where it is felt [75-79]. Finally, until recently, MRI and US did not reveal abnormalities within muscle tissue, other than intramuscular ruptures. However, MRI combined with elastography and high resolution US have shown tissue characteristics that are characteristic features of myofascial trigger points (MTrPs). This makes the concept of myofascial pain caused by MTrPs more acceptable for physicians and therapists.

Problems studied in this thesis

This thesis aims to contribute to the knowledge of the role of MTrPs in shoulder pain. In our physical therapy practice, we treat patients with shoulder pain using a comprehensive therapy approach specifically aimed at treating MTrPs. Although patients and therapists

have been satisfied with our treatment for many years, we felt a need to study the effectiveness in a methodologically well-designed study, which was the main motivation for the research presented in this thesis. If effectiveness can be proven, continuation and possibly wider implementation of the comprehensive therapy targeted at MTrPs would be recommendable.

Objectives of the thesis

The aim of this thesis was to determine the importance of MTrPs in patients with chronic unilateral shoulder pain. We wanted to explore three major questions:

- Can we reliably identify MTrPs in shoulder muscles under controlled conditions?
- How common are MTrPs in patients with chronic shoulder pain?
- What is the effectiveness of treatment of MTrPs in patients with chronic unilateral shoulder pain?

Outline of the thesis

This thesis consists of three studies: an interrater reliability study, an observational study, and a randomized controlled trial conducted in a primary care physical therapy practice specializing in musculoskeletal disorders of the arm, shoulder and neck.

Chapter 2 provides an evidence-informed review of the current scientific understanding of MTrPs with regard to their etiology, pathophysiology and clinical implications.

Chapter 3 presents the results of an interrater reliability study of a sample of three shoulder muscles, which were of importance in patients with shoulder pain according to our daily clinical experience.

Chapter 4 presents the design of the randomized controlled trial, evaluating the effectiveness of a physical therapy treatment in patients with unilateral non-traumatic chronic shoulder pain. All subjects had unilateral shoulder pain for at least six months and were referred to a physical therapy practice specializing in musculoskeletal disorders of the neck, shoulder and arm. After the initial assessment, patients were randomly assigned to either an intervention group or a control group (wait and see).

Chapter 5 presents the results of an observational study that aimed to assess the prevalence of muscles with MTrPs and their potential impact on patients with chronic non-traumatic unilateral shoulder pain. Subjects were recruited from patients included in a clinical trial studying the effectiveness of physical therapy treatment in patients with unilateral non-traumatic shoulder pain.

Chapter 6 presents the results of a single blinded randomized controlled trial. We assessed the outcome in a group of patients with shoulder pain who received comprehensive treatment given by a physical therapist for 12 weeks and compared this with the outcome in a comparable group with patients who remained on a waiting list for 12 weeks

Finally, *Chapter 7* provides the general discussion and summary of the results.

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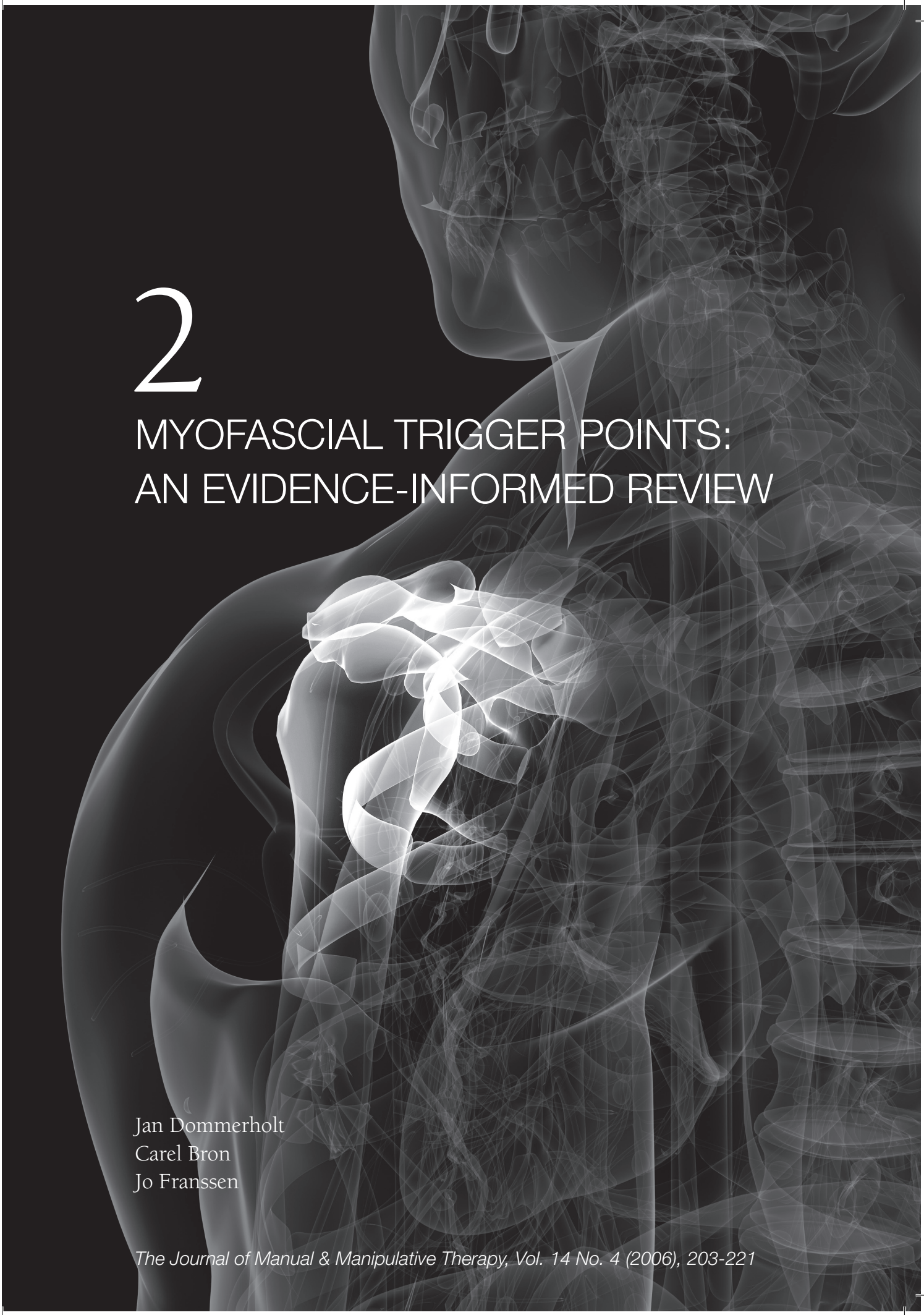

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MYOFASCIAL TRIGGER POINTS: AN EVIDENCE-INFORMED REVIEW

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MYOFASCIAL TRIGGER POINTS: AN EVIDENCE-INFORMED REVIEW

Abstract: This article provides a best evidence-informed review of the current scientific understanding of myofascial trigger points with regard to their etiology, pathophysiology, and clinical implications. Evidence-informed manual therapy integrates the best available scientific evidence with individual clinicians' judgments, expertise, and clinical decision-making. After a brief historical review, the clinical aspects of myofascial trigger points, the interrater reliability for identifying myofascial trigger points, and several characteristic features are discussed, including the taut band, local twitch response, and referred pain patterns. The etiology of myofascial trigger points is discussed with a detailed and comprehensive review of the most common mechanisms, including low-level muscle contractions, uneven intramuscular pressure distribution, direct trauma, unaccustomed eccentric contractions, eccentric contractions in unconditioned muscle, and maximal or sub-maximal concentric contractions. Many current scientific studies are included and provide support for considering myofascial trigger points in the clinical decision-making process. The article concludes with a summary of frequently encountered precipitating and perpetuating mechanical, nutritional, metabolic, and psychological factors relevant for physical therapy practice. Current scientific evidence strongly supports that awareness and working knowledge of muscle dysfunction and in particular myofascial trigger points should be incorporated into manual physical therapy practice consistent with the guidelines for clinical practice developed by the International Federation of Orthopaedic Manipulative Therapists. While there are still many unanswered questions in explaining the etiology of myofascial trigger points, this article provides manual therapists with an up-to-date evidence-informed review of the current scientific knowledge.

During the past few decades, myofascial trigger points (MTrPs) and myofascial pain syndrome (MPS) have received much attention in the scientific and clinical literature. Researchers worldwide are investigating various aspects of MTrPs, including their specific etiology, pathophysiology, histology, referred pain patterns, and clinical applications. Guidelines developed by the International Federation of Orthopaedic Manipulative Therapists (IFOMT) confirm the importance of muscle dysfunction for orthopedic manual therapy clinical practice. The IFOMT has defined orthopedic manual therapy as "a specialized area of physiotherapy/physical therapy for the management of neuromusculoskeletal conditions, based on clinical reasoning, using highly specific treatment approaches including manual techniques and therapeutic exercises." The educational standards of IFOMT require that skills will be demonstrated in—among others—"analysis and specific tests for functional status of the muscular system," "a high level of skill in other manual and physical therapy techniques required to mobilize the articular, muscular or neural systems," and "knowledge of various manipulative therapy approaches as practiced within physical therapy, medicine, osteopathy and chiropractic"[1].

However, articles about muscle dysfunction in the manual therapy literature are sparse and they generally focus on muscle injury and muscle repair mechanisms[2] or on muscle recruitment[3]. Until very recently, the current scientific knowledge and clinical implications of MTrPs were rarely included[4-7]. It appears that orthopedic manual therapists have not paid much attention to the pathophysiology and clinical manifestations of MTrPs. Manual therapy educational programs in the US seem to reflect this orientation and tend to place a strong emphasis on joint dysfunction, mobilizations, and manipulations with only about 10-15% of classroom education devoted to muscle pain and muscle dysfunction.

This review of the MTrP literature is based on current best scientific evidence. The field of manual therapy has joined other medical disciplines by embracing evidence-based medicine, which proposes that the results of scientific research need to be integrated into clinical practice[8]. Evidence-based medicine has been defined as "the conscientious, explicit, and judicious use of current best-evidence in making decisions about the care of individual patients"[9,10]. Within the evidencebased medicine paradigm, evidence is not restricted to randomized controlled trials, systematic reviews, and meta-analyses, although this restricted view seems to be prevalent in the medical and physical therapy literature. Sackett et al[9,10] emphasized that external clinical evidence can inform but not replace individual clinical expertise. Clinical expertise determines whether external clinical evidence applies to an individual patient, and if so, how it should be integrated into clinical decision making. Pencheon[11] shared this perspective and suggested that high-quality healthcare is about combining "wisdom produced by years of experience" with "evidence produced by generalizable research" in "ways with which patients are happy." He suggested shifting from evidence-based to evidence-informed medicine, where clinical decision making is informed by research evidence but not driven by it, and always includes knowledge from experience. Evidence-informed manual therapy involves integrating the best available external scientific

evidence with individual clinicians' judgments, expertise, and clinical decision-making[12]. The purpose of this article is to provide a best evidence-informed review of the current scientific understanding of MTrPs, including the etiology, pathophysiology, and clinical implications, against the background of extensive clinical experience.

Brief Historical Review

While Dr. Janet Travell (1901-1997) is generally credited for bringing MTrPs to the attention of healthcare providers, MTrPs have been described and rediscovered for several centuries by various clinicians and researchers[13,14]. As far back as the 16th century, de Baillou (1538-1616), as cited by Ruhmann, described what is now known as myofascial pain syndrome (MPS)[15]. MPS is defined as the "sensory, motor, and autonomic symptoms caused by MTrPs" and has become a recognized medical diagnosis among pain specialists[16,17]. In 1816, British physician Balfour, as cited by Stockman, described "nodular tumors and thickenings which were painful to the touch, and from which pains shot to neighboring parts"[18]. In 1898, the German physician Strauss discussed "small, tender and apple-sized nodules and painful, pencil-sized to little-finger-sized palpable bands"[19]. The first trigger point manual was published in 1931 in Germany nearly a decade before Travell became interested in MTrPs[20]. While these early descriptions may appear a bit archaic and unusual—for example, in clinical practice one does not encounter "apple-sized nodules"—these and other historic papers did illustrate the basic features of MTrPs quite accurately[14].

In the late 1930s, Travell, who at that time was a cardiologist and medical researcher, became particularly interested in muscle pain following the publication of several articles on referred pain[21]. Kellgren's descriptions of referred pain patterns of many muscles and spinal ligaments after injecting these tissues with hypertonic saline[22-25] eventually moved Travell to shift her medical career from cardiology to musculoskeletal pain. During the 1940s, she published several articles on injection techniques of MTrPs[26-28]. In 1952, she described the myofascial genesis of pain with detailed referred pain patterns for 32 muscles[29]. Other clinicians also became interested in MTrPs. European physicians Lief and Chaitow developed a treatment method, which they referred to as "neuromuscular technique"[30]. German physician Gutstein described the characteristics of MTrPs and effective manual therapy treatments in several papers under the names of Gutstein, Gutstein-Good, and Good[31-34]. In Australia, Kelly produced a series of articles about fibrositis, which paralleled Travel's writings[35-38].

In the US, chiropractors Nimmo and Vannerson[39] described muscular "noxious generative points," which were thought to produce nerve impulses and eventually result in "vasoconstriction, ischaemia, hypoxia, pain, and cellular degeneration." Later in his career, Nimmo adopted the term "trigger point" after having been introduced to Travell's writings. Nimmo maintained that hypertonic muscles are always painful to pressure, a statement that later became known as "Nimmo's law." Like Travell, Nimmo described distinctive referred pain patterns and recommended releasing these dysfunctional points by applying the proper degree of manual pressure. Nimmo's "receptor-tonus control method" continues to be popular

among chiropractic physicians[39,40]. According to a 1993 report by the National Board of Chiropractic Economics, over 40% of chiropractors in the US frequently apply Nimmo's techniques[41]. Two spin-offs of Nimmo's work are St. John Neuromuscular Therapy (NMT) method and NMT American version, which have become particularly popular among massage therapists[30].

In 1966, Travell founded the North American Academy of Manipulative Medicine, together with Dr. John Mennell, who also published several articles about MTrPs[42,43]. Throughout her career Travell promoted integrating myofascial treatments with articular treatments[16]. One of her earlier papers described a technique for reducing sacroiliac displacement[44]. However, Travell, as cited by Paris[45], maintained the opinion that manipulations were the exclusive domain of physicians and she rejected membership in the North American Academy of Manipulative Medicine by physical therapists.
In the early 1960s, Dr. David Simons was introduced to Travell and her work, which became the start of a fruitful collaboration eventually resulting in several publications, including the *Trigger Point Manuals*, consisting of a 1983 first volume (upper half of the body) and a 1992 second volume (lower half of the body)[46,47]. The first volume has since been revised and updated and a second edition was released in 1999[16]. The *Trigger Point Manuals* are the most comprehensive review of nearly 150 muscle referred-pain patterns based on Travell's clinical observations, and they include an extensive review of the scientific basis of MTrPs. Both volumes have been translated into several foreign languages, including Russian, German, French, Italian, Japanese, and Spanish. Several other clinicians worldwide have also published their own trigger point manuals[48-54]

Clinical aspects of Myofascial Trigger Points

An MTrP is described as "a hyperirritable spot in skeletal muscle that is associated with a hypersensitive palpable nodule in a taut band"[16]. Myofascial trigger points are classified into active and latent trigger points[16]. An active MTrP is a symptom-producing MTrP and can trigger local or referred pain or other paraesthesiae. A latent MTrP does not trigger pain without being stimulated. Myofascial trigger points are the hallmark characteristics of MPS and feature motor, sensory, and autonomic components. Motor aspects of active and latent MTrPs may include disturbed motor function, muscle weakness as a result of motor inhibition, muscle stiffness, and restricted range of motion[55,56]. Sensory aspects may include local tenderness, referral of pain to a distant site, and peripheral and central sensitization. Peripheral sensitization can be described as a reduction in threshold and an increase in responsiveness of the peripheral ends of nociceptors, while central sensitization is an increase in the excitability of neurons within the central nervous system. Signs of peripheral and central sensitization are allodynia (pain due to a stimulus that does not normally provoke pain) and hyperalgesia (an increased response to a stimulus that is normally painful). Both active and latent MTrPs are painful on compression. Vecchiet et al[57,59]

described specific sensory changes over MTrPs. They observed significant lowering of the pain threshold over active MTrPs when measured by electrical stimulation, not only in the muscular tissue but also in the overlying cutaneous and subcutaneous tissues. In contrast, with latent MTrPs, the sensory changes did not involve the cutaneous and subcutaneous tissues[57-59]. Autonomic aspects of MTrPs may include, among others, vasoconstriction, vasodilatation, lacrimation, and piloerection[16,60-63].

A detailed clinical history, examination of movement patterns, and consideration of muscle referred pain patterns assist clinicians in determining which muscles may harbor clinically relevant MTrPs[64]. Muscle pain is perceived as aching and poorly localized. There are no laboratory or imaging tests available that can confirm the presence of MTrPs. Myofascial trigger points are identified through either a flat palpation technique *(Figure 1)* in which a clinician applies finger or thumb pressure to muscle against underlying bone tissue, or a pincer palpation technique *(Figure 2)* in which a particular muscle is palpated between the clinician's fingers.

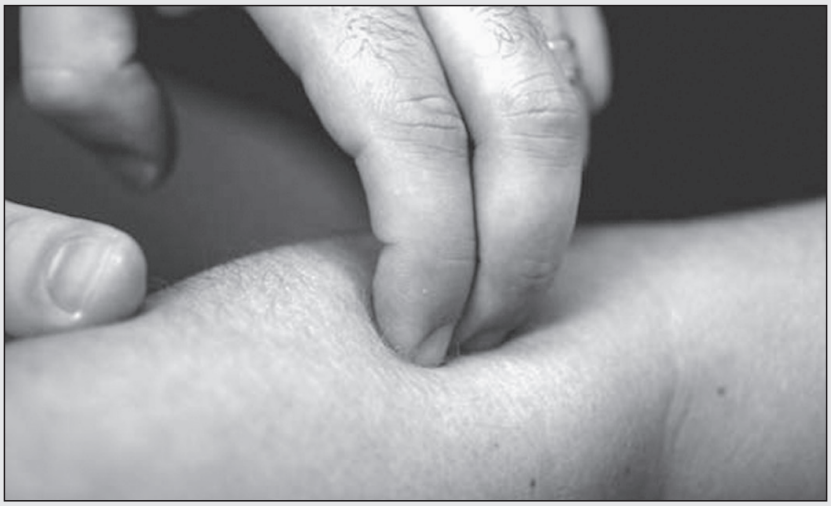


Fig. 1: *Flat palpation*

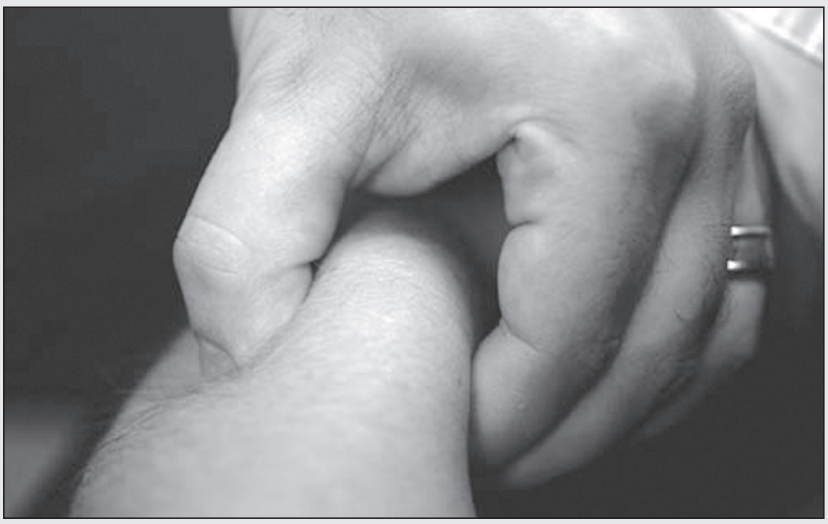


Fig. 2: *Pincer palpation*

By definition, MTrPs are located within a taut band of contractured muscle fibers *(Figure 3)*, and palpating for MTrPs starts with identifying this taut band by palpating perpendicular to the fiber direction. Once the taut band is located, the clinician moves along the taut band to find a discrete area of intense pain and hardness.

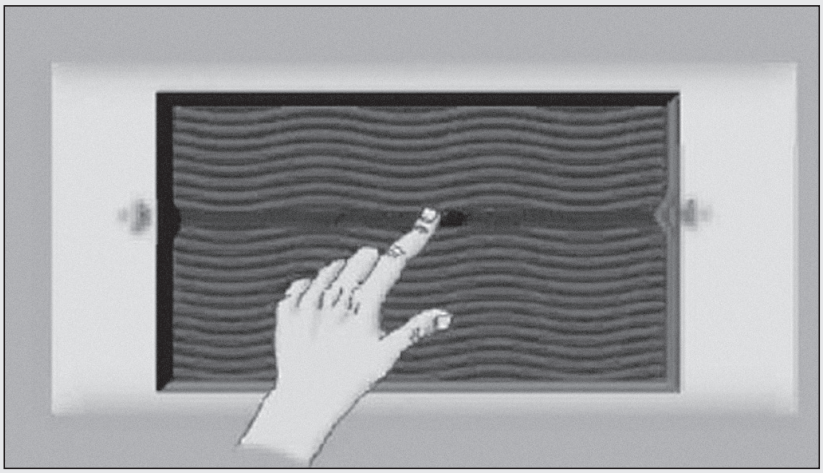
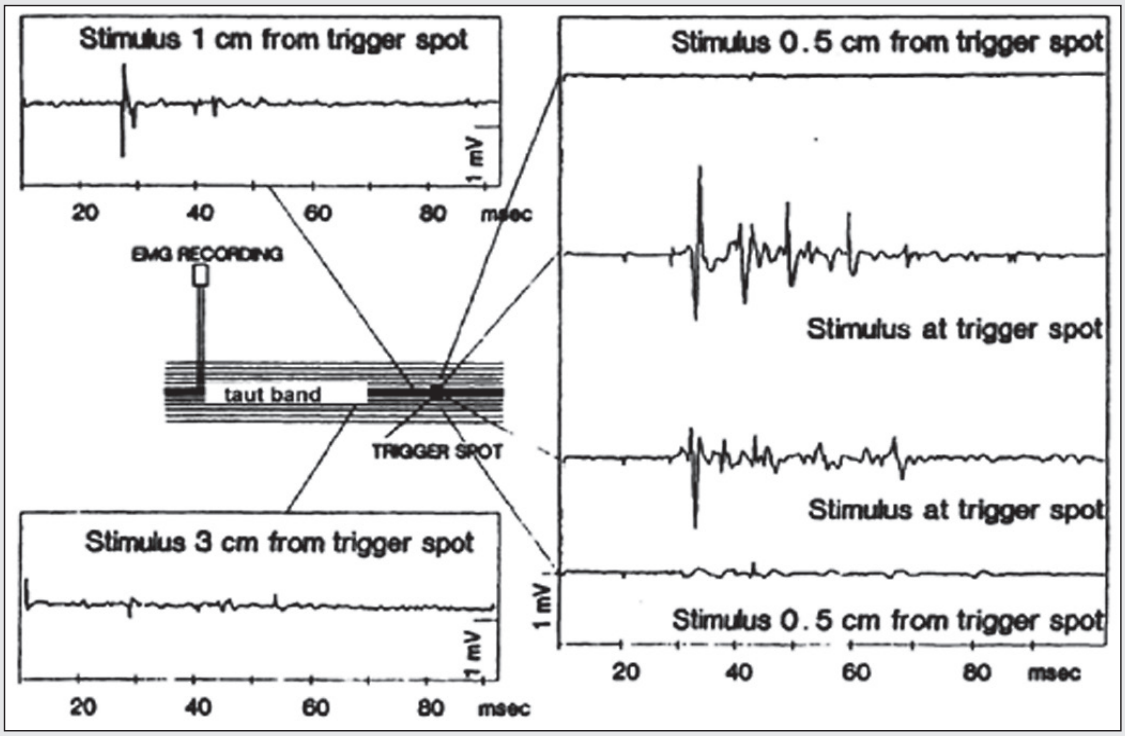


Fig. 3: *Palpation of a trigger point within a taut band (reproduced with permission from Weisskircher H-W. Head Pains Due to Myofascial Trigger Points. CD-ROM, www. trigger-point. com, 1997)*

Two studies have reported good overall interrater reliability for identifying taut bands, MTrPs, referred pain, and local twitch responses[65,66]. The minimum criteria that must be satisfied in order to distinguish an MTrP from any other tender area in muscle are a taut band and a tender point in that taut band[65]. Although Janda maintained that systematic palpation can differentiate between myofascial taut bands and general muscle spasms, electromyography is the gold standard to differentiate taut bands from contracted muscle fibers[67,68]. Spasms can be defined as electromyographic (EMG) activity as the result of increased neuromuscular tone of the entire muscle, and they are the result of nerve-initiated contractions. A taut band is an endogenous localized contracture within the muscle without activation of the motor endplate[69] . From a physiological perspective, the term "contracture" is more appropriate then "contraction" when describing chronic involuntary shortening of a muscle without EMG activity. In clinical practice, surface EMG is used in the diagnosis and management of MTrPs in addition to manual examinations[67,70,71]. Diagnostically, surface EMG can assist in assessing muscle behavior during rest and during functional tasks. Clinicians use the MTrP referred pain patterns in determining which muscles to examine with surface EMG. Muscles that harbor MTrPs responsible for the patient's pain complaint are examined first. EMG assessments guide the clinician with postural training, ergonomic interventions, and muscle awareness training[67] .

The patient's recognition of the elicited pain further guides the clinician. The presence of a so-called local twitch response (LTR), referred pain, or reproduction of the person's symptomatic pain increases the certainty and specificity of the diagnosis of MPS. Local twitch responses are spinal reflexes that appear to be unique to MTrPs. They are characterized by a sudden contraction of muscle fibers within a taut band, when the taut band is

Fig. 4: *Local twitch response in a rabbit trigger spot. Local twitch responses are elicited only when the needle is placed accurately within the trigger spot. Moving as little as 0.5 cm away from the trigger spot virtually eliminates the local twitch response.*
(reproduced with permission from Hong C-Z, 1994)

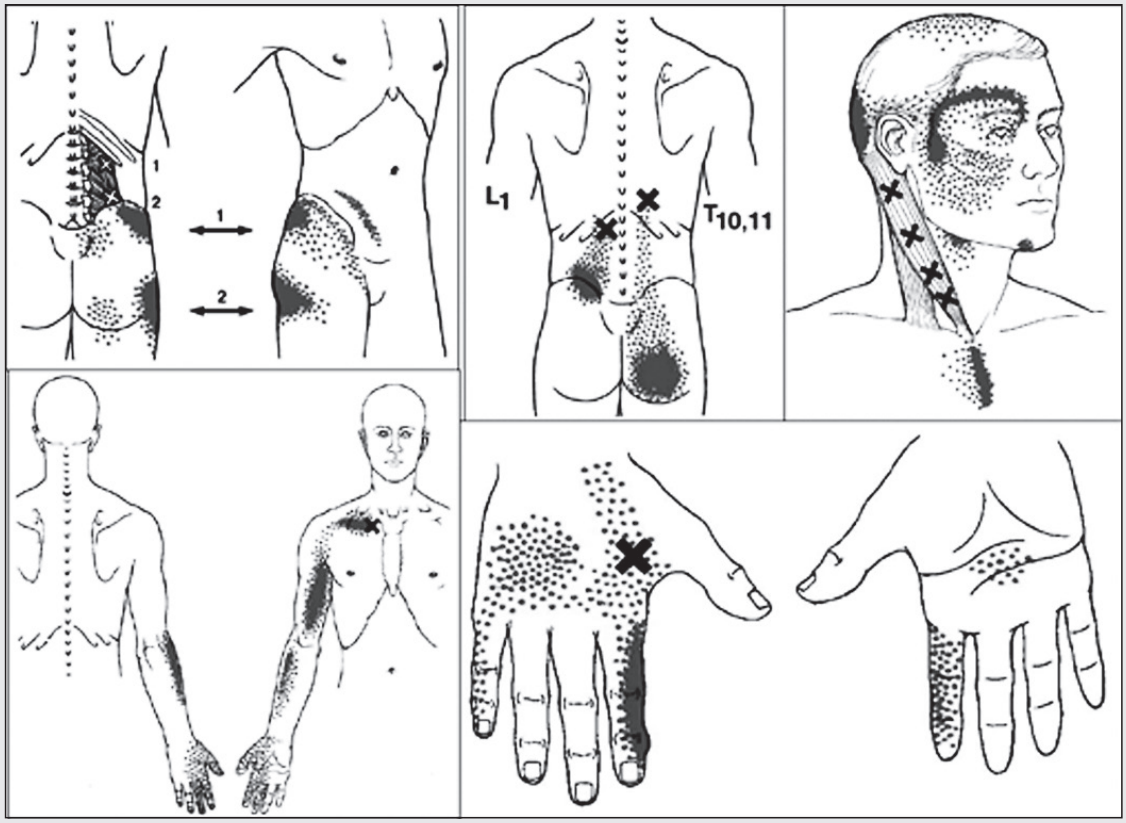


strummed manually or needled. The sudden contractions can be observed visually, can be recorded electromyographically, or can be visualized with diagnostic ultrasound[72]. When an MTrP is needled with a monopolar teflon-coated EMG needle, LTRs appear as high-amplitude poly-phasic EMG discharges[73-78].

In clinical practice, there is no benefit in using needle EMG or sonography, and its utility is limited to research studies. For example, Audette et al[79] established that in 61.5% of active MTrPs in the trapezius and levator scapulae muscles, dry needling an active MTrP elicited an LTR in the same muscle on the opposite side of the body. Needling of latent MTrPs resulted in unilateral LTRs only. In this study, LTRs were used to research the nature of active versus latent MTrPs. Studies have shown that clinical outcomes are significantly improved when LTRs are elicited in the treatment of patients with dry needling or injection therapy[74,80,81]. The taut band, MTrP, and LTR *(Figure 4)* are objective criteria, identified solely by palpation, that do not require a verbal response from the patient[82].

Active MTrPs refer pain usually to a distant site. The referred pain patterns *(Figure 5)* are not necessarily restricted to single segmental pathways or to peripheral nerve distributions. Although typical referred pain patterns have been established, there is considerable variation between patients[16,48].

Fig. 5: *MTrP referred pain patterns (reproduced with permission from MEDICLIP, Manual Medicine 1 & 2, Version 1.0a, 1997, Williams & Wilkins)*



Usually, the pain in reference zones is described as "deep tissue pain" of a dull and aching nature. Occasionally, patients may report burning or tingling sensations, especially in superficial muscles such as the platysma muscle[83,84]. By mechanically stimulating active MTrPs, patients may report the reproduction of their pain, either immediately or after a 10-15 second delay. Normally, skeletal muscle nociceptors require high intensities of stimulation and they do not respond to moderate local pressure, contractions, or muscle stretches[85]. However, MTrPs cause persistent noxious stimulation, which results in increasing the number and size of the receptive fields to which a single dorsal horn nociceptive neuron responds, and the experience of spontaneous and referred pain[86]. Several recent studies have determined previously unrecorded referred pain patterns of different muscles and MTrPs[87-90]. Referred pain is not specific to MPS but it is relatively easy to elicit over MTrPs[91]. Normal muscle tissue and other body tissues, including the skin, zygapophyseal joints, or internal organs, may also refer pain to distant regions with mechanical pressure, making referred pain elicited by stimulation of a tender location a nonspecific finding[84,92-95]. Gibson et al[96] found that referred pain is actually easier to elicit in tendon-bone junctions and tendon than in the muscle belly. However, after exposing the

muscle to eccentric exercise, significantly higher referred pain frequency and enlarged pain areas were found at the muscle belly and the tendon-bone junction sites following injection with hypotonic saline. The authors suggested that central sensitization may explain the referred pain frequency and enlarged pain areas[97].

While a survey of members of the American Pain Society showed general agreement that MTrPs and MPS exist as distinct clinical entities, MPS continues to be one of the most commonly missed diagnoses[17,98]. In a recent study of 110 adults with low back pain, myofascial pain was the most common finding affecting 95.5% of patients, even though myofascial pain was poorly defined as muscle pain in the paraspinal muscles, piriformis, or tensor fasciae latae[99]. A study of adults with frequent migraine headaches diagnosed according to the International Headache Society criteria showed that 94% of the patients reported migrainous pain with manual stimulation of cervical and temporal MTrPs, compared with only 29% of controls[100,101]. In 30% of the migraine group, palpation of MTrPs elicited a "full-blown migraine attack that required abortive treatment." The researchers found a positive relationship between the number of MTrPs and the frequency of migraine attacks and duration of the illness[100]. Several studies have confirmed that MTrPs are common not only in persons attending pain management clinics but also in those seeking help through internal medicine and dentistry[102-107]. In fact, MTrPs have been identified with nearly every musculoskeletal pain problem, including radiculopathies[104], joint dysfunction[108], disk pathology[109], tendonitis[110], craniomandibular dysfunction[111-113], migraines[100,114], tension-type headaches[7,87], carpal tunnel syndrome[115], computer-related disorders[116], whiplash-associated disorders[60,117], spinal dysfunction[118], and pelvic pain and other urologic syndromes[119-122]. Myofascial trigger points are associated with many other pain syndromes[123], including, for example, post-herpetic neuralgia[124,125], complex regional pain syndrome[126,127], nocturnal cramps[128], phantom pain[129,130], and other relatively uncommon diagnoses such as Barré-Liéou syndrome[131] and neurogenic pruritus[132]. A recent study suggested that there might be a relationship between MTrPs in the upper trapezius muscle and cervical spine dysfunction at the C3 and C4 vertebrae, although a cause-and-effect relationship was not established in this correlational study[133]. Another study described that persons with mechanical neck pain had significantly more clinically relevant MTrPs in the upper trapezius, sternocleidomastoid, levator scapulae, and suboccipital muscles as compared to healthy controls[5].

Etiology of MTrPs

Several possible mechanisms can lead to the development of MTrPs, including low-level muscle contractions, uneven intramuscular pressure distribution, direct trauma, unaccustomed eccentric contractions, eccentric contractions in unconditioned muscle, and maximal or submaximal concentric contractions.

Low-level muscle contractions

Of particular interest in the etiology of MTrPs are low-level muscle exertions and the so-called Cinderella Hypothesis developed by Hägg in 1988[134]. The Cinderella Hypothesis postulates that occupational myalgia is caused by selective overloading of the earliest recruited and last de-recruited motor units according to the ordered recruitment principle or Henneman's "size principle"[134,135]. Smaller motor units are recruited before and de-recruited after larger ones; as a result, the smaller type 1 fibers are continuously activated during prolonged motor tasks[135]. According to the Cinderella Hypothesis, muscular force generated at sub-maximal levels during sustained muscle contractions engages only a fraction of the motor units available without the normally occurring substitution of motor units during higher force contractions, which in turn can result in metabolically overloaded motor units, prone to loss of cellular Ca^{2+}-homeostasis, subsequent activation of autogenic destructive processes, and muscle pain[136,137]. The other pillar of the Cinderella Hypothesis is the finding of an excess of ragged red fibers in myalgic patients[136]. Indeed, several researchers have demonstrated the presence of ragged red fibers and moth-eaten fibers in subjects with myalgia, which are indications of structural damage to the cell membrane and mitochondria and a change in the distribution of mitochondria or the sarcotubular system respectively[138-142].

There is growing evidence that low-level static muscle contractions or exertions can result in degeneration of muscle fibers[143]. Gissell[144,145] has shown that low-level exertions can result in an increase of Ca^{2+}-release in skeletal muscle cells, muscle membrane damage due to leakage of the intracellular enzyme lactate dehydrogenase, structural damage, energy depletion, and myalgia. Low-level muscle stimulation can also lead to the release of interleukin 6 (IL-6) and other cytokines[146,147].

Several studies have confirmed the Cinderella Hypothesis and support the idea that in low-level static exertions, muscle fiber recruitment patterns tend to be stereotypical with continuous activation of smaller type 1 fibers during prolonged motor tasks[148-152]. As Hägg indicated, the continuous activity and metabolic overload of certain motor units does not occur in all subjects[136]. The Cinderella Hypothesis was recently applied to the development of MTrPs[116]. In a well-designed study, Treasters et al[116] established that sustained low-level muscle contractions during continuous typing for as little as 30 minutes commonly resulted in the formation of MTrPs. They suggested that MTrPs might provide a useful explanation for muscle pain and injury that can occur from low-level static exertions[116]. Myofascial trigger points are common in office workers, musicians, dentists, and other occupational groups exposed to low-level muscle exertions[153]. Chen et al[154] also suggested that low-level muscle

exertions can lead to sensitization and development of MTrPs. Forty piano students showed significantly reduced pressure thresholds over latent MTrPs after only 20 minutes of continuous piano playing[154].

Intramuscular pressure distribution

Otten[155] has suggested that circulatory disturbances secondary to increased intramuscular pressure may also lead to the development of myalgia. Based on mathematical modeling applied to a frog gastrocnemius muscle, Otten confirmed that during static low-level muscle contractions, capillary pressures increase dramatically especially near the muscle insertions *(Figure 6)*. In other words, during low-level exertions, the intramuscular pressure near the muscle insertions might increase rapidly, leading to excessive capillary pressure, decreased circulation, and localized hypoxia and ischaemia[155].

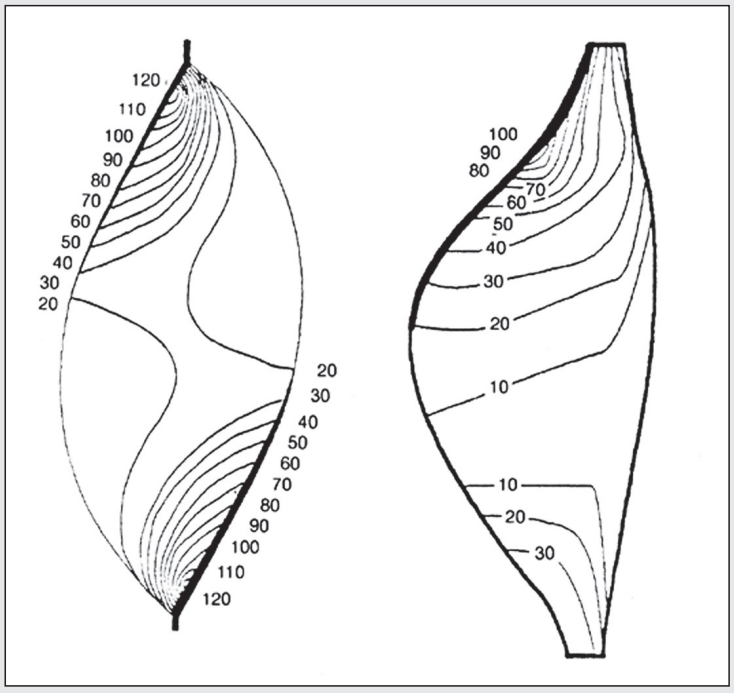


Fig. 6: *Intramuscular pressure distribution in the gastrocnemius muscle of the toad (reproduced with permission from E. Otten, 2006)*

With higher level contractions in between 10% and 20% of maximum voluntary effort, the intramuscular pressure increases also in the muscle belly[156,157]. According to Otten, the increased pressure gradients during low-level exertions may contribute to the development of pain at the musculotendinous junctions and eventually to the formation of MTrPs (personal communication, 2005).

In 1999, Simons introduced the concept of "attachment trigger points" to explain pain at the musculotendinous junctions in persons with MTrPs, based on the assumption that taut bands would generate sufficient sustained force to induce localized enthesopathies[16,158]. More recently, Simons concluded that there is no convincing evidence that the tension

generated in shortened sarcomeres in a muscle belly would indeed be able to generate passive or resting force throughout an entire taut band resulting in enthesopathies, even though there may be certain muscles or conditions where this could occur (personal communication, 2005). To the contrary, force generated by individual motor units is always transmitted laterally to the muscle's connective tissue matrix, involving at least two protein complexes containing vinculin and dystrophin, respectively[159]. There is also considerable evidence that the assumption that muscle fibers pass from tendon to tendon is without basis[160]. Trotter[160] has demonstrated that skeletal muscle is comprised of in-series fibers. In other words, there is evidence that a single muscle fiber does not run from tendon to tendon. The majority of fibers are in series with inactive fibers, which makes it even more unlikely that the whole muscle length-tension properties would be dictated by the shortest contractured fibers in the muscle[161].

In addition, it is important to consider the mechanical and functional differences between fast and slow motor units[162,163]. Slow motor units are always stiffer than fast units, although fast units can produce more force. If there were any transmission of force along the muscle fiber, as Simons initially suggested, fast fibers would be better suited to accomplish this. Yet, fast motor units have larger series of elastic elements, which would absorb most of the force displacement[164,165]. Fast fibers show a progressive decrease in cross-sectional area and end in a point within the muscle fascicle, making force transmission even more unlikely[163]. Fast fibers rely on transmitting a substantial proportion of their force to the endomysium, transverse cytoskeleton, and adjacent muscle fibers[162,163]. In summary, the development of so-called "attachment trigger points" as a result of increased tension by contractured sarcomeres in MTrPs is not clear and more research is needed to explain the clinical observation that MTrPs appear to be linked to pain at the musculotendinous junction. The increased tension in the muscle belly is likely to dissipate across brief sections of the taut band on both sides of the MTrP and laterally through the transverse cytoskeleton[166-168]. Instead, Otten's model of increased intramuscular pressure, decreased circulation, localized hypoxia, and ischaemia at the muscle insertions provides an alternative model for the clinically observed pain near the musculotendinous junction and osseous insertions in persons with MTrPs, even though the model does not explain why taut bands are commonly present[155].

Direct trauma

There is general agreement that acute muscle overload can activate MTrPs, although systematic studies are lacking[169]. For example, people involved in whiplash injuries commonly experience prolonged muscle pain and dysfunction[170-173]. In a retrospective review, Schuller et al[174] found that 80% of 1096 subjects involved in low-velocity collisions demonstrated evidence of muscle pain with myogeloses among the most common findings. Although Schuller et al[174] did not define these myogeloses, Simons has suggested that a myogelosis describes the same clinical entity as an MTrP[175]. Baker[117] reported that the splenius capitis, semispinalis capitis, and sternocleidomastoid muscles developed symptomatic MTrPs in 77%, 62%, and 52% of 52 whiplash patients, respectively. In a

retrospective review of 54 consecutive chronic whiplash patients, Gerwin and Dommerholt[176] reported that clinically relevant MTrPs were found in every patient, with the trapezius muscle involved most often. Following treatment emphasizing the inactivation of MTrPs and restoration of normal muscle length, approximately 80% of patients experienced little or no pain, even though the average time following the initiating injury was 2.5 years at the beginning of the treatment regimen. All patients had been seen previously by other physicians and physical therapists who apparently had not considered MTrPs in their thought process and clinical management[176]. Fernández-de-las-Peñas et al[177,178] confirmed that inactivation of MTrPs should be included in the management of persons suffering from whiplashassociated disorders. In their research-based treatment protocol, the combination of cervical and thoracic spine manipulations with MTrP treatments proved superior to more conventional physical therapy consisting of massage, ultrasound, home exercises, and low-energy high-frequency pulsed electromagnetic therapy[177].

Direct trauma may create a vicious cycle of events wherein damage to the sarcoplasmic reticulum or the muscle cell membrane may lead to an increase of the calcium concentration, a subsequent activation of actin and myosin, a relative shortage of adenosine triphosphate (ATP), and an impaired calcium pump, which in turn will increase the intracellular calcium concentration even more, completing the cycle. The calcium pump is responsible for returning intracellular Ca^{2+} to the sarcoplasmic reticulum against a concentration gradient, which requires a functional energy supply. Simons and Travell[179] considered this sequence in the development of the so-called "energy crisis hypothesis" introduced in 1981. Sensory and motor system dysfunction have been shown to develop rapidly after injury and actually may persist in those who develop chronic muscle pain and in individuals who have recovered or continue to have persistent mild symptoms[172,180]. Scott et al[181] determined that individuals with chronic whiplash pain develop more widespread hypersensitivity to mechanical pressure and thermal stimuli than those with chronic idiopathic neck pain. Myofascial trigger points are a likely source of ongoing peripheral nociceptive input, and they contribute to both peripheral and central sensitization, which may explain the observation of widespread allodynia and hypersensitivity[60,62,63]. In addition to being caused by whiplash injury, acute muscle overload can occur with direct impact, lifting injuries, sports performance, etc.[182].

Eccentric and (sub)maximal concentric contractions

Many patients report the onset of pain and activation of MTrPs following either acute, repetitive, or chronic muscle overload[183]. Gerwin et al[184] suggested that likely mechanisms relevant for the development of MTrPs included either unaccustomed eccentric exercise, eccentric exercise in unconditioned muscle, or maximal or sub-maximal concentric exercise. A brief review of pertinent aspects of exercise follows, preceding linking this body of research to current MTrP research.

Eccentric exercise is associated with myalgia, muscle weakness, and destruction of muscle fibers, partially because eccentric contractions cause an irregular and uneven

lengthening of muscle fibers[185-187]. Muscle soreness and pain occur because of local ultrastructural damage, the release of sensitizing algogenic substances, and the subsequent onset of peripheral and central sensitization[85,188-190]. Muscle damage occurs at the cytoskeletal level and frequently involves disorganization of the A-band, streaming of the Z-band, and disruption of cytoskeletal proteins, such as titin, nebulin, and desmin, even after very short bouts of eccentric exercise[186,189-194]. Loss of desmin can occur within 5 minutes of eccentric loading, even in muscles that routinely contract eccentrically during functional activities, but does not occur after isometric or concentric contractions[193,195]. Lieber and Fridén[193] suggested that the rapid loss of desmin might indicate a type of enzymatic hydrolysis or protein phosphorylation as a likely mechanism.

One of the consequences of muscle damage is muscle weakness[196-198]. Furthermore, concentric and eccentric contractions are linked to contraction-induced capillary constrictions, impaired blood flow, hypoperfusion, ischaemia, and hypoxia, which in turn contribute to the development of more muscle damage, a local acidic milieu, and an excessive release of protons (H^+), potassium (K^+), calcitonin-gene-related-peptide (CGRP), bradykinin (BK), and substance P (SP), and sensitization of muscle nociceptors[184,188]. There are striking similarities with the chemical environment of active MTrPs established with microdialysis, suggesting an overlap between the research on eccentric exercise and MTrP research[184,199]. However, at this time, it is premature to conclude that there is solid evidence that eccentric and sub-maximal concentric exercise are absolute precursors to the development of MTrPs. In support of this hypothesized causal relation, Itoh et al[200] demonstrated in a recent study that eccentric exercise can lead to the formation of taut and tender ropy bands in exercised muscle, and they hypothesized that eccentric exercise may indeed be a useful model for the development of MTrPs.

Eccentric and concentric exercise and MTrPs have been associated with localized hypoxia, which appears to be one of the most important precursors for the development of MTrPs[201]. As mentioned, hypoxia leads to the release of multiple algogenic substances. In this context, recent research by Shah et al[199] at the US National Institutes of Health is particularly relevant. Shah et al analyzed the chemical milieu of latent and active MTrPs and normal muscles. They found significantly increased concentrations of BK, CGRP, SP, tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), serotonin, and norepinephrine in the immediate milieu of active MTrPs only[199]. These substances are well-known stimulants for various muscle nociceptors and bind to specific receptor molecules of the nerve endings, including the so-called purinergic and vanilloid receptors[85,202].

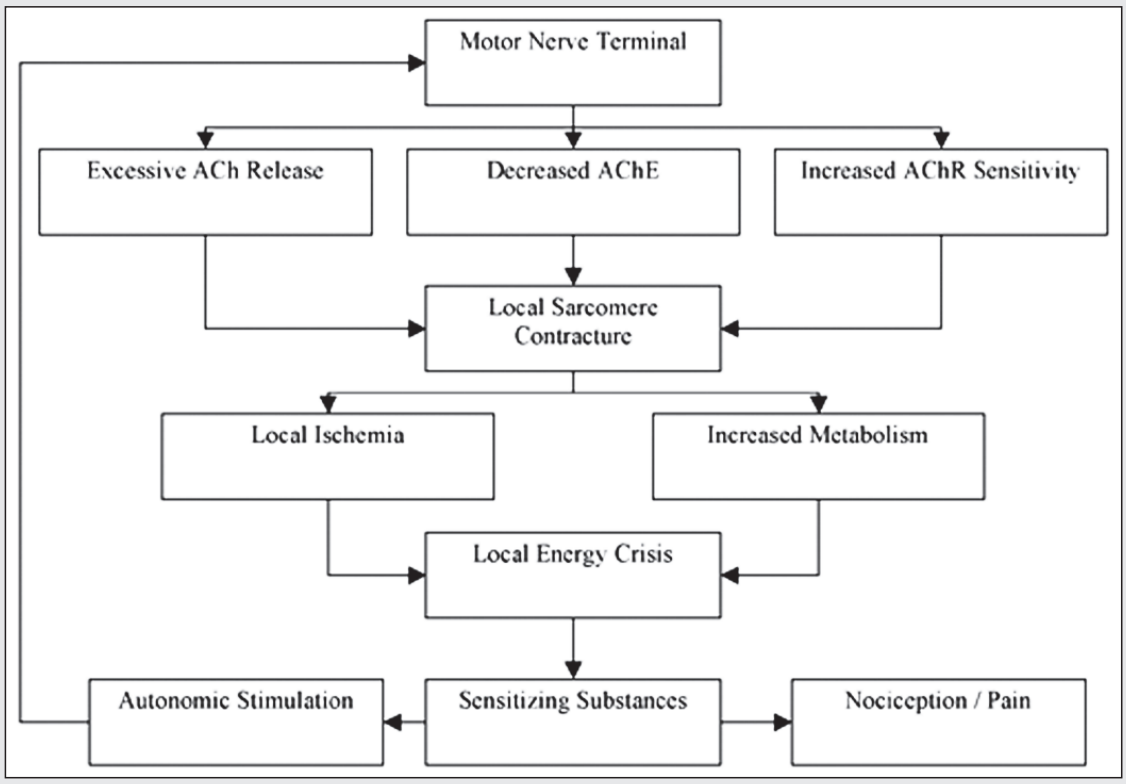
Muscle nociceptors are dynamic structures whose receptors can change depending on the local tissue environment. When a muscle is damaged, it releases ATP, which stimulates purinergic receptors, which are sensitive to ATP, adenosine diphosphate, and adenosine. They bind ATP, stimulate muscle nociceptors, and cause pain. Vanilloid receptors are sensitive to heat and respond to an increase in H^+-concentration, which is especially relevant under conditions with a lowered pH, such as ischaemia, inflammation, or prolonged and exhaustive muscle contractions[85]. Shah et al[199] determined that the pH at

active MTrP sites is significantly lower than at latent MTrP sites. A lowered pH can initiate and maintain muscle pain and mechanical hyperalgesia through activation of acid-sensing ion channels[203,204]. Neuroplastic changes in the central nervous system facilitate mechanical hyperalgesia even after the nociceptive input has been terminated (central sensitization)[203,204]. Any noxious stimulus sufficient to cause nociceptor activation causes bursts of SP and CGRP to be released into the muscle, which have a significant effect on the local biochemical milieu and microcirculation by stimulating "feed-forward" neurogenic inflammation. Neurogenic inflammation can be described as a continuous cycle of increasing production of inflammatory mediators and neuropeptides and an increasing barrage of nociceptive input into wide dynamic-range neurons in the spinal cord dorsal horn[184].

The integrated Trigger point Hypothesis

The integrated trigger point hypothesis *(Figure 7)* has evolved since its first introduction as the "energy crisis hypothesis" in 1981. It is based on a combination of electrodiagnostic and histopathological evidence[179,183].

Fig. 7: *The integrated trigger point hypothesis. Ach-acetylcholine; AchE-acetylcholinesterase; AchR- acetylcholine receptor*



As early as 1957, Weeks and Travell[205] had published a report that outlined a characteristic electrical activity of an MTrP. It was not until 1993 that Hubbard et al[206] confirmed that this EMG discharge consists of low-amplitude discharges in the order of 10-50 μV and intermittent high-amplitude discharges (up to 500 μV) in painful MTrPs. Initially, the electrical activity was termed "spontaneous electrical activity" (SEA) and thought to be related to dysfunctional muscle spindles[206]. Best available evidence now suggests that the SEA is in fact endplate noise (EPN), which is found much more commonly in the endplate zone near MTrPs than in an endplate zone outside MTrPs[207-209]. The electrical discharges occur with frequencies that are 10-1,000 times that of normal endplate potentials, and they have been found in humans, rabbits, and recently even in horses[209,210]. The discharges are most likely the result of an abnormally excessive release of acetylcholine (ACh) and indicative of dysfunctional motor endplates, contrary to the commonly accepted notion among electromyographers that endplate noise arises from normal motor endplates[183]. The effectiveness of botulinum toxin in the treatment of MTrPs provides indirect evidence of the presence of excessive ACh[211]. Botulinum toxin (BoTox) is a neurotoxin that blocks the release of ACh from presynaptic cholinergic nerve endings. A recent study in mice demonstrated that the administration of botulinum toxin resulted in a complete functional repair of dysfunctional endplates[212]. There is some early evidence that muscle stretching and hypertonicity may also enhance the excessive release of ACh[213,214]. Tension on the integrins in the presynaptic membrane at the motor nerve terminal is hypothesized to mechanically trigger an ACh release that does not require Ca^{2+} [213-215]. Integrins are receptor proteins in the cell membrane involved in attaching individual cells to the extracellular matrix.

Excessive ACh affects voltage-gated sodium channels of the sarcoplasmic reticulum and increases the intracellular calcium levels, which triggers sustained muscle contractures. It is conceivable that in MTrPs, myosin filaments literally get stuck in the Z-band of the sarcomere. During sarcomere contractions, titin filaments are folded into a gel-like structure at the Z-band. In MTrPs, the gel-like titin may prevent the myosin filaments from detaching. The myosin filaments may actually damage the regular motor assembly and prevent the sarcomere from restoring its resting length[216]. Muscle contractures are also maintained because of the relative shortage of ATP in an MTrP, as ATP is required to break the cross-bridges between actin and myosin filaments. The question remains whether sustained contractures require an increase of oxygen availability.

At the same time, the shortened sarcomeres compromise the local circulation causing ischaemia. Studies of oxygen saturation levels have demonstrated severe hypoxia in MTrPs[201]. Hypoxia leads to the release of sensitizing substances and activates muscle nociceptors as reviewed above. The combined decreased energy supply and possible increased metabolic demand would also explain the common finding of abnormal mitochondria in the nerve terminal and the previously mentioned ragged red fibers. In mice, the onset of hypoxia led to an immediate increased ACh release at the motor endplate[217].

The combined high-intensity mechanical and chemical stimuli may cause activation and sensitization of the peripheral nerve endings and autonomic nerves, activate second order neurons including so-called "sleeping" receptors, cause central sensitization, and lead to the formation of new receptive fields, referred pain, a long-lasting increase in the excitability of nociceptors, and a more generalized hyperalgesia beyond the initial nociceptive area. An expansion of a receptive field means that a dorsal horn neuron receives information from areas it has not received information from previously[218]. Sensitization of peripheral nerve endings can also cause pain through SP activating the neurokin-1 receptors and glutamate activating N-methyl-D-aspartate receptors, which opens post-synaptic channels through which Ca^{2+} ions can enter the dorsal horn and activate many enzymes involved in the sensitization[85].

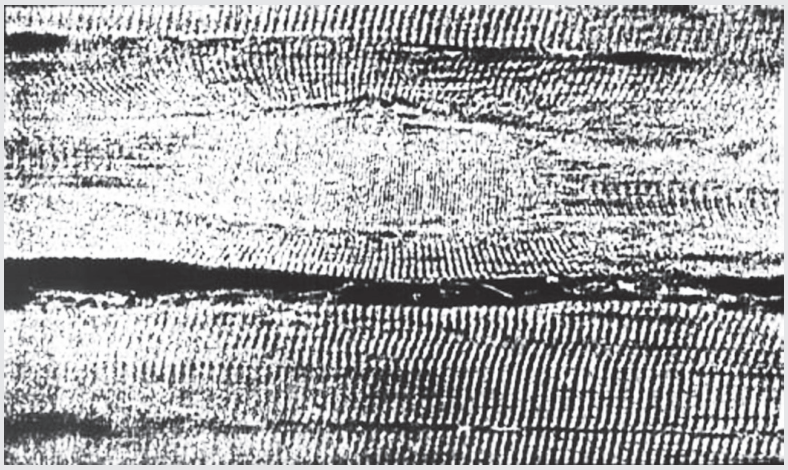


Fig. 8: *Longitudinal section of a contraction knot in a canine gracilis muscle (reproduced with permission from: Simons DG, Travell JG, Simons LS. Travell and Simons' Myofascial Pain and Dysfunction: The Trigger Point Manual. Vol. 1. 2nd ed. Baltimore, MD: Williams & Wilkins, 1999)*

Several histological studies offer further support for the integrated trigger point hypothesis. In 1976, Simons and Stolov published the first biopsy study of MTrPs in a canine muscle and reported multiple contraction knots in various individual muscle fibers *(Figure 8)* [219]. The knots featured a combination of severely shortened sarcomeres in the center and lengthened sarcomeres outside the immediate MTrP region[219].

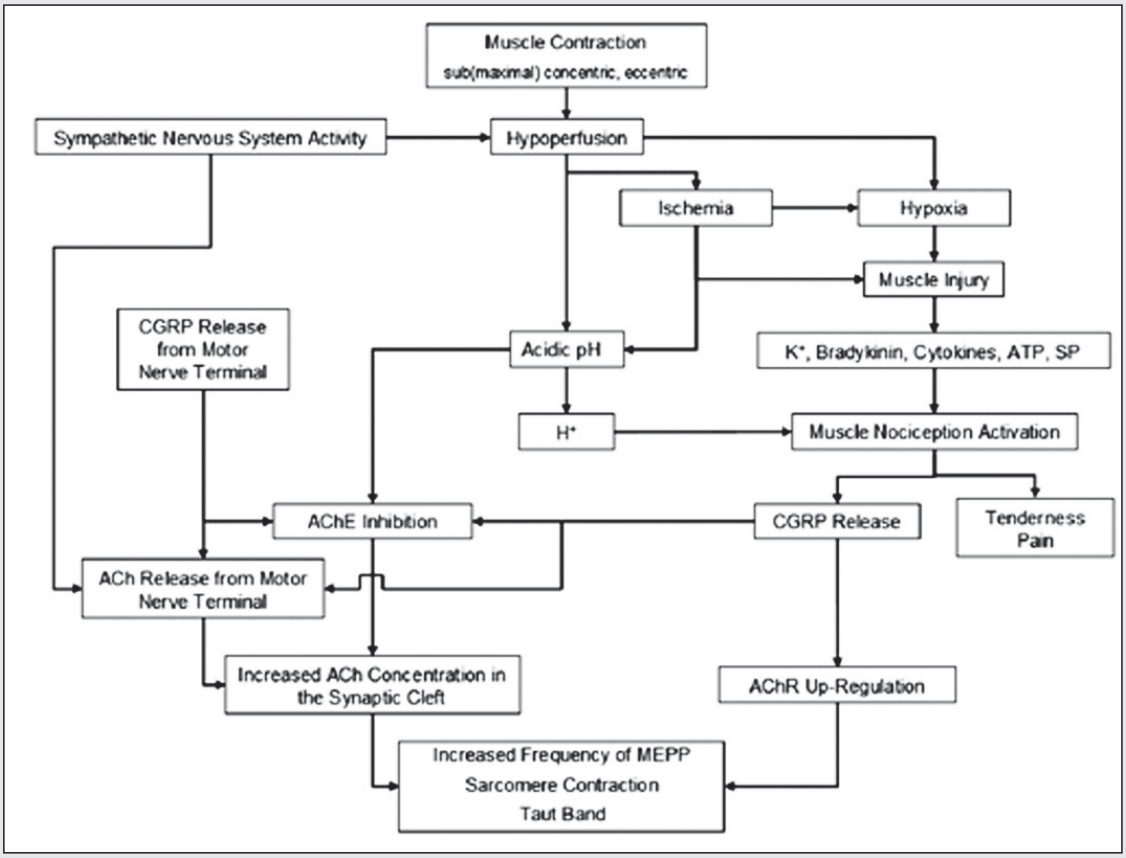
Reitinger et al[220] reported pathologic alterations of the mitochondria as well as increased width of A-bands and decreased width of I-bands in muscle sarcomeres of MTrPs in the gluteus medius muscle. Windisch et al[221] determined similar alterations in a post-mortem histological study of MTrPs completed within 24 hours of time of death. Mense et al[222] studied the effects of electrically induced muscle contractions and a cholinesterase blocker on muscles with experimentally induced contraction knots and found evidence of localized contractions, torn fibers, and longitudinal stripes. Pongratz and Spath[223, 224] demonstrated evidence of a contraction disk in a region of an MTrP using light microscopy. New MTrP histopathological studies are currently being conducted at the Friedrich Baur Institute in Munich, Germany. Gariphianova[225] described pathological changes with biopsy studies of MTrPs, including a decrease in quantity of mitochondria, possibly indicating metabolic distress. Several older

histological studies are often quoted, but it is not clear to what extent those findings are specific for MTrPs. In 1951, Glogowsky and Wallraff[226] reported damaged fibril structures. Fassbender[227] observed degenerative changes of the I-bands, in addition to capillary damage, a focal accumulation of glycogen, and a disintegration of the myofibrillar network.

There is growing evidence for the integrated trigger point hypothesis with regard to the motor and sensory aspects of MTrPs, but many questions remain about the autonomic aspects. Several studies have shown that MTrPs are influenced by the autonomic nervous system. Exposing subjects with active MTrPs in the upper trapezius muscles to stressful tasks consistently increased the electrical activity in MTrPs in the upper trapezius muscle but not in control points in the same muscle, while autogenic relaxation was able to reverse the effects[228-231]. The administration of the sympathetic blocking agent phentolamine significantly reduced the electrical activity of an MTrP[228,232,233]. The interactions between the autonomic nervous system and MTrPs need further investigation. Hubbard[228] maintained that the autonomic features of MTrPs are evidence that MTrPs may be dysfunctional muscle spindles. Gerwin et al[184] have suggested that the presence of alpha and beta adrenergic receptors at the endplate provide a possible mechanism for autonomic interaction. In a rodent, stimulation of the alpha and beta adrenergic receptors stimulated the release of ACh in the phrenic nerve[234]. In a recent study, Ge et al[61] provided for the first time experimental evidence of sympathetic facilitation of mechanical sensitization of MTrPs, which they attributed to a change in the local chemical milieu at the MTrPs due to increased vasoconstriction, an increased sympathetic release of noradrenaline, or an increased sensitivity to noradrenaline. Another intriguing possibility is that the cytokine interleukin-8 (IL-8) found in the immediate milieu of active MTrPs may contribute to the autonomic features of MTrP. IL-8 can induce mechanical hyperalgesia, which is inhibited by beta adrenergic receptor antagonists[235]. Shah et al found significantly increased levels of IL-8 in the immediate milieu of active MTrPs (Shah, 2006, personal communication).

The findings of Shah et al[199] mark a major milestone in the understanding and acceptance of MTrPs and support parts of the integrated trigger point hypothesis[183]. The possible consequences of several of the chemicals present in the immediate milieu of active MTrPs have been explored by Gerwin et al[184]. As stated, Shah et al found significantly increased concentrations of H^+, BK, CGRP, SP, TNF-α, IL-1β, serotonin, and norepinephrine in active MTrPs only. There are many interactions between these chemicals that all can contribute to the persistent nature of MTrPs through various vicious feedback cycles[236]. For example, BK is known to activate and sensitize muscle nociceptors, which leads to inflammatory hyperalgesia, an activation of high-threshold nociceptors associated with C-fibers, and even an increased production of BK itself. Furthermore, BK stimulates the release of TNF-α, which activates the production of the interleukins IL-1β, IL-6, and IL-8. Especially IL-8 can cause hyperalgesia that is independent from prostaglandin mechanisms. Via a positive feedback loop, IL-1β can also induce the release of BK[237]. Release of BK, K^+, H^+, and cytokines from injured muscle activates the muscle nociceptors, thereby causing tenderness and pain[184].

Fig. 9: *The expanded MTrP hypothesis (reproduced with permission from: Gerwin RD, Dommerholt J, Shah J. An expansion of Simons' integrated hypothesis of trigger point formation. Curr Pain Headache Rep 2004;8:468-475). Ach-acetylcholine; AchE-acetylcholinesterase; AchR- acetylcholine receptor; ATP-adenosine triphosphate; SP-substance P; CGRP-calcitonin gene-related peptide; MEPP-miniature endplate potential*



Calcitonin gene-related peptide can enhance the release of ACh from the motor endplate and simultaneously decrease the effectiveness of acetylcholinesterase (AChE) in the synaptic cleft, which decreases the removal of ACh[238,239]. Calcitonin gene-related peptide also upregulates the ACh-receptors (AChR) at the muscle and thereby creates more docking stations for ACh. Miniature endplate activity depends on the state of the AChR and on the local concentration of ACh, which is the result of ACh-release, reuptake, and breakdown by AChE. In summary, increased concentrations of CGRP lead to a release of more ACh, and increase the impact of ACh by reducing AChE effectiveness and increasing AChR efficiency. Miniature endplate potential frequency is increased as a result of greater ACh effect. The observed lowered pH has several implications as well. Not only does a lower pH enhance the release of CGRP, it also contributes to a further down-regulation of AChE. The multiple chemicals and lowered pH found in active MTrPs can contribute to the chronic

nature of MTrPs, enhance the segmental spread of nociceptive input into the dorsal horn of the spinal cord, activate multiple receptive fields, and trigger referred pain, allodynia, hypersensitivity, and peripheral and central sensitization that are characteristic of active myofascial MTrPs[184]. There is no other evidence-based hypothesis that explains the phenomena of MTrPs in as much detail and clarity as the expanded integrated trigger point hypothesis *(Figure 9)*.

Perpetuating Factors

There are several precipitating or perpetuating factors that need to be identified and, if present, adequately managed to successfully treat persons with chronic myalgia. Even though several common perpetuating factors are more or less outside the direct scope of manual physical therapy, familiarity with these factors is critical especially considering the development of increasingly autonomous physical therapy practice. Simons, Travell, and Simons[16] identified mechanical, nutritional, metabolic, and psychological categories of perpetuating factors. Mechanical factors are familiar to manual therapists and include the commonly observed forward head posture, structural leg length inequalities, scoliosis, pelvic torsion, joint hypermobility, ergonomic stressors, poor body mechanics, etc.[16,102,116,240]. In recent review articles, Gerwin[241,242] provided a comprehensive update with an emphasis on non-structural perpetuating factors. Management of these factors usually requires an interdisciplinary approach, including medical and psychological intervention[64,82]. Common nutritional deficiencies or insufficiencies involve vitamin B1, B6, B12, folic acid, vitamin C, vitamin D, iron, magnesium, and zinc, among others. The term "insufficiency" is used to indicate levels in the lower range of normal, such as those associated with biochemical or metabolic abnormalities or with subtle clinical signs and symptoms. Nutritional or metabolic insufficiencies are frequently overlooked and not necessarily considered clinically relevant by physicians unfamiliar with MTrPs and chronic pain conditions. Yet any inadequacy that interferes with the energy supply of muscle is likely to aggravate MTrPs[242]. The most common deficiencies and insufficiencies will be reviewed briefly.

Vitamin B12 deficiencies are rather common and may affect as many as 15-20% of the elderly and approximately 16% of persons with chronic MTrPs[103,243]. B12 deficiencies can result in cognitive dysfunction, degeneration of the spinal cord, and peripheral neuropathy, which is most likely linked to complaints of diffuse myalgia seen in some patients. Serum levels of vitamin B12 as high as 350 pg/ml may be associated with a metabolic deficiency manifested by elevated serum or urine methylmalonic acid or homocysteine and may be clinically symptomatic[244]. However, there are patients with normal levels of methylmalonic acid and homocysteine, who do present with metabolic abnormalities of B12 function[242]. Folic acid is closely linked to vitamin B12 and should be measured as well. While folic acid is able to correct the pernicious anaemia associated with vitamin B12 deficiency, it does not influence the neuromuscular aspects.

Iron deficiency in muscle occurs when ferritin is depleted. Ferritin represents the tissue-bound non-essential iron stores in muscle, liver, and bone marrow that supply the essential iron for oxygen transport and iron-dependent enzymes. Iron is critical for the generation of energy through the cytochrome oxidase enzyme system and a lack of iron may be a factor in the development and maintenance of MTrPs[242]. Interestingly, lowered levels of cytochrome oxidase are common in patients with myalgia[140]. Serum levels of 15-20 ng/ml indicate a depletion of ferritin. Common symptoms are chronic tiredness, coldness, extreme fatigue with exercise, and muscle pain. Anaemia is common at levels of 10 ng/ml or less. Although optimal levels of ferritin are unknown, Gerwin[242] suggested that levels below 50 ng/ml may be clinically significant.

Close to 90% of patients with chronic musculoskeletal pain may have vitamin D deficiency[245]. Vitamin D deficiencies are identified by measuring 25-OH vitamin D levels. Levels above 20 ng/ml are considered normal, but Gerwin[242] suggested that levels below 34 ng/ml may represent insufficiencies. Correction of insufficient levels of vitamin B12, vitamin D, and iron levels may take many months, during which patients may not see much improvement.

Even when active MTrPs have been identified in a particular patient, clinicians must always consider that MTrPs may be secondary to metabolic insufficiencies or other medical diagnoses. It is questionable whether physical therapy and—as an integral part of physical therapy management—manual therapy intervention can be successful when patients have nutritional or metabolic insufficiencies or deficiencies. A close working relationship with physicians familiar with this body of literature is essential. Therapists should consider the possible interactions between arthrogenic or neurogenic dysfunction and MTrPs[4,5,118,133,246,247].

Clinically, physical therapists should address all aspects of the dysfunction. There are many other conditions that feature muscle pain and MTrPs, including hypothyroidism, systemic lupus erythematosis, Lyme disease, babesiosis, ehrlichiosis, candida albicans infections, myoadenylate deaminase deficiency, hypoglycaemia, and parasitic diseases such as fascioliasis, amoebiasis, and giardia[64, 242]. Therapists should be familiar with the symptoms associated with these medical diagnoses[64].

Psychological stress may activate MTrPs. Electromyographic activity in MTrPs has been shown to increase dramatically in response to mental and emotional stress, whereas adjacent non-trigger point muscle EMG activity remained normal[229, 230]. Relaxation techniques, such as autogenic relaxation, can diminish the electrical activity[231]. In addition, many patients with persistent MTrPs are dealing with depression, anxiety, anger, and feelings of hopelessness[248]. Pain-related fear and avoidance can lead to the development and maintenance of chronic pain[249]. Sleep disturbance can also be a major factor in the perpetuation of musculoskeletal pain and must be addressed. Sleep problems may be related to pain, apnea, or to mood disorders like depression or anxiety. Management can be both pharmacologic and non-pharmacologic. Pharmacologic treatment utilizes drugs that promote normal sleep patterns and induce and maintain sleep through the night without causing daytime sedation. Non-pharmacologic treatment emphasizes sleep hygiene, such

as using the bed only for sleep and sex, and not for reading, television viewing, and eating[250]. Therapists must be sensitive to the impact of psychological and emotional distress and refer patients to clinical social workers or psychologists when appropriate.

The role of Manual Therapy

Although the various management approaches are beyond the scope of this article, manual therapy is one of the basic treatment options and the role of orthopedic manual physical therapists cannot be overemphasized[82,158]. Myofascial trigger points are treated with manual techniques, spray and stretch, dry needling, or injection therapy. Dry needling is within the scope of physical therapy practice in many countries including Canada, Spain, Ireland, South Africa, Australia, the Netherlands, and Switzerland. In the United States, the physical therapy boards of eight states have ruled that physical therapists can engage in the practice of dry needling: New Hampshire, Maryland, Virginia, South Carolina, Georgia, Kentucky, New Mexico, and Colorado[80]. A promising new development used in the diagnosis and treatment of MTrPs involves shockwave therapy, but as of yet, there are no controlled studies substantiating its use[251,252].

Conclusion

Although MTrPs are a common cause of pain and dysfunction in persons with musculoskeletal injuries and diagnoses, the importance of MTrPs is not obvious from reviewing the orthopedic manual therapy literature. Current scientific evidence strongly supports that awareness and a working knowledge of muscle dysfunction; in particular, MTrPs should be incorporated into manual physical therapy practice consistent with the IFOMT guidelines for clinical practice. While there are still many unanswered questions with regard to explaining the etiology of MTrPs, this article provides manual therapists with an up-to-date evidence-informed review of the current scientific knowledge.

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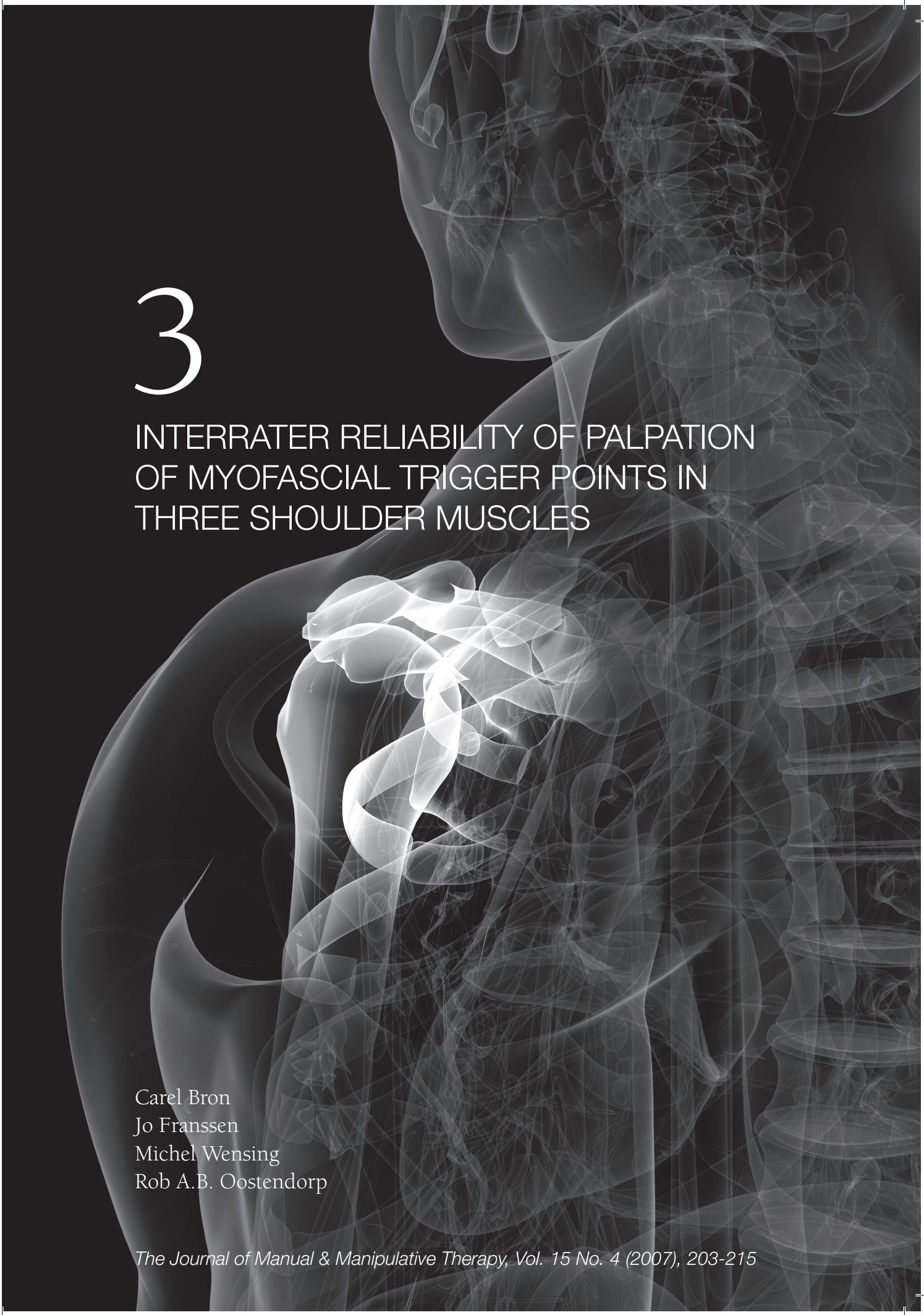

3

INTERRATER RELIABILITY OF PALPATION OF MYOFASCIAL TRIGGER POINTS IN THREE SHOULDER MUSCLES

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3

INTERRATER RELIABILITY OF PALPATION OF MYOFASCIAL TRIGGER POINTS IN THREE SHOULDER MUSCLES

Abstract: This observational study included both asymptomatic subjects (n=8) and patients with unilateral or bilateral shoulder pain (n=32). Patient diagnoses provided by the referring medical physicians included subacromial impingement, rotator cuff disease, tendonitis, tendinopathy, and chronic subdeltoid-subacromial bursitis. Three raters bilaterally palpated the infraspinatus, the anterior deltoid, and the biceps brachii muscles for clinical characteristics of a total of 12 myofascial trigger points (MTrPs) as described by Simons et al. The raters were blinded to whether the shoulder of the subject was painful. In this study, the most reliable features of trigger points were the referred pain sensation and the jump sign. Percentage of pair-wise agreement (PA) was ≥ 70% (range 63–93%) in all but 3 instances for the referred pain sensation. For the jump sign, PA was ≥ 70% (range 67–77%) in 21 instances. Finding a nodule in a taut band (PA = 45–90%) and eliciting a local twitch response (PA = 33–100%) were shown to be least reliable. The best agreement about the presence or absence of MTrPs was found for the infraspinatus muscle (PA = 69–80%). This study provides preliminary evidence that MTrP palpation is a reliable and, therefore, potentially useful diagnostic tool in the diagnosis of myofascial pain in patients with non-traumatic shoulder pain.

Shoulder complaints are very common in modern industrial countries. Recent reviews[1-4] have indicated a one-year prevalence ranging from 4.7 to 46.7%. These reviews have also reported a lifetime prevalence between 6.7 and 66.7%. This wide variation in reported prevalence can be explained by the different definitions used for shoulder complaints and by differences in the age and other characteristics of the various study populations. Because making a specific structure-based diagnosis for patients with shouldercomplaints is considered difficult due to the lack of reliable tests for shoulder examination, recent guidelines developed by the Dutch Society of General Practitioners have recommended instead using the term "shoulder complaints" as a working diagnosis[5]. Shoulder complaints have been defined in a similarly non-specific manner as signs and symptoms of pain in the deltoid and upper arm region, and stiffness and restricted movements of the shoulder, often accompanied by limitations in daily activities[6].

Despite the absence of reliable diagnostic tests to implicate these structures, the currently prevailing assumption is that in non-traumatic shoulder complaints, mostly the anatomical structures in the subacromial space are involved, i.e., the subacromial bursa, the rotator cuff tendons, and the tendon of the long head of the biceps muscle[7-9]. However, this assumption does not take into account that muscle tissue itself can also give rise to pain in the shoulder region[10]. In our clinical experience, myofascial trigger points (MTrPs) may lead to myofascial pain in the shoulder and upper arm region and contribute to the burden of shoulder complaints.

The term myofascial pain was first introduced by Travell[10], who described it as "the complex of sensory, motor, and autonomic symptoms caused by myofascial trigger points." An MTrP is a hyperirritable spot in skeletal muscle that is associated with a hypersensitive palpable nodule in a taut band. In addition, the spot is painful on compression and may produce characteristic referred pain, referred tenderness, motor dysfunction, and autonomic phenomena. Two different types of MTrPs have been described: active and latent. Active trigger points are associated with spontaneous complaints of pain. In contrast, latent trigger points do not cause spontaneous pain, but pain may be elicited with manual pressure or with needling of the trigger point. Despite not being spontaneously painful, latent MTrPs have been hypothesized to restrict range of motion[11] and to alter motor recruitment patterns[12].

As noted above, referred pain is a key characteristic of myofascial pain. Referred pain is felt remote from the site of origin[13]. The area of referred pain may be discontinuous from the site of local pain or it can be segmentally related to the lesion, both of which may pose a serious problem for the correct diagnosis and subsequent appropriate treatment of muscle-related pain. The theoretical model for this phenomenon of referred pain was first proposed by Ruch[14] and later modified by Mense[13-15] and Hoheisel[14]. Referred pain patterns originating in muscles have been documented using injection of hypertonic saline, electrical stimulation, or pressure on the most sensitive spot in the muscle[17-21]. In the clinical setting, palpation is the only method capable of diagnosing myofascial pain. Therefore, reliable MTrP palpation is the necessary prerequisite for considering myofascial pain as a valid

diagnosis[22]. Published interrater studies have reported poor to good reliability for MTrP palpation[23-29]. However, only one study has included a muscle that could produce shoulder pain: Gerwin et al[27] reported a percent agreement (PA) of 83% for tenderness in the infraspinatus muscle (κ=0.48), 83% (κ=0.40) for the taut band, 59% (κ=0.17) for the local twitch response, and 89% (κ=0.84) for the referred pain.

In light of this near absence of data, of the societal impact of shoulder complaints as noted above, and of the potential role of myofascial pain syndrome with regard to shoulder pain, the aim of this study was to determine the interrater reliability of MTrP palpation in three human shoulder muscles deemed by us to be clinically relevant, i.e., the infraspinatus, the anterior deltoid, and the biceps brachii muscles.

Methods and Materials

Subjects

Subjects were recruited from a consecutive sample of patients with unilateral or bilateral shoulder pain referred by their physician to a physical therapy private practice specializing in the management of persons with neck, shoulder, and upper extremity musculoskeletal disorders. To decrease limited variation within the data set and to control for rater bias, we also included asymptomatic subjects.

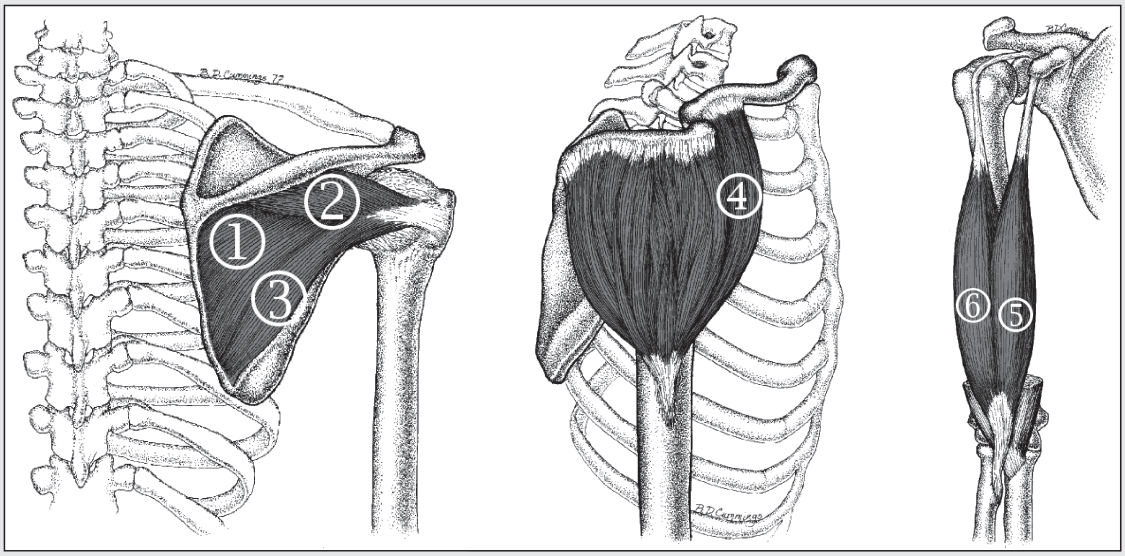
All subjects were unacquainted with and had not met the raters. Additional inclusion criteria for participation in the study were age between 18 and 75 years and the ability to read and understand the Dutch language. Exclusion criteria were known serious rheumatological, neurological, orthopaedic, or internal diseases, such as adhesive capsulitis, rotator cuff tears, cervical radiculopathy, diabetes mellitus, recent shoulder or neck trauma, or shoulder/upper extremity complaints of uncertain origin as diagnosed by the referring physicians. After reading a brief synopsis of the aim of the study and the test procedure, all subjects signed an informed consent form. The Committee on Research involving Human Subjects of the district Arnhem-Nijmegen approved the study design, the protocols, and the informed consent procedure.

Raters and Observers

The raters were three physical therapists: rater A with 29, rater B with 28, and rater C with 16 years of clinical experience, respectively. All were employed at the private practice where this study was conducted. The raters had all specialized in the diagnosis and management of patients with musculoskeletal disorders of the neck, shoulder, and upper extremity; and they had 21, 16, and 2 years of experience, respectively, with regard to diagnosis and management of MTrPs.

The observers were three physical therapists who also had experience in treating patients with myofascial pain. Prior to the study, they were informed by the lead investigator (CB) about the study protocol, and they participated in the training sessions with the raters.

Fig 1. *The localization of trigger points in the infraspinatus, biceps brachii, and the anterior deltoid muscles. The numbers correspond with the sequence of palpation during the test.*



Illustrations courtesy of Lifeart/Mediclip, Manual Medicine 1, Version 1.0a, Williams & Wilkins, 1997.

Both raters and observers participated in a total of eight hours of training. During these sessions, they were able to practice their skills, to compare with each other, and to discuss palpation technique, subject positioning, the amount of pressure used by the examiners[30], and the location of the MTrPs *(Figure 1)*. Before proceeding with the study, they reached consensus about all aspects of the examination.

Trigger Point Examination

Simons et al[31] documented 11 muscles in total that could refer pain to the frontal or lateral region of the shoulder and arm *(Table 1)*. Based on our clinical observation that these muscles are frequently involved in patients with shoulder pain, we chose to study the infraspinatus, the anterior deltoid, and the biceps brachii. Without providing specific data on prevalence, Simons et al[31] reported that the infraspinatus is very often involved in shoulder pain. Hong[32] noted that the deltoid and the biceps brachii could give rise to satellite MTrPs of the infraspinatus muscle. Hsieh[33] provided evidence for the existence of a key-satellite relation between the infraspinatus muscle and the anterior deltoid muscle. A satellite trigger point may develop in the referral zone of a key MTrP located in the key muscle. It may also develop in an overloaded synergist that is substituting for the muscle that is harboring the key MTrP, in an antagonist countering the increased tension of the key muscle, or in a muscle that is linked apparently only neurogenically to the key MTrP. Sometimes this hierarchy is obvious but it is not always evident. Key and satellite trigger

Table 1. Muscles with a known referred pain pattern to the frontal or lateral region of the shoulder and/or arm [31]

Muscle
Infraspinatus
Deltoid [anterior and middle part]
Biceps brachii
Supraspinatus
Coracobrachialis
Lattisimus dorsi
Scalene
Pectoralis major
Pectoralis minor
Subclavius
Sternalis

points are related to each other; our clinical observations indicate that signs and symptoms related to satellite trigger points diminish when key MTrPs are treated appropriately.

Another reason for our choice of these specific muscles is that all three muscles studied here are part of the same functional unit with all three muscles acting as synergists active during shoulder flexion. Although the infraspinatus muscle is traditionally known as an external rotator, this is only true for the anatomical position. This muscle is one of the rotator cuff muscles that is active during flexion of the upper arm to provide stability of the glenohumeral joint during arm movements[34,35].

Although MTrPs may be found anywhere in the muscle belly, we agreed to palpate for their presence only in close proximity to the motor endplate zones. The reason for this choice of location is that Simons et al[31] have suggested that the primary abnormality responsible for MTrP formation is associated with individual dysfunctional endplates in the endplate zone or motor point.

We bilaterally palpated these three muscles for MTrPs using four of the criteria proposed for the palpatory diagnosis of MTrPs[31]:

1 Presence of a taut band with a nodule. The rater examined the subject by palpating the muscle perpendicular to the muscle fiber orientation with either a flat palpation (infraspinatus muscle and the anterior deltoid muscle) or a pincer palpation (biceps brachii muscle). When a taut band was identified, the rater palpated along the taut band to locate the nodule. The raters were asked to search for multiple MTrPs in each muscle. The palpatory findings were more important than the exact location of the MTrPs as indicated by Simons et al[31].

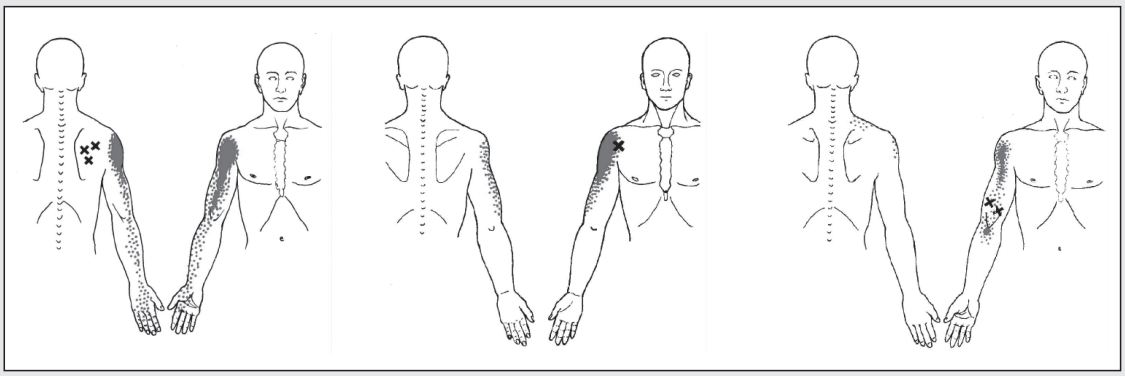


Fig. 2. *The localization of trigger points in the infraspinatus, biceps brachii and the anterior deltoid muscles and the referred pain patterns according to Simons et al[31].*

X = trigger point
Solid gray shows the essential referred pain zone, nearly present in all patients, while the stippling represents the spillover zone, present in some but not all patients[31].

Illustrations courtesy of Lifeart/Mediclip, Manual Medicine 1, Version 1.0a, Williams & Wilkins, 1997.

2 Reported painful sensation during compression in an area consistent with the established referred pain pattern of the involved muscle. While compressing the palpable nodule in the taut band, the subject was asked if he or she felt any pain or any sensation (e.g., tingling or numbness) in an area remote from the compressed point. When the subjects reported referred sensation, they were asked to describe this area. The rater then decided whether this area was comparable to the established referred pain zone *(Figure 2)*.
3 Presence of a visible or palpable local twitch response (LTR) during snapping palpation. The rater quickly rolled the taut band under the fingertip, while examining the skin above the muscle fibers for this characteristic short and rapid movement.
4 Presence of a general pain response during palpation, also known as a jump sign. While compressing the MTrP, the rater carefully examined the subject's reaction. A positive jump sign was defined as the subject withdrawing from palpation, wincing, or producing any pain-related vocalization.

All four criteria were scored dichotomously:
- Yes if the rater was certain of presence of a parameter
- No if the rater was sure of the absence of a parameter or if the rater was unsure of presence or absence

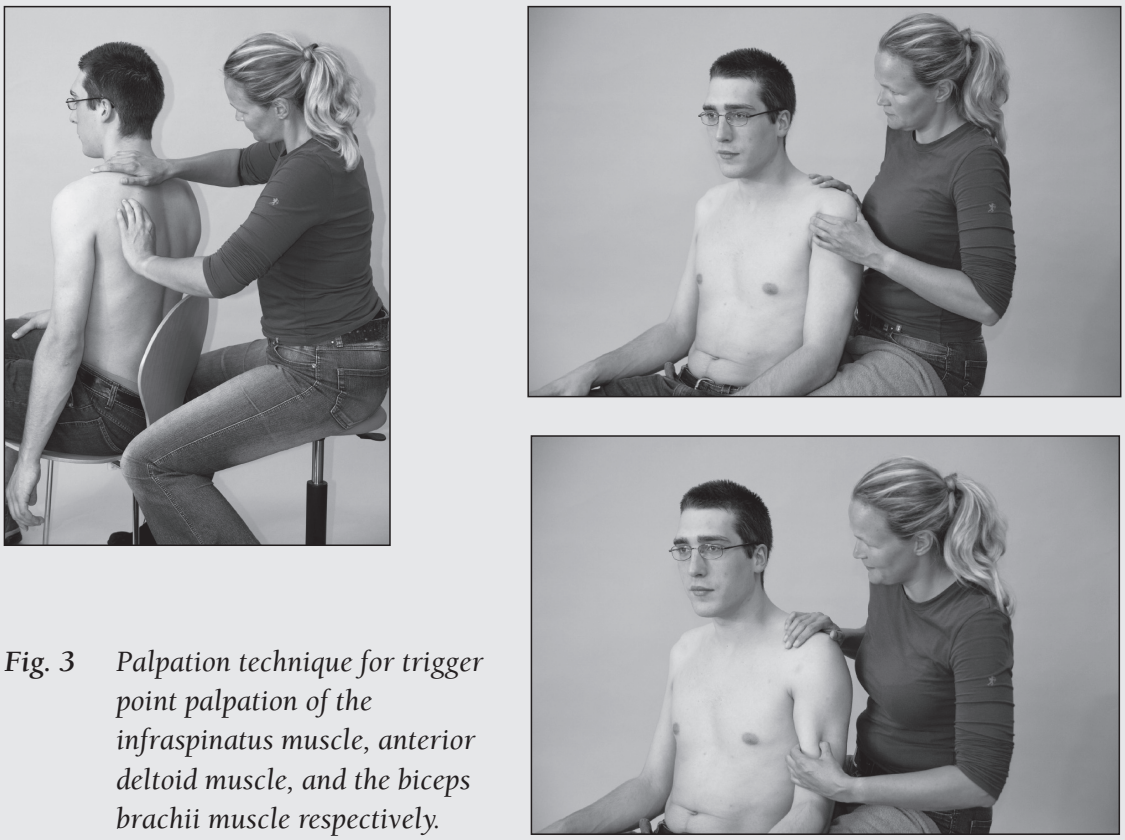


Fig. 3 *Palpation technique for trigger point palpation of the infraspinatus muscle, anterior deltoid muscle, and the biceps brachii muscle respectively.*

Examination of the infraspinatus muscle was performed with the subjects seated with the arms hanging down by the side of the body. Examination of the anterior deltoid and biceps brachii muscles was performed with the forearms supported with slight elbow flexion *(Figure 3)*.

The raters were blinded to subject status; i.e., the subjects were not allowed to indicate whether they were symptomatic. They were instructed to inform the raters when they felt pain somewhere else than the palpation site or when they experienced a referred sensation. However, they were not allowed to tell the rater whether they felt a recognizable pain because that would negate attempts at rater blinding.

In addition to scoring the separate criteria, the raters were asked to judge whether a trigger point was present or absent. Simons et al[31] suggested that minimal diagnostic criteria for an MTrP consist of a palpable nodule present in a palpable taut band. Simons et al also required that this produce the patient's recognizable pain upon compression, but we should note that in this study, the subjects were not allowed to inform the examiners of their symptom status. Therefore, in this study the examiners decided that the MTrP was present when the palpable nodule in the taut band was present together with at least one or more of the other clinical characteristics. In all other combinations, it was said that the MTrP was absent. As a result of this study design, no distinction was made between active and latent MTrPs, as the examiners were not allowed to inquire whether subjects recognized

the pain from palpation. Therefore, examiners may have reported on both active and latent MTrPs in symptomatic and asymptomatic subjects.

Methods

During two morning sessions separated by a one-week interval, two different groups of 20 subjects each were examined. The raters completed the assessment of each of the four characteristics for the three bilateral muscles within a 10 minute period. Subjects were examined in groups of three with each subject in a separate, private treatment room. Following the first assessment, the raters were randomly assigned to one of the two other rooms to assess another subject until all three raters had assessed all subjects. Upon completion of the assessment of the initial group of three subjects, three new subjects were assigned to the examination rooms and the procedures were repeated. An observer was present in each room during all examinations to verify correct implementation of the testing procedures, but the observer did not interfere with the examination. According to the observers, all examinations were performed in an appropriate manner.

Table 2. The contingency matrix

		Rater 1		
		Positive	Negative	
Rater 2	Positive	a	b	g_1
	Negative	c	d	g_2
Total		f_1	f_2	n

Statistical Analysis

For the statistical analysis, we used the Statistical Package for the Social Sciences for Windows version 12.0.1 (SPSS Inc., Chicago, IL). Frequencies were calculated for the subject demographic information.

To express interrater reliability, we calculated both pairwise percentages of agreement (PA) and pair-wise Cohen Kappa-values (κ). The PA-value is defined as the ratio of the number of agreements to the total number of ratings made[36].

Using the terminology from the contingency matrix provided in *Table* 2, PA = (a+d)/n. Cohen's κ is a coefficient of agreement beyond chance: $\kappa = (PA - P_e)/(1 - P_e)$. The agreement based on chance alone (P_e) is calculated by the sum of the multiplied marginal totals corresponding to each cell divided by the square of the total number of cases (n): $P_e = (f_1g_1 + f_2g_2) / n^2$.

The κ-value is widely used for dichotomous variables in interrater reliability studies, although there is no universally accepted value for good agreement[37]. Landis and Koch[38] proposed that a κ-value < 0.00 be considered indicative of poor reliability and a value of

0.001–0.20 slight, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial or good, and 0.81–1.00 almost perfect or very good reliability. In this study, we considered a PA-value ≥ 70% indicative of interrater reliability acceptable for clinical use, because under ideal circumstances, i.e., equal prevalence of negative and positive findings, when using a dichotomous test, a PA-value ≥ 70% leads to a $\kappa \geq 0.40$.

Table 3a. Example of the influence of a high value of the prevalence index on the κ value (Example used: Trigger point 3, right shoulder, couple A/C, palpation of a nodule)

		Observer 1		
		Positive	Negative	
Observer 2	Positive	35	2	37
	Negative	2	1	3
Total		37	3	40

In this case, the percentage of agreement is high (0.90), but because the prevalence index is also high (0.85), the κ-value indicates only fair agreement (0.28).

Table 3b. Example of the influence of a low value of the prevalence index on the κ value (Example used: Trigger point 2, right shoulder, couple B/C, palpation of a nodule)

		Observer 1		
		Positive	Negative	
Observer 2	Positive	19	0	19
	Negative	5	16	21
Total		24	16	40

In this case the percentage of agreement is high (0.85), but the prevalence index is low (0.08), so despite slightly lower percentage agreement than in Table 3a, the κ-value (0.75) indicates good agreement.

A major drawback to using κ as an index of agreement is that this statistic is very sensitive to the prevalence of positive and negative findings. To quantify this effect on the κ values calculated, in this study we also determined the prevalence index (P_i), which is the absolute value of the difference between the number of agreements on positive findings (a) and agreements on negative findings (d) divided by the total number of observations (n): $P_i = | a - d | / n$ [39]. If P_i is high (closer to 1), chance agreement (P_e) is also high and κ is reduced

accordingly. If the P_i is closer to 0, chance agreement (P_e) is low and κ will increase. This means that the κ-statistic is more useful as an index of agreement in case of a low P_i than it is with higher P_i-values. *Table 3* provides examples of the influence of variations in P_i on κ-values. With κ-values in this study strongly influenced by variations in prevalence as indicated by the wide range of P_i, we were forced to focus on the PA-values for the interpretation of our findings.

To compare the three pairs of raters, we used the Kruskal-Wallis test, which is a non-parametric one-way analysis of variance. The test statistic H will increase with increased variation. For graphical presentation, we used the box-and-whisker plot. To compare several data sets, this semi-graphical way of summarizing data, which provides median value, lower and upper quartiles, and the extreme values, is considered simple and useful[37].

Results

Patient Characteristics

Thirty-two subjects with unilateral or bilateral shoulder pain and eight subjects without shoulder pain were included in this study. The mean age of subjects was 40 (SD = 11.5; range 18 to 70). Of these 40 subjects, 24 (60%) were female and 16 (40%) were male. The study population had a gender and age profile similar to the patient population of the physical therapy practice where the study was conducted. Most of the subjects (53%) were not diagnosed with a specific medical diagnosis for their shoulder complaints as suggested in the guidelines developed by the Dutch Society of General Practitioners[5]. *Table 4* provides physician referral diagnoses for the 32 patients involved in this study.

Table 4. Patient diagnosis and referral information

Referral diagnosis	Number of subjects	Percentage
No medical diagnosis. *The physician referred the patient to the practice without mentioning any medical diagnosis. This follows to the Dutch guidelines for general practioners.*	17	53%
Calcifying tendonitis	2	6%
Tendonitis / bursitis / tendinosis	3	9%
Soft tissue disorder	7	22%
Degenerative changes in the acromioclavicular or glenohumeral joint	2	6%
Subacromial impingement syndrome	1	3%
Total	**32**	**100%**

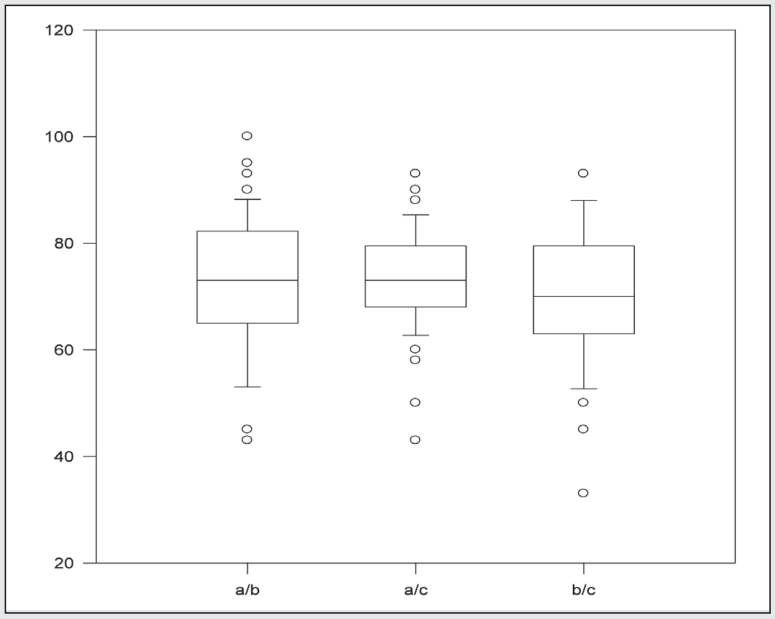


Fig. 4. *This box-and-whisker plot shows the graphical expression [i.e., median, lower and upper quartile, minimum and the maximum value] of the dataset from the pairs of raters. This graphic shows only small differences (not statistically or clinically relevant differences) between the three pairs of observers.*

Pair-Wise Interrater Agreement

Tables 5 to 8 present the data of the various clinical characteristics of the MTrP in the 80 shoulders of our 40 subjects, i.e., palpable nodule in a taut band, referred pain sensation, LTR, and the jump sign, respectively. The column PA provides the percentage agreement values for the three pairs of observers for both the left and right shoulder. The column κ shows the corresponding κ-value; the third column shows the corresponding prevalence index (P_i). Although we have insufficient information to calculate mean agreement values for all rater pairs, we can cautiously conclude that the rater pairs seemed to be demonstrating similar reliability. When comparing the pair-wise PA-values for the presence or absence of MTrPs, we found no significant difference between the rater pairs (Kruskal-Wallis oneway ANOVA on ranks, H=0.841, P > 0.05; *Figure 4*).

Palpable Nodule in a Taut Band

The PA-value for the palpable nodule in a taut band in the muscle varied from 45% in the medial head of the biceps brachii muscle to 90% in the infraspinatus muscle. The PA tended to be higher in trigger point 3 (83–90%) than in point 1 (63–73%). In the anterior deltoid muscle the PA varied from 63% to 75%. The PA for the biceps brachii varied from 45% to 75%. Only the rater pair A/C agreed in both points more than 70%. The κ-value varied from 0.11 to 0.75 *(Table 5)*.

Referred Pain Sensation

The agreement on the referred pain sensation elicited by pressure on the nodule reached a PA-value $\geq$ 70% in all but 3 cases (range 63-93%). The scores for referred pain sensation were the lowest in the infraspinatus (trigger point 1). The κ-value varied from –0.13 to 0.64 *(Table 6)*.

Table 5. Percentage of agreement (PA), kappa coefficient (κ), and the prevalence index (Pind) calculated for palpation of a nodule in a taut band in 6 localizations in 3 muscles (left and right).

		Rater pairs								
		A/B			A/C			B/C		
TrP	Side	PA%	κ	P*ind*	PA%	κ	P*ind*	PA%	κ	P*ind*
1	Left	65	0.22	0.40	68	0.30	0.38	68	0.34	0.13
	Right	73	0.40	0.32	63	0.24	0.13	70	0.47	0.30
2	Left	70	0.35	0.30	80	0.60	0.10	65	0.30	0.20
	Right	73	0.44	0.18	70	0.43	0.05	88	0.75	0.08
3	Left	83	0.26	0.73	90	0.30	0.85	88	0.25	0.83
	Right	85	0.33	0.75	90	0.28	0.85	85	0.33	0.75
4	Left	63	0.34	0.03	70	0.40	0.20	63	0.25	0.18
	Right	75	0.50	0.15	63	0.26	0.13	68	0.35	0.03
5	Left	45	0.16	0.00	68	0.27	0.38	53	0.14	0.18
	Right	53	0.16	0.13	80	0.58	0.20	53	0.11	0.18
6	Left	53	0.22	0.03	73	0.25	0.53	45	0.15	0.05
	Right	53	0.22	0.03	75	0.44	0.35	58	0.24	0.13

The numbers 1, 2, and 3 in the first column correspond with the localization in the infraspinatus muscle, 4 is localized in the anterior deltoid muscle, and 5 and 6 are localized in the biceps brachii muscle. In the second row, the three raters are mentioned as A, B, and C. The number of subjects is 40.

Table 6. Percentage of agreement (PA), kappa coefficient (κ), and the prevalence index (Pind) calculated for palpation of referred pain in 6 localizations in 3 muscles (left and right).

		Rater pairs								
		A/B			A/C			B/C		
TrP	Side	PA%	κ	P*ind*	PA%	κ	P*ind*	PA%	κ	P*ind*
1	Left	78	0.48	0.38	63	0.19	0.28	65	0.21	0.35
	Right	78	0.51	0.33	75	0.41	0.40	73	0.41	0.28
2	Left	88	0.38	0.78	88	0.55	0.68	80	0.23	0.70
	Right	80	0.25	0.70	85	0.33	0.75	85	0.53	0.6
3	Left	73	0.46	0.08	63	0.26	0.13	70	0.36	0.25
	Right	83	0.64	0.18	78	0.54	0.13	80	0.58	0.2
4	Left	78	0.13-	0.78	85	0.31	0.75	78	0.13-	0.78
	Right	88	0.55	0.68	80	0.25	0.70	88	0.22	0.83
5	Left	93	0.36	0.88	83	0.29	0.73	80	0.13	0.75
	Right	85	0.19	0.80	93	0.63	0.78	88	0.06-	0.88
6	Left	90	0.45	0.80	75	0.25	0.60	70	0.03	0.65
	Right	88	0.38	0.78	75	0.15	0.65	78	0.20	0.68

Table 7. Percentage of agreement (PA), kappa coefficient (κ), and the prevalence index (P*ind*) calculated for palpation of a local twitch response in 6 localizations in 3 muscles (left and right).

		Rater pairs								
		A/B			A/C			B/C		
TrP	Side	PA%	κ	Pind	PA%	κ	Pind	PA%	κ	Pind
1	Left	80	0.09	0.75	73	0.21	0.58	78	0.36	0.58
	Right	85	0.04-	0.85	75	0.05-	0.75	75	0.15	0.65
2	Left	100	n.c	1.00	73	n.c.	0.73	73	n.c.	0.73
	Right	95	n.c.	0.95	78	n.c.	0.78	78	0.11	0.73
3	Left	53	0.05	0.13	58	0.15	0.38	50	0.16	0.25
	Right	70	0.15	0.55	43	0.13	0.13	33	0.07	0.03
4	Left	73	0.04	0.68	63	0.14	0.38	65	0.11	0.55
	Right	65	0.21	0.35	60	0.20	0.20	60	0.20	0.15
5	Left	43	0.00	0.28	50	0.04	0.00	58	0.00	0.48
	Right	53	0.01	0.43	73	0.45	0.08	60	0.13	0.45
6	Left	53	0.17	0.28	68	0.32	0.28	50	0.16	0.25
	Right	60	0.23	0.35	63	0.25	0.08	58	0.21	0.33

n.c. = not calculated

The numbers 1, 2, and 3 in the first column correspond with the localization in the infraspinatus muscle, 4 is localized in the anterior deltoid muscle, and 5 and 6 are localized in the biceps brachii muscle. In the second row, the three raters are mentioned as A, B, and C. The number of subjects is 40.

Local Twitch Response

The LTR had only acceptable agreement for two locations in the infraspinatus. The lowest PA was 33% in trigger point 3, which is the most central point in the infraspinatus muscle. All three raters were unable to elicit an LTR in trigger point 2 (also in the infraspinatus muscle) in almost any of the subjects. This led to an agreement of 100% in one case; in most cases it was not possible to calculate a κ-value because of the absence of the LTR in all cases of one rater *(table 7)*.

Table 8. Percentage of agreement (PA), kappa coefficient (κ), and the prevalence index (Pind) calculated for palpation of the jump sign in 6 localizations in 3 muscles (left and right).

		Rater pairs								
		A/B			A/C			B/C		
TrP	Side	PA%	κ	Pind	PA%	κ	Pind	PA%	κ	Pind
1	Left	75	0.47	0.25	83	0.60	0.38	78	0.51	0.33
	Right	63	0.27	0.18	73	0.36	0.38	65	0.31	0.15
2	Left	70	0.07	0.60	68	0.12	0.53	88	0.68	0.53
	Right	68	0.02	0.63	75	0.19	0.65	93	0.58	0.43
3	Left	70	0.29	0.40	68	0.22	0.43	78	0.38	0.53
	Right	75	0.47	0.25	75	0.49	0.15	80	0.58	0.25
4	Left	78	0.56	0.18	65	0.31	0.15	73	0.36	0.38
	Right	78	0.54	0.18	78	0.48	0.43	70	0.34	0.40
5	Left	68	0.30	0.33	68	0.33	0.18	65	0.22	0.35
	Right	68	0.31	0.28	68	0.31	0.28	65	0.16	0.4
6	Left	68	0.35	0.28	70	0.40	0.05	63	0.28	0.18
	Right	70	0.37	0.25	83	0.64	0.18	73	0.41	0.28

The numbers 1, 2, and 3 in the first column correspond with the localization in the infraspinatus muscle, 4 is localized in the anterior deltoid muscle, and 5 and 6 are localized in the biceps brachii muscle. In the second row, the three raters are mentioned as A, B, and C. The number of subjects is 40.

Jump Sign

The raters achieved the highest PA (93%) on the jump sign in the infraspinatus muscle and the lowest PA (63%) in the infraspinatus muscle and the biceps brachii muscle. The κ varied from 0.07 to 0.68 *(Table 8)*.

Table 9. Percentage of agreement, kappa [κ] coefficient, and the prevalence index for agreement on presence or absence of myofascial trigger points

	Raters	PA%	κ	Pind
1 Left	A-B	75	0.50	0.05
	A-C	70	0.40	0.05
	B-C	70	0.40	0.05
1 Right	A-B	65	0.33	0.00
	A-C	65	0.29	0.15
	B-C	70	0.41	0.05
2 Left	A-B	78	0.38	0.53
	A-C	75	0.44	0.35
	B-C	73	0.38	0.38
2 Right	A-B	70	0.19	0.55
	A-C	73	0.29	0.53
	B-C	88	0.72	0.33
3 Left	A-B	73	0.18	0.58
	A-C	80	0.25	0.70
	B-C	83	0.29	0.73
3 Right	A-B	73	0.30	0.48
	A-C	78	0.40	0.53
	B-C	85	0.48	0.65
4 Left	A-B	63	0.31	0.13
	A-C	58	0.18	0.03
	B-C	65	0.25	0.30
4 Right	A-B	80	0.60	0.00
	A-C	68	0.35	0.03
	B-C	63	0.25	0.08
5 Left	A-B	53	0.22	0.13
	A-C	60	0.19	0.20
	B-C	58	0.18	0.28
5 Right	A-B	58	0.15	0.28
	A-C	73	0.45	0.03
	B-C	55	0.12	0.25
6 Left	A-B	58	0.28	0.08
	A-C	73	0.33	0.43
	B-C	50	0.20	0.00
6 Right	A-B	60	0.27	0.15
	A-C	80	0.58	0.20
	B-C	60	0.27	0.15

The numbers 1, 2, and 3 correspond with the localization in the infraspinatus muscle, 4 is localized in the anterior deltoid muscle, and 5 and 6 are localized in the biceps brachii muscle. PA= Percentage of Agreement, κ = kappa coefficient, and Pind = prevalence index.

Overall agreement

The percentage of agreement on MTrP presence or absence was acceptable for the infraspinatus muscle. In two out of three trigger point locations, PA-values exceeded 70%. In the anterior deltoid muscle and in the biceps brachii muscle, the PA-value was < 70% *(Table 9)*.

Discussion

Palpation is the only method available for the clinical diagnosis of myofascial pain. Therefore, reliable MTrP palpation is the necessary prerequisite to considering myofascial pain as a valid diagnosis. This study indicated that referred pain was the most reliable criterion for palpatory diagnosis in all six MTrPs in all three muscles on both sides. Only in three of the 36 MTrP locations did the PA-value not reach the predetermined value of 70%. This finding is consistent with the results of other interrater reliability studies of MTrP examination[26,27]. The nodule in the taut band, the LTR, and the jump sign were more reliable in the infraspinatus muscle than in the anterior deltoid and biceps brachii muscle. In general, the jump sign also proved a reliable palpatory characteristic in this study. This is in contrast to other studies, which may indicate that the raters in this study were more successful in standardizing the amount of pressure during the palpation. In general, the LTR was not a reliable characteristic although it did prove reliable for MTrP 1 and 2 in the infraspinatus on either side. Palpation of the nodule in the taut band had sufficient reliability for the diagnosis of MTrPs in the infraspinatus muscle, but less for diagnosis of MTrPs in the anterior deltoid and biceps brachii muscles. There was also a high level of agreement for the presence or absence of MTrPs in the infraspinatus muscle. This agreement was lower for the anterior deltoid and biceps brachii muscles.

Compared to various other commonly used physical examination tests such as the assessment of intervertebral motion or muscle strength, whose established interrater relia bility ranges from 41% to 97%[40-43], the interrater agreement with regard to MTrP palpation in these three shoulder muscles seemed acceptable. However, the degree of agreement seemed to be strongly dependent on the muscle that was examined. Clinical experience suggests that some muscles are more accessible to palpation than others. There may even be differences within particular muscles. For trigger point 3 of the infraspinatus muscle, the raters achieved the highest agreement. Because MTrPs are often in close proximity to each other, raters did not always agree on which MTrP they were evaluating. For example, the raters may have had difficulty in distinguishing trigger points in the infraspinatus muscle, the teres minor muscle, and the posterior deltoid muscle. The area of referred pain may help in determining which muscle was palpated. However, recognition of pain elicited by palpation, as normally would occur in the clinical situation, was not determined in this study, as this could have endangered the blinding of the raters. Recognition of this characteristic pain by the patient may be an important aspect of reliable MTrP identification.

For the biceps brachii muscle, the raters may have had difficulty distinguishing between the lateral and the medial head of the muscle. It is conceivable that such difficulties could contribute to the lower level of agreement noted for this muscle.

We realize that by collapsing rating categories in this study to absent or present and by not including a third category of indeterminate findings, we may have artificially inflated reliability findings. We decided to score dichotomously for the presence or absence of MTrPs and not include this indeterminate category because the treatment choice would have been similar independent of a negative or indeterminate finding. When MTrPs are absent or when the physical therapist is unsure about the presence or absence of an MTrP, in the clinical situation no treatment will be directed to the MTrP.

We should again note that in this study no distinction was made between active and latent MTrPs, as the examiners were not allowed to inquire whether subjects recognized the pain from palpation. Therefore, examiners may have reported on both active and latent MTrPs in symptomatic and asymptomatic subjects. This may affect external validity in this study in that its findings cannot be directly extrapolated to the clinical situation where patient report of recognition of pain is available and the distinction between active and latent trigger points, therefore, can be made.

In the interpretation of the study findings, we chose to emphasize PA over κ-values. PA-values do not take into account the agreement that would be expected purely by chance. True agreement is the agreement beyond this expected agreement by chance, and κ is a measure of true, chance-corrected agreement. However, as we earlier mentioned, the κ-statistic is probably inappropriate for studies in which the positive and negative findings are not equally distributed[39,44-46]. In this study, even asymptomatic subjects had some (obviously latent) trigger points in the shoulder muscles. Subjects with unilateral shoulder pain often also may have latent or active trigger points in the contralateral shoulder47,48. Both may have contributed to the high prevalence of positive findings in this study. The resultant P*i* resulted in generally low κ-values despite high PA-values, making the κ-statistic less appropriate for the statistical representation and subsequent interpretation of study findings.

Training would seem important to achieve sufficient agreement, even when raters have considerable clinical experience. Prior to conducting this interrater reliability study, consensus about the standardization of manual palpation of MTrPs was achieved between raters. In this study, there was no statistically significant difference between the rater pairs, even though one rater had only two years of clinical experience with MTrP diagnosis and management. We recognize that this consensus training may impact external validity in that the results of this study may not apply to situations and clinicians where such training has not occurred. Future studies are needed to determine how many years of experience and what extent of pre-study consensus training is needed to achieve sufficient interrater reliability.

Conclusion

In this study, three blinded raters were able to reach acceptable pair-wise interrater agreement on the presence or absence of TrPs as described by Simons et al[31]. Referred pain was the most reliable feature in all six MTrPs in all three shoulder muscles on both sides. The nodule in the taut band, the LTR, and the jump sign were more reliable in the infraspinatus muscle than in the anterior deltoid and biceps muscle.

The results of this study support the idea that experienced raters can obtain acceptable agreement when diagnosing MTrPs by palpation in the three shoulder muscles studied. Allowing for patient report of pain recognition may provide for even better interrater reliability results. Interrater agreement seems dependent on the muscle and even on the location of the trigger point within a muscle, and findings indicating acceptable interrater reliability cannot be generalized to all shoulder muscles. The distinction between active and latent trigger points should be considered in future studies as should the effect of pre-study consensus training and clinical experience. However, in summary we conclude that this study provides preliminary evidence that MTrP palpation is a reliable and, therefore, potentially useful diagnostic tool in the diagnosis of myofascial pain in patients with non-traumatic shoulder pain.

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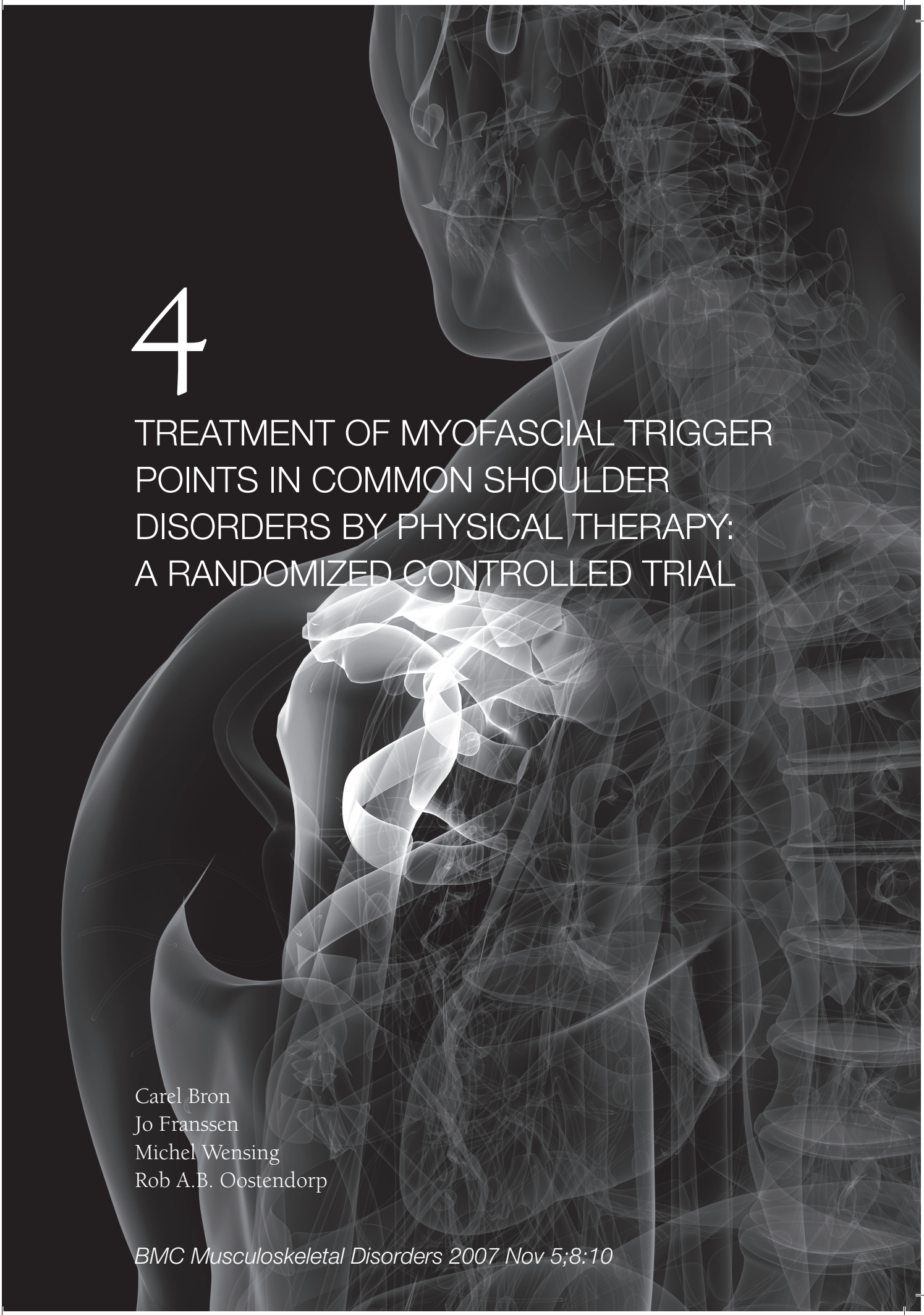

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TREATMENT OF MYOFASCIAL TRIGGER POINTS IN COMMON SHOULDER DISORDERS BY PHYSICAL THERAPY: A RANDOMIZED CONTROLLED TRIAL

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4

TREATMENT OF MYOFASCIAL TRIGGER POINTS IN COMMON SHOULDER DISORDERS BY PHYSICAL THERAPY: A RANDOMIZED CONTROLLED TRIAL

Abstract Background: Shoulder disorders are a common health problem in western societies. Several treatment protocols have been developed for the clinical management of persons with shoulder pain. However available evidence does not support any protocol as being superior over others. Systematic reviews provide some evidence that certain physical therapy interventions (i.e. supervised exercises and mobilisation) are effective in particular shoulder disorders (i.e. rotator cuff disorders, mixed shoulder disorders and adhesive capsulitis), but there is an ongoing need for high quality trials of physical therapy interventions. Usually, physical therapy consists of active exercises intended to strengthen the shoulder muscles as stabilizers of the glenohumeral joint or perform mobilisations to improve restricted mobility of the glenohumeral or adjacent joints (shoulder girdle). It is generally accepted that a-traumatic shoulder problems are the result of impingement of the subacromial structures, such as the bursa or rotator cuff tendons. Myofascial trigger points (MTrPs) in shoulder muscles may also lead to a complex of symptoms that are often seen in patients diagnosed with subacromial impingement or rotator cuff tendinopathy. Little is known about the treatment of MTrPs in patients with shoulder disorders.

The primary aim of this study is to investigate whether physical therapy modalities to inactivate MTrPs can reduce symptoms and improve shoulder function in daily activities in a population of chronic a-traumatic shoulder patients when compared to a wait-and-see strategy. In addition we investigate the recurrence rate during a one-year-follow-up period.

Methods/Design: This paper presents the design for a randomized controlled trial to be conducted between September 2007 – September 2008, evaluating the effectiveness of a physical therapy treatment for non-traumatic shoulder complaints. One hundred subjects are included in this study. All subjects have unilateral shoulder pain for at least six months and are referred to a physical therapy practice specialized in musculoskeletal disorders of the neck-, shoulder-, and arm.

After the initial assessment patients are randomly assigned to either an intervention group or a control-group (wait and see). The primary outcome measure is the overall score of the Dutch language version of the DASH (Disabilities of Arm, Shoulder and Hand) questionnaire.

Discussion: Since there is only little evidence for the efficacy of physical therapy interventions in certain shoulder disorders, there is a need for further research. We found only a few studies examining the efficacy of MTrP therapy for shoulder disorders. Therefore we will perform a randomised clinical trial of the effect of physical therapy interventions aimed to inactivate MTrPs, on pain and impairment in shoulder function in a population of chronic a-traumatic shoulder patients. We opted for an intervention strategy that best reflects daily practice. Manual high velocity thrust techniques and dry-needling are excluded. Because in most physical therapy interventions, blinding of the patient and the therapist is not possible, we will perform a randomised, controlled and observer-blinded study.

Trial Registration: This randomized clinical trial is registered at current controlled trials ISRCTN75722066.

Background

Shoulder pain is a common health problem in western societies. There are substantial differences in reported prevalence in the general population. The one-year prevalence of shoulder disorders has been reported to range from 20% to 50%. This wide range is strongly influenced for example by the definition of shoulder disorders, including or excluding limited motion, age, gender and anatomic area [1-3]. Of all shoulder patients who attend primary care physicians 50% recover within 6 months, meaning they do not seek any medical help after the first episode [1,4-6]. Chronicity and recurrence of symptoms are common [7,8]. According to the guidelines of the Dutch College of General Practioners [9], the recommended management of shoulder symptoms starts with educational information about the natural course of shoulder pain combined with the advise to avoid irritating and loading activities. The use of analgesics or NSAIDs is recommended for the first two weeks. When no recovery occurs within two weeks, subacromial or intra-articular injection therapy with corticosteroids are administered and eventually repeated. Finally, physical therapy is only recommended after a 6-week period when there are functional limitations (specifically an activating and time-contingent approach). International guidelines for shoulder pain, including the Clinical Guideline of Shoulder pain of the American Academy of Orthopaedic Surgeons [10] and the Shoulder Guideline of the New Zealand Guidelines Group [11] differ more or less from the Dutch guidelines in classification, recommended interventions and timeline, and order of interventions. Scientific evidence from randomized clinical trials, meta-analyses or systematic reviews for either the efficacy of multimodal rehabilitation, injection therapy, medication, surgery or physical therapy or the order of application of commonly used therapies is lacking [12-16].

An alternative approach to the management of persons with shoulder problems consists of a treatment aimed at inactivating MTrPs and eliminating factors that perpetuate them. MTrPs may be inactivated by manual techniques (such as compression on the trigger point or other massage techniques), cooling the skin with ethyl chloride spray or with ice-cubes followed by stretching of the involved muscle, trigger point needling using an acupuncture needle, or injection with local anaesthetics or Botulinum toxin, followed by ergonomic advises, active exercises, postural correction, and relaxation (with or without biofeedback) [17,18]. Over the years, MTrPs are increasingly accepted in the medical literature. Clinical, histological, biochemical and electrophysiological research has provided biological plausibility for the existence of MTrPs [19-24].

MTrPs are defined as exquisitely tender spots in discrete taut bands of hardened muscle that produce symptoms [25,26]. A previous study showed that MTrPs can be detected reliably by trained physiotherapists [27]. Palpation is still the only reliable method to diagnose myofascial pain clinically. In reviews addressing the efficacy of interventions in shoulder patients, MTrP therapy and myofascial pain are rarely mentioned [15.] However, some published case studies suggest that treatment of MTrPs in shoulder patients may be beneficial [28-31].

The primary aim of this study is to investigate the effectiveness of inactivation of MTrPs in shoulder muscles by physical therapy on symptoms and functioning of the shoulder in daily

activities in a population of chronic a-traumatic shoulder patients when compared to a wait-and-see strategy. In addition, we investigate the recurrence rate during a one-year-follow-up period.

Methods/Design

An examiner-blinded randomized controlled trial will be conducted, which has been approved by the ethics committee of the Radboud University Nijmegen Medical Centre, the Netherlands [CMO 2007/022].

Participants/Study sample

Between September 2007 and September 2008, all consecutive patients referred to a physical therapy practice specialized in the treatment of individuals with musculoskeletal disorders of the neck, shoulder and arm are potential study participants. The referring physicians include general practitioners, orthopaedic surgeons, neurologists and physiatrists. Patients are eligible if they have unilateral shoulder complaints (described as pain felt in the shoulder or upper arm) for at least six months. The patients present with persistent shoulder pain that has not spontaneously recovered. The patients are between 18 and 65 years old. Because the questionnaires are in the Dutch language, subjects must understand written and verbal Dutch. Patients who have been diagnosed (prior to the referral) with shoulder instability, shoulder fractures, systemic diseases (such as rheumatoid arthritis, Reiter's syndrome, diabetes), or who's medical history or examination suggests neurological diseases, or other severe medical or psychiatric disorders will be excluded from the study. The project leader will check all the available information from referral letters, additional information from the general practitioner and from the patients. All eligible patients will be informed of the study and will be invited to participate. Patients who are willing to participate will be asked to review and sign the written informed consent.

Measurements

Before randomization, all participants will be assessed during an individual baseline test session. They will complete a battery of questionnaires and tests, determining data on social, demographic, and physical factors, and baseline values for the outcome measures. In addition, subjects will complete the DASH, RAND-36-dutch language version, and passive range of motion tests of the shoulder (PROM). During the initial assessment, MTrPs will be identified, based on compression-produced pain that is recognized by patients as their own shoulder pain. If no MTrPs are detected, the subjects will be excluded from the study. All measurements will be performed by the same independent observer, who is not employed by the physical therapy practice (This is to create optimal blinding of the observer, who is now not able to recognise the subjects). The observer is trained in identifying MTrPs and has several years of clinical experience in MTrP therapy. The observer participated in a former reliability study of MTrP palpation. The baseline measurements will be at T0, the second measurement (T1) will

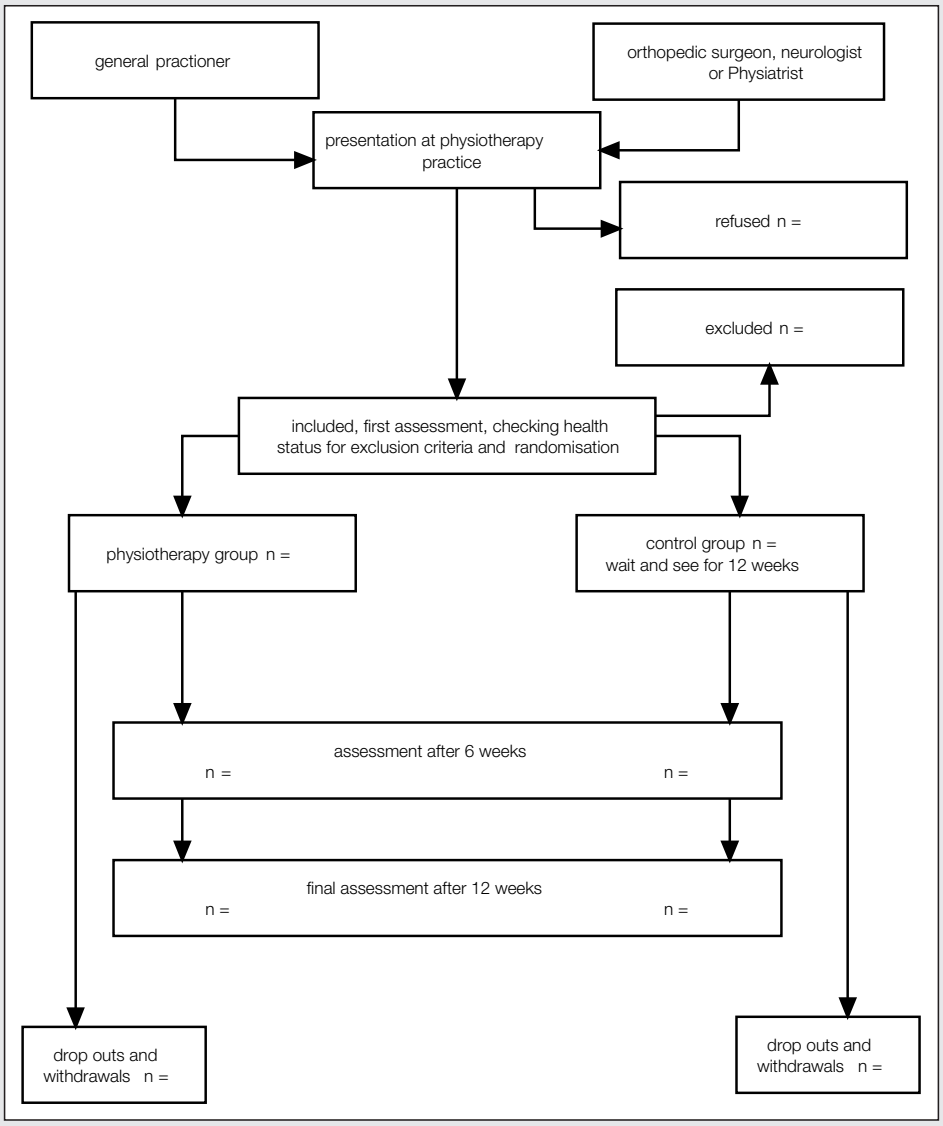
be 6 weeks after the first assessment session, the third (T2) will be 12 weeks after the first assessment session. All measurements *(see table 1)* will be performed outside the physical therapy practice to assure that the observer will not recognize any of the study participants when they come to the physical therapy practice for their treatment. After this first assessment, the patients will be randomly assigned to one of two groups: the intervention group or the control group. The patients in the control group will stay on the waiting list and will not receive any treatment. They are allowed to use over-the-counter painkillers during this 12-week period. After 6 weeks and 12 weeks, respectively, they will be examined by the same blinded observer. After 12 weeks they will receive the same physical therapy program as the experimental group *(see Figure 1)*. The initial trial ends after 12 weeks, but 6 months and 12 months after the start of the experimental intervention shoulder function of the subjects will be re-evaluated with the DASH-Dutch language version.

Table 1: Overview of variables

Variable	T0 Baseline	T1 After 6 wk	T2 After 12 wk	Measured by
Age*	X			Interview
Gender*	X			Interview
Work	X			Interview
Dominant side affected	X			Interview
Duration of the complaints*	X			Interview
DASH DLV	X	X	X	Questionnaire
Use of **medication**	X	X	X	Interview
Use of **other therapy**	X	X	X	Interview
Work %	X	X	X	Interview
Improvement (percentage of perceived improvement)		X	X	Interview
Number of involved muscles	X	X	X	Assessment
No. of treatment sessions			X	Assessment
Health status for baseline comparison	X			RAND-36 DLV
Existence and severity of symptoms of depression	X	Beck Depression Inventory		
Shoulder Passive ROM	X	X	X	Goniometry
• flexion	X	X	X	
• abduction	X	X	X	
• external rotation	X	X	X	
• internal rotation	X	X	X	
• cross body adduction	X	X	X	

*Age, gender and duration of the complaints seem to be important prognostic variables [53].

Figure 1 Recruitment and experimental plan



Intervention

The patients in the intervention group will be treated by a physical therapist once a week for a maximum period of 12 weeks. All participating physiotherapists are experienced in treating patients with long-lasting shoulder symptoms and patients with MTrPs and myofascial pain, especially in the upper part of the body. They are trained and skilled in the identification of MTrPs and received a certification in manual trigger point therapy. The treatment starts with inactivation of the active (pain producing) MTrPs by using manual techniques (compression on the trigger point, manual stretching of the trigger point area and the taut band) combined with "intermittent cold application by using ice-cubes followed by stretching the muscle" according to Travell [32] to further inactivate the MTrPs.

Manual pressure will decrease the sensitivity of the painful nodule in the muscle while other massage techniques will mobilize and stretch the contracted muscle fibres. The application of the ice-cubes has a desensitizing effect, and makes it easier to stretch shoulder muscles. Each treatment session will end with a heat application to increase the circulation of the involved muscles.

Patients will be advised to do stretching exercises and will be taught to perform these correctly by means of surfaceelectromyography-assisted stretching [33,34]. Furthermore they will be advised to perform relaxation exercises, and to apply heat (like a hot shower, hot packs) several times (at least twice) a day. If there is abnormal measurable higher electromyographic activity in the upper trapezius muscle (measured by surface Electromyography (sEMG) using a Myomed 932 (Enraf Nonius, Delft, the Netherlands) during standing and/or sitting [35], relaxation exercises will be performed using a portable myofeedback device (Myotrac I, Thought Technology, Quebec, Canada). Abnormal sEMG activity is defined as a constantly measured value above 1–5% of the maximally voluntary contraction [36-39], which is in general above 10 microvolt, during several minutes and the patient is not able to relax the muscle spontaneously or on request. Finally, all patients will receive ergonomic recommendations, and instructions to assume and maintain "good" posture [40,41]. Manual high velocity thrust techniques of the cervical spine and the shoulder and dry needling are excluded from the treatment protocol, because not all participating physical therapists are skilled to perform these techniques. The content of each session may vary as it depends on the findings during the first treatment session and the results of the previous treatment sessions. Thus, there are differences in the content of the individual treatments, but within the limits of the treatment protocol.

Stoprule

The treatment ceases when the patient is completely symptom-free or the patient and the therapist agree that treatment will not further benefit the patient, although their participation in the study will prolong. If patients decide that they no longer wish to participate in the study they are free to withdraw from the study at any moment.

Control of intervention integrity

To enhance the integrity of this complex intervention, every week all participating physical therapists will discuss the content of each therapy session with the researcher (CB) without mentioning names or other information which will assure the blinding of the independent researcher (CB). After 6 and 12 weeks, the patients of the intervention group will be interviewed about the content of the received treatment sessions to assure that all patients will be treated according to the protocol. If patients are not treated according to the protocol, they will be identified and participation may be discontinued.

Expectations regarding treatment outcome

At the start of the trial (T0) both the patients and physical therapists will complete a questionnaire regarding the anticipated treatment outcome.

Setting

The study will be conducted in a physical therapy practice specialized in management of persons with musculoskeletal disorders of the neck, shoulder and arm. After randomisation every patient assigned to the experimental group will be treated by the same physical therapist.

Objectives

In the current study we will test the following hypothesis (H0).

A physical therapy treatment to inactivate MTrPs within a three months' period is as effective as a "wait and see" approach of patients with chronic shoulder complaints in a three month period.

Population characteristics

- To identify potential confounding factors, demographic information for all subjects will be collected including age, gender, education, occupation, sports and leisure activities, duration of the complaints, and type of onset, among others.
- The Dutch language version of the RAND-36 item Health Survey will be used for base line characteristics of the study population. The RAND-36, which is almost identical to the MOS SF-36 [42], scores the functional status and quality of life and is widely used for screening health status in medical, social and epidemiological research. The RAND-36 consists of 36 items divided into 8 subscales concerning physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy and fatigue, emotional wellbeing, social functioning, pain, general health perception and health change. This questionnaire is considered to be a reliable instrument for comparing groups (internal consistency Cronbach's alpha > 0.70). The test-retest stability is sufficient (0.58 – 0.82) and the questionnaire is responsive when scoring after at least 4 weeks. The construct validity was estimated by comparing the RAND-36 with other Health questionnaires (like the Nottingham Health Profile (NHP) and the Groninger Activities Restriction Scale (GARS). There are significant correlations between the subscales of the RAND-36 and the subscales of the NHP (correlation coefficient 0.42 – 0.69). The correlation coefficient between the subscale physical functioning and the GARS is 0.65. A higher score (maximum is 100 points) defines a more favourable health status.
- The Beck Depression Inventory (BDI) is used to discriminate between patients with major depression and those without or with minor depressive feelings. The BDI is included because depression may be a confounding factor. The BDI is widely accepted and used in clinical and experimental research and its predictive value is rated as good. A BDI-score equally or higher than 21 indicates a major depression (specificity 78.4%) [43].

Outcomes

The following outcome parameters will be used:

Primary

The overall score of the DASH (Disability of Arm Shoulder and Hand) questionnaire – Dutch language version will be used as the primary outcome measure. The DASH is a multidimensional (physical, emotional and social) 30-item self-report measure focussing on physical function pain and other symptoms. At least 27 of the 30 items must be completed for a score to be calculated. The assigned values for all completed responses are simply summed and averaged. This value is then transformed to a score out of 100 by subtracting one and multiplying by 25. The transformation is done to make the score easier to compare to other measures using a 0–100 scale. A higher score indicates greater disability.

$$\text{DASH disability/sympton score} = \frac{[(\text{sum of n responses}) - 1]}{n} \times 25$$

where n is equal to the number of completed responses.

Scoring is on a 5-point Likert scale from no difficulty (0 points) to very difficult (5 points). The range of the total score is from 0 to 100, where 0 means no symptoms (pain, tingling, weakness or stiffness) and no difficulty in performing daily activities, while 100 means extreme, severe symptoms and unable to perform any daily activity. Content and face validity of the DASH were confirmed by a variety of experts of the American Academy of Orthopaedic Surgeons (AAOS), the council of Musculoskeletal Speciality Societies (COMSS) and the institute for Work and Health (Toronto, Ontario, Canada) throughout the development process [44].

Its internal consistency was excellent (Cronbach's alpha = 0.96) during field-testing. The test-retest reliability was excellent (ICC2.1 = 0.92 and 0.96) in two studies [45,46] and satisfactory in one study (Pearson 0.98 and kappa 0.67). The minimal detectable Change (MDC) was calculated in a population of 172 patients with several upper limb disorders (Osteoarthritis, Carpal Tunnel syndrome, Rotator Cuff syndrome, Rheumatoid Arthritis and Tennis Elbow) [47]. The Minimal Detectable Change (MDC) varied between 10.70 (at 90% confidence level) and 12.75 (at 95% confidence level). The DASH demonstrated to be a responsive questionnaire.

The inter- and intra-observer reliability is good to excellent (intra-observer reliability Pearson r = 0.96 to 0.98; ICC = 0.91 to 0.96; Inter-observer agreement Cohen's kappa = 0.79).

The construct validity was estimated by comparing the DASH to several other questionnaires. The correlation with other instruments like the SPADI (Shoulder Pain and Disability Index) is good (Pearson's r = 0.82 to 0.88). The DASH questionnaire is one of the best among 16 other questionnaires for shoulder symptoms [48].

Secondary

An independent examiner will perform the following tests.

- The total number of shoulder muscles with MTrPs will be counted and compared to the baseline measurement findings.

- Passive range of motion of the shoulder will be measured by a handheld digital inclinometer (The Saunders group Inc, Chaska, MN). The range of motion of the non-painful shoulder will be used as reference [49,49,50]. Because the normal range of motion differs from one individual to another, we focus on improvement of limited range of motion during the experiment (both experimental group and control group).
  - For the measurement of passive external rotation, the patient is in a supine position, with the shoulder in 0° of abduction and rotation, the elbow flexed at 90° and the forearm in a neutral position. This position is defined as the position of 0°. The observer then performs external rotation until pain limits the range of motion or the extreme of the range is reached. The inclinometer is placed against the volar side of the forearm. This range of motion is recorded in degrees. The normal range of motion for external rotation is between 70° and 90°.
  - For the measurement of passive glenohumeral abduction, the patient is seated upright, and the position of 0° is defined as the upper arm is in a neutral position. While palpating the lower angle of the scapula with the thumb, the examiner elevates the upper arm of the patient until the scapula begins to rotate or pain limits further motion. The inclinometer is placed against the lateral side of the upper arm near the elbow. The range of motion is recorded in degrees. The normal range of motion is 90°.
  - For the measurement of passive elevation (through flexion), the patient is in the supine position with the arm along the side. This position is defined as the position of 0°. The observer than performs elevation until pain limits the range of motion or the extreme of the range is reached. Then the inclinometer is placed against the medial side of the upper arm near the elbow. The range of motion is recorded in degrees. The normal range of motion is between 165° and 180°
  - For the measurement of internal rotation the patient is in a prone position. The shoulder is 90° abduction, and the forearm is in neutral position. This position is defined as the position of 0°. The observer than performs internal rotation until pain limits the range of motion or the extreme of the range is reached. The sensor is placed against the volar side of the forearm. The normal range of motion is 70°
  - For the measurement of horizontal adduction the patient is in a supine position. The arm is in 90° abduction. This position is defined as the position of 0°. The observer performs adduction, while the arm stays in the vertical plane, until pain limits the range of motion or the extreme of the range is reached. The normal range of motion is 135°

- Finally the total number of treatment sessions will be counted. This is done by an assistant, who is not involved in the study by using the administration-software of the practice *(see Table 1)*.

Sample size

The initial sample size is based on the assumption that the overall score of the primary outcome measure DASH shows a mean improvement of 15 points (SD = 22) [51].

To test the null hypothesis of equality of treatment at α = .05 with 90% power and assuming a uniform dropout rate of 5%, it was calculated that 52 patients in each group would be sufficient.

Randomization

After inclusion the patients will be randomly assigned to either the intervention group or the "wait and see" group. The randomisation will be performed by an assistant not otherwise involved in the study by generating random numbers using computer software. Stratification or blocking strategies will not be used.

Informed consent

The patients will be informed about the study prior to the first assessment and will be asked to give written informed consent.

Blinding

Blinding of the patients or the physical therapists, who are involved in the treatment, is impossible due to the treatment characteristics.

An independent observer will collect baseline data and outcome data. The independent observer is blinded. The successfulness of the blinding procedure will be evaluated by asking the observer to which group she believes the subjects belong.

Statistical analysis

For comparisons of prognostic variables on baseline we will use the Student's t test for continuous variables with normal distribution and the chi-square test for categorical variables or continuous variables with non-normal distribution [52]. For the overall score of the DASH (primary outcome measure) we will use the unpaired t-test for normally distributed data or Mann-Whitney Rank Sum-test for non-normally distributed data to assess the difference between the two groups after the treatments. Regression analyses will be used to include prognostic factors, such as the baseline scores like age, gender and duration of the complaints, in the analyses. All significance levels will be set at $p < 0.05$. All data will be analysed primarily according to intention-to-treat principle. We will use Sigmastat 3.11 and Systat 12 for Windows (Systat Inc. Richmond, California, USA) for the statistical analyses.

Discussion

Since there is little evidence for the efficacy of physical therapy interventions in some shoulder disorders, there is a need for further research. Therefore we will perform a randomised clinical trial dealing with the effect of physical therapy interventions aimed to inactivate MTrPs on pain and impairment in shoulder function in a population of chronic a-traumatic shoulder patients. To the best of our knowledge, few studies of the efficacy of MTrP therapy are published. We choose for an intervention strategy that best reflects daily practice. We excluded manual high velocity thrust techniques and intramuscular MTrP release by dry needling, because these interventions are not commonly used by Dutch physical therapists and not all participating therapists were skilled to perform these techniques at the beginning of the study. In most physical therapy interventions, blinding of the patient and the therapist is not possible. The observers will be blinded for the allocation procedure. The results of this trial will be presented as soon as they are available.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

All authors read, edited and approved the final manuscript. CB is the lead investigator, and developed the design of the study, will carry out data-acquisition, analysis, interpretations, and prepared as primary author the manuscript. MW and RO were responsible for the design, project supervision and writing of the manuscript. JF will assist in carrying out data acquisition and was involved in preparing the study design and in writing the manuscript.

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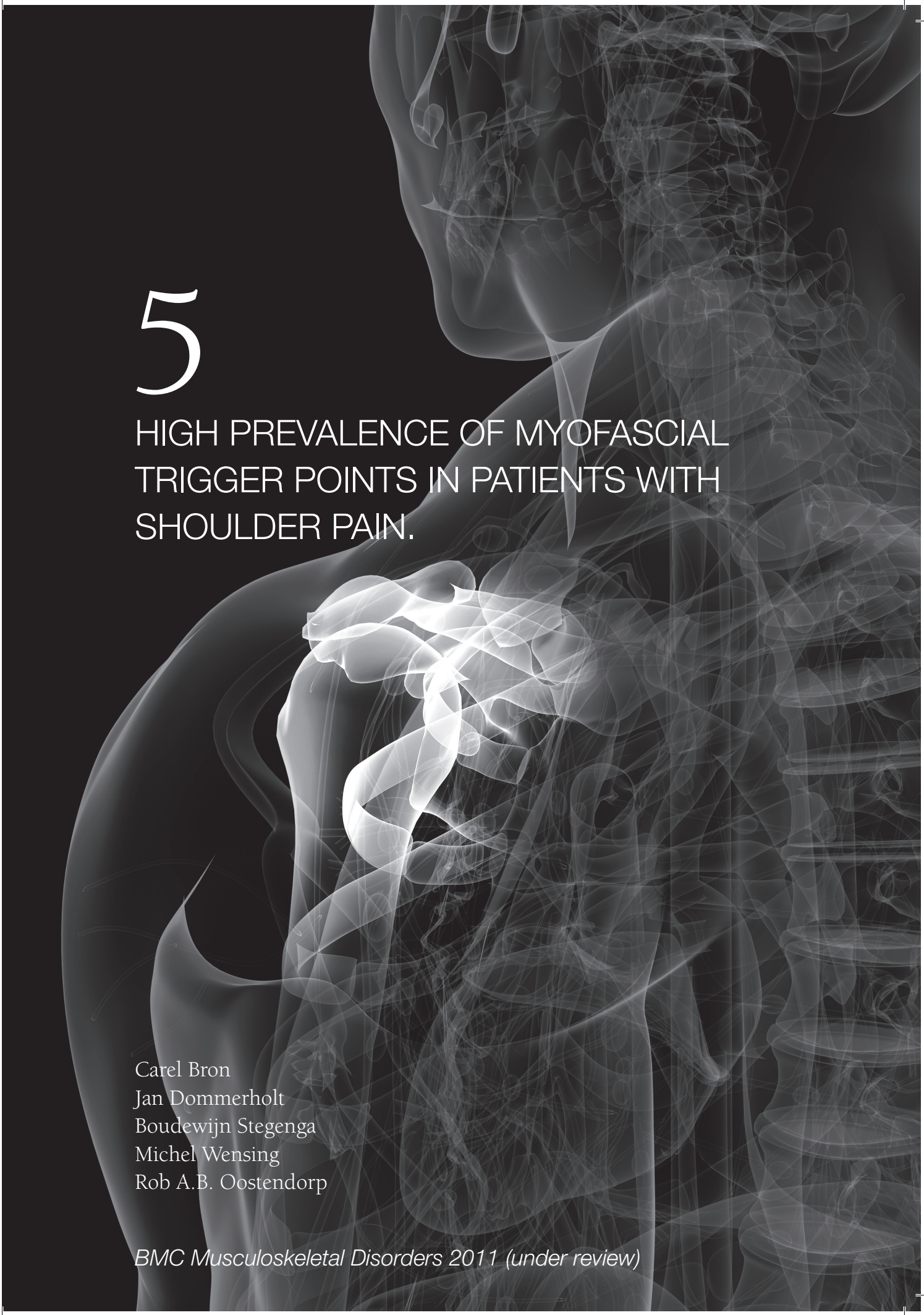

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HIGH PREVALENCE OF MYOFASCIAL TRIGGER POINTS IN PATIENTS WITH SHOULDER PAIN.

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HIGH PREVALENCE OF MYOFASCIAL TRIGGER POINTS IN PATIENTS WITH SHOULDER PAIN.

Abstract

Background: Shoulder pain is reported to be highly prevalent and tends to be recurrent or persistent despite medical treatment. The pathophysiological mechanisms of shoulder pain are poorly understood. Furthermore, there is little evidence supporting the effectiveness of current treatment protocols. Although myofascial trigger points (MTrPs) are rarely mentioned in relation to shoulder pain, they may present an alternative underlying mechanism, which would provide new treatment targets through MTrP inactivation. While previous research has demonstrated that trained physiotherapists can reliably identify MTrPs in patients with shoulder pain, the percentage of patients who actually have MTrPs remains unclear. The aim of this observational study was to assess the prevalence of muscles with MTrPs and the association between MTrPs and the severity of pain and functioning in patients with chronic non-traumatic unilateral shoulder pain.

Methods: An observational study was conducted. Subjects were recruited from patients participating in a controlled trial studying the effectiveness of physical therapy on patients with unilateral non-traumatic shoulder pain. Sociodemographic and patient-reported symptom scores, including the Disabilities of the Arm, Shoulder, and Hand (DASH) Questionnaire, and Visual Analogue Scales for Pain were compared with other studies. To test for differences in age, gender distribution, and education level between the current study population and the populations from Dutch shoulder studies, the one sample T-test was used. One observer examined all subjects (n=72) for the presence of MTrPs. Frequency distributions, means, medians, standard deviations, and 95% confidence intervals were calculated for descriptive purposes. The Spearman's rank-order correlation (ρ) was used to test for association between variables.

Results: MTrPs were identified in all subjects. The median number of muscles with MTrPs per subject was 6 (active MTrPs) and 4 (latent MTrPs). Active MTrPs were most prevalent in the infraspinatus (77%) and the upper trapezius muscles (58%), whereas latent MTrPs were most prevalent in the teres major (49%) and anterior deltoid muscles (38%). The number of muscles with active MTrPs was only moderately correlated with the DASH score.

Conclusion: The prevalence of muscles containing active and latent MTrPs in a sample of patients with chronic non-traumatic shoulder pain was high.

INTRODUCTION

Shoulder pain, which is often persistent or recurrent, is one of the major reasons patients consult with primary healthcare providers [1-6]. However, the pathophysiological mechanisms underlying shoulder pain are poorly understood. Although subacromial impingement is often suggested to be a potential source of shoulder pain [7, 8], solid evidence is lacking. In fact, calcifications, acromion spurs, subacromial fluid, or signs of tendon degeneration are equally prevalent in healthy subjects and in patients with shoulder pain [9-12]. Furthermore, physical examination tests of subacromial impingement are not reliable [13-15], and the results of imaging diagnostics do not correlate well with pain [9, 10, 16, 17]. In addition, interventions targeting subacromial problems are, at most, only moderately effective at treating shoulder complaints [18-24].

Myofascial trigger points (MTrPs) may offer an alternative explanation for the pathophysiological mechanisms underlying shoulder pain. In recent years, our understanding of the etiology, pathophysiology, and management of MTrPs has increased [25-30]. MTrPs are local points, that are highly sensitive to pressure, the application of which causes characteristic referred sensations, including pain, muscle dysfunction [26], and sympathetic hyperactivity [31-33].

MTrPs are classified into active and latent myofascial trigger points. Active MTrPs are characterized by the presence of clinical pain and constant tenderness. Specifically, active MTrPs prevent full lengthening and weakening of the muscle. Diagnostically, active MTrPs refer patient-recognized pain upon compression and mediate a local twitch response in muscle fibers when stimulated. When compressed within the patients' level of pain tolerance, active MTrPs produce referred motor phenomena and often sympathetic hyperactivity, (generally in the pain reference zone), and cause tenderness in the pain reference zone. In contrast, latent MTrPs are clinically quiescent, and are only painful when palpated. With the exception of spontaneous pain, a latent MTrP can present with all the clinical characteristics of active MTrPs. In addition, latent MTrPs are within a taut band that increases muscle tension and restricts patients' range of motion [26]. Although the exact pathophysiology of MTrPs is not yet fully understood, abnormal electrical activity, called endplate noise, has been associated with both latent and active MTrPs, and several pain-inducing and pro-inflammatory substances have been found at active MTrP in humans [27, 34].

In clinical practice, identification of MTrPs is usually performed by palpation. In a recent study [35], we confirmed that this technique is a reliable method for detecting MTrPs in shoulder muscles. Although prevalence studies are sparse [36-42], based on clinical experience, MTrPs seem to be associated with shoulder pain, disability, and dysfunction [43-45]. Still, little is known about the impact of MTrPs on pain and functioning in patients with shoulder disorders [46]. Because MTrPs refer pain to the shoulder, they may contribute substantially to the clinical picture of shoulder pain *(Figure 1)*. Experimental muscle pain, clinical muscle pain, and MTrPs have all been shown to alter motor activation patterns in a similar manner as the kinematic disturbances seen in shoulder pain patients often referred to as SIS [47-49].

The aim of this study was to determine the prevalence of MTrPs and the correlation between MTrPs and pain and functioning, in a sample of patients presenting with chronic, non-traumatic unilateral shoulder complaints.

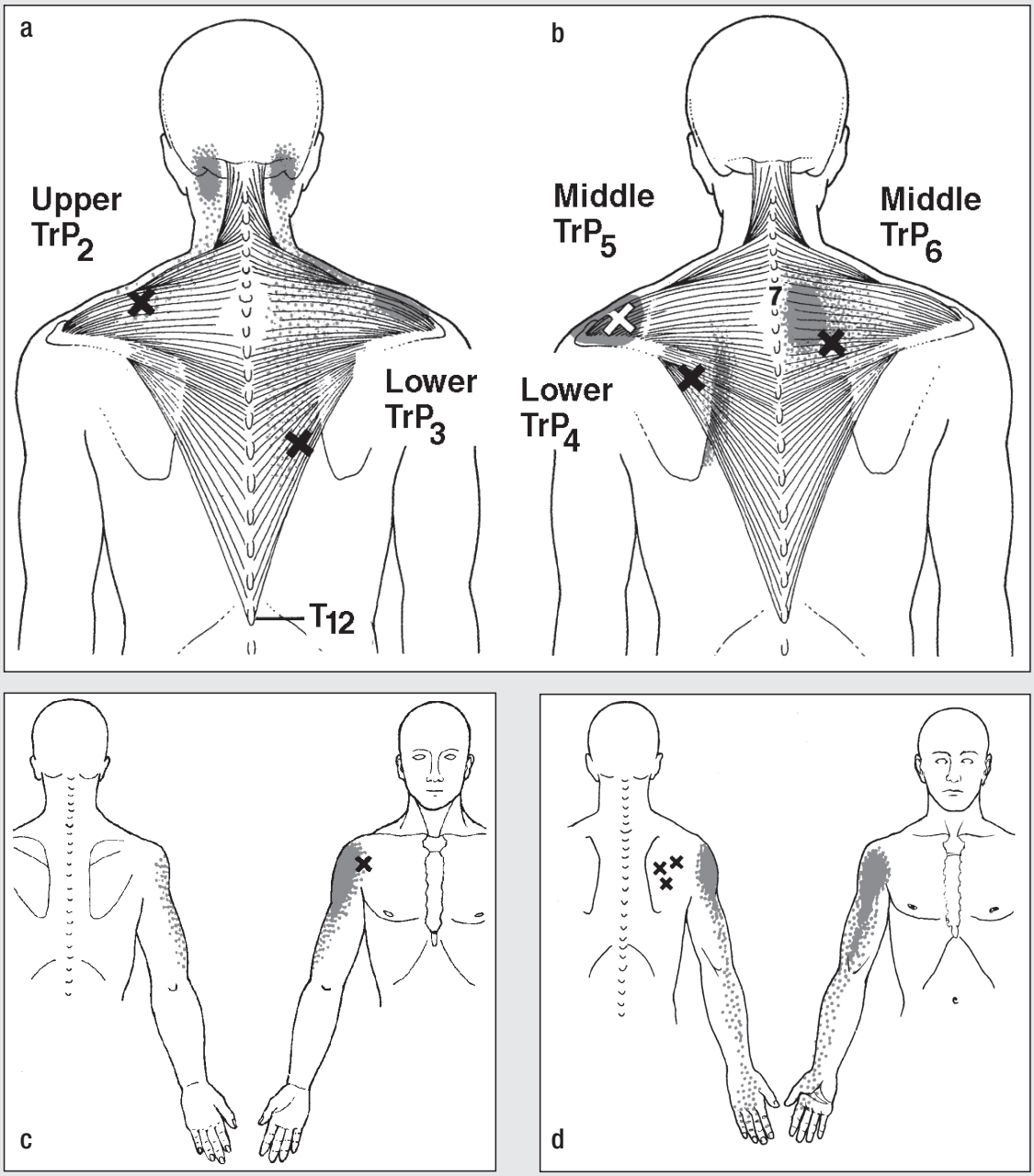


***Figure 1**: Referred pain patterns (gray) from the lower trapezius (a), upper trapezius (b), anterior deltoid (c), and infraspinatus (d) muscle MTrPs (Xs), according to Simons et al. Illustrations courtesy of LifeART/MEDICLIP, Manual Medicine 1, Version 1.0a, Lippincott,Williams & Wilkins, 1997*

Material and methods

Study design

This observational study was embedded in a clinical trial (registered at current controlled trials ISRCTN75722066) addressing a specific treatment of patients with shoulder pain [50]. The Committee of Human Research of the region Nijmegen-Arnhem, the Netherlands, has approved the study protocol [CMO 2007/22].

Study Participants

Study participants were recruited from patients participating in a controlled trial investigating the effectiveness of physical therapy on patients with unilateral, non-traumatic shoulder pain. This study was conducted at a primary care practice for physical therapy, which specializes in the treatment of patients with disorders of the shoulder, the neck, and upper extremities. A power analysis was performed prior to beginning this study, and it was calculated that 104 subjects were needed for the clinical trial.

All patients who contacted the practice for non-specific shoulder complaints from September 2007 until September 2009, were requested to participate in the study. The inclusion criteria were 1) age between 18 and 66 years; 2) unilateral non-traumatic shoulder pain; and 3) duration of symptoms of more than six months. Patients were excluded from the study if they presented with a prior diagnosis of shoulder instability, shoulder fractures, any systemic diseases, or a medical history or examination suggestive for the presence of neurological disease, internal diseases, or psychiatric disorders. All patients signed a written informed consent before participating in the study.

General Applicability

To determine the potential general applicability of this study to primary care shoulder pain patients, we searched for Dutch studies conducted on primary care patients from 1995 until 2009. Eight studies were found and sociodemographic data (age, gender, education level, and duration of shoulder pain) were analyzed and compared to the current study population [2, 5, 51-55].

Measures

At baseline, age, gender, hand dominance, and education level were recorded. For comparison reasons we classified the education level as high education (university and higher vocational school), medium education (middle vocational school and higher or middle general secondary school), and low education (lower vocational school, lower general secondary school, primary school, or no education) [54]. Shoulder-pain related data (duration of shoulder-pain, recurrence rate and location of the complaints) were collected and the study subjects were asked to complete a set of standardized self-report measures, including the Disabilities of the Arm, Shoulder, and Hand outcome measure - Dutch Language Version (DASH-DLV), Visual Analogue Scale for Pain (VAS-P) and the Beck Depression

Inventory- Second Version- Dutch Language Version (BDI-II-DLV) [50]. The BDI-II-DLV is used to discriminate between patients with major depression and those with only minor depressive feelings or no depression, which may be a confounding factor. The BDI-II has good predictive value, is widely accepted, and is commonly used in both clinical and experimental research. A BDI-II-DLV score equally or ≥ 21 indicates major depression (specificity 78.4%) [56].

For every study participant, one of the two available observers measured the passive range of motion (PROM) of the shoulder in flexion, internal and external rotation, abduction, and (horizontal or cross-body) adduction with a handheld digital inclinometer (The Saunders Group Inc, Chaska, MN). Range of motion was expressed in degrees and presented as the sum of the value measured for the non-affected shoulder minus the value measured for the affected shoulder. A positive value means that the affected shoulder had impaired range of motion as compared to the non-affected shoulder. Next, the observer examined each subject for the presence of MTrPs in the shoulder muscles of their affected shoulder according to the guidelines outlined in Simons et al [26]; the non-affected shoulder was examined as a control. Following these guidelines, an MTrP is defined as: a nodule in a taut band that is extremely painful upon compression, and may produce referred pain or sensations. MTrPs were classified as either 'active' when the pain was recognized by the patient as a familiar pain, and 'latent' when the observer found a firm nodule in a taut band, which was painful on compression, but did not produce a recognizable pain. The inter-examiner reliability of trigger point palpation has been established in several studies [35, 57, 58]. All 17 muscles that are known to produce pain in the shoulder or may result in dysfunction of shoulder muscles were systematically examined and the number of muscles with MTrPs in the affected shoulder was counted, regardless of the number of MTrPs per muscle *(Table 1)*. The two observers were physical therapists, each with 30 years of clinical experience in primary care practice. Both observers had attended an extensive, postgraduate course on MTrP diagnosis and therapy and had more than 5 years experience in identifying MTrPs and treating patients with MTrPs prior to the start of the study.

Table 1. List of muscles examined for presence of MTrPs

upper trapezius muscle	middle trapezius muscle	lower trapezius muscle
infraspinatus muscle	supraspinatus muscle	subscapularis muscle
teres minor muscle	teres major muscle	anterior deltoid muscle
middle deltoid muscle	posterior deltoid muscle	pectoralis major muscle
pectoralis minor muscle	biceps brachii muscle	triceps brachii muscle
scalene muscles	subclavius muscle	

The DASH-DLV is a widely used multidimensional (physical, emotional and social) 30-item self-reporting questionnaire that focuses on physical function, pain and other symptoms. DASH-DLV scores ranges from 0 to 100, with higher scores indicating greater disability. DASH is a reliable and valid questionnaire, with good to excellent intra- and inter-rater reliability, and good correlation with the Shoulder Pain and Disability Index. Because of these advantages, DASH is considered to be one of the best questionnaires available for shoulder symptoms (http://www.dash.iwh.on.ca/) [59, 60].

The VAS-P is a self-report scale consisting of a 100 mm horizontal line anchored by word descriptions on each side [61]. VAS-P can be used to measure pain current pain levels (VAS-P1), the average pain over the last 7 days (VAS-P2), and the most severe pain over the last 7 (VAS-P3). VAS-P scores ranges from 0 (no pain) to 100 (the worst pain imaginable). The Visual Analogue Scale has properties consistent with a linear scale for patients with mild to moderate pain.

Data was collected and transferred to a worksheet by a research assistant (who was not involved in the physical examination or palpation of MTrP).

Data analysis

Frequency distributions, means, medians, standard deviations, and 95% confidence intervals were calculated for descriptive purposes. The Shapiro-Wilk W test was used to test for normality of the data. Because the number of muscles with MTrPs (active, latent and total) was not normally distributed we used the Spearman's rank-order correlation (ρ) test for all variables. For interpretation of the ρ-values, we used the classification proposed by Feinstein [62]. A correlation coefficient < 0.30 was considered to be indicative of a poor correlation. A correlation coefficient ≥ 0.30 and ≤ 0.70 was considered to be indicative of moderate correlation, and a correlation coefficient ≥ 0.70 was defined as substantial or a good correlation. To test for differences in age, gender distribution, and education level between the current study population and study populations from Dutch shoulder studies (from 1995 until 2009), we used a one sample T-test. The α level for statistical significance was set at 0.05. All analyses were performed using Systat 12 or Sigmastat 3.1 for Windows (Systat Software, Inc. Chicago, IL, USA).

Results

A flowchart describing patient participation is depicted in *Figure 2*. Out of 211 patients who were treated for shoulder disorders, between September 2007 and September 2009, 72 patients (50 females and 22 males; mean age 43.9 years, SD 12.3; 95% CI 41.0 to 46.0) presented with unilateral, non-traumatic shoulder complaints, met the study inclusion criteria, and agreed to participate in this study. Twenty-six subjects were suffering from their first episode of shoulder pain, while for 19 subjects, this was their second episode.

The remaining 27 subjects had suffered from ≥ 3 episodes of shoulder pain. Study participants' characteristics are summarized in Table 2. A comparison of data obtained from the present study with data from previous Dutch studies is presented in Table 3. The mean age of the present study population was lower ($p < 0.05$) and the proportion of female subjects was higher ($p < 0.05$) compared to these other studies. In addition, the current study population was more highly educated ($p < 0.05$) than the previous study populations for which educational data was reported [3, 5, 52]. Comparison of the duration of shoulder pain was not possible because different classifications were used.

Figure 2: *Flow chart showing a schematic summary of patient participation in this study*

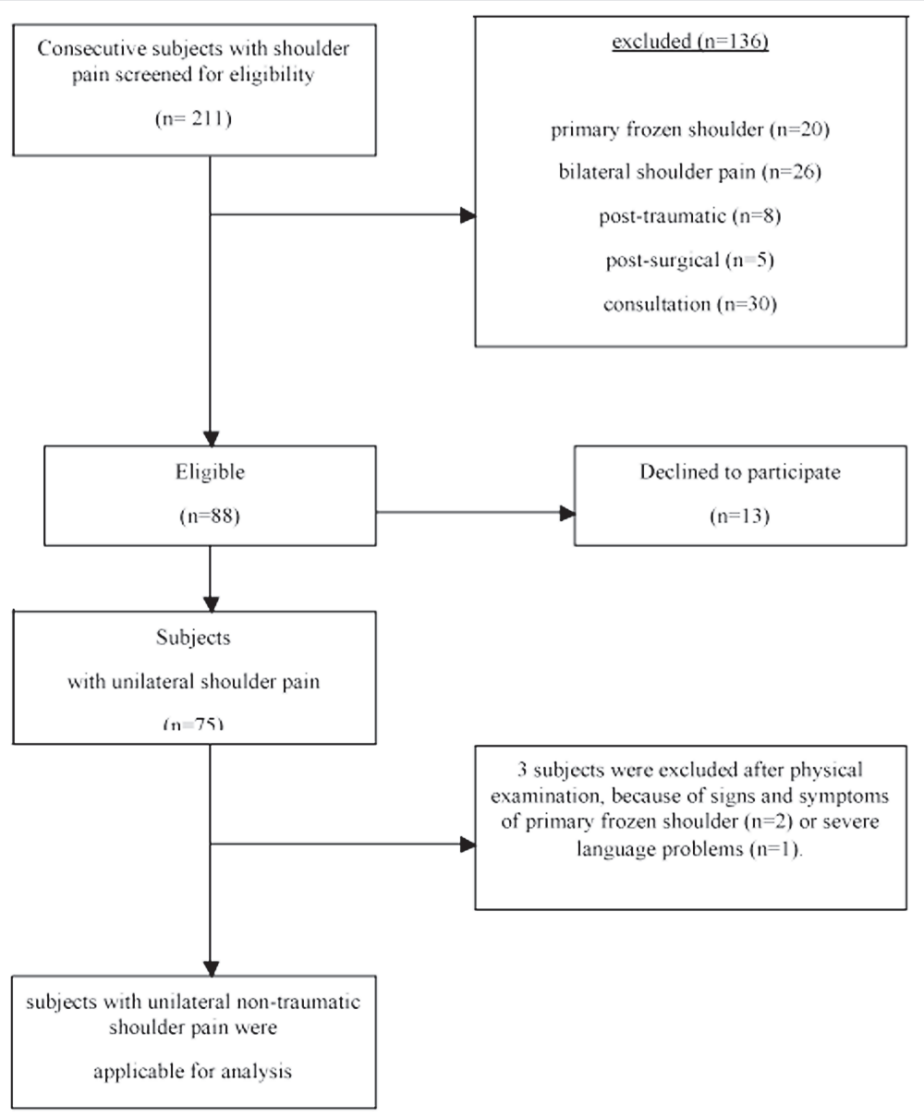


Table 2 Characteristics of patients participating in this study (n=72).

Characteristics	n (%)	mean (SD; 95% CI); median
Age (years)		43.9 (12.3; 41.0 – 46.8); 45.0
Gender, female	50(69.4)	
Duration of shoulder pain		
6-9 months	17(23.6)	
9-12 months	14(19.4)	
1-2 years	13(18.0)	
2-5 years	14(19.4)	
>5 years	14(19.4)	
Recurrence rate		
1st episode	26(36.1)	
2nd episode	19(26.4)	
3rd > episode	27(37.5)	
Hand dominance, left-handed	4(5.6)	
Side of complaints right	48 (66.7)	
DASH-DLV (0 – 100)a		30.8 (14.1; 27.5 – 34.1); 28.3
VAS-P1 (0-100)b		30.0 (23.9; 27.0 – 39.9); 30.0
VAS-P2 (0-100)b		42.1 (17.7; 37.4 – 50.0); 40.0
VAS-P3 (0-100)b		56.6 (19.8; 51.2 – 61.9); 57.0
BDI-II-DLV (0 – 63)c		6.1 (6.0; 4.7 – 7.6); 5.00
0-13	68 (94.4)	
14-19	3 (4.3)	
20-28	0 (0.0)	
28-63	1 (1.4)d	

a Higher Dash-DLV (Disabilities of the Arm, Shoulder and Hand outcome measure- Dutch Language Version) scores mean more disability with a maximum of 100 (range from 0 to 100)[59].

b Higher VAS-P scores (Visual Analogue Scales for Pain) mean more pain, with a maximum of 100 (range from 0 to 100). VAS-P1 represents the current pain score, VAS-P2 represents the average pain score over the past seven days, and VAS-P3 represents the most severe pain score over the past seven days.

c Higher scores on the BDI-II-DLV (Beck Depression Inventory-second edition- Dutch Language Version) mean more symptoms of depression. Clinical interpretation of scores is accomplished through criterion-referenced procedures utilizing the following interpretive ranges: 0-13 minimal depression; 14-19 mild depression; 20-28 moderate depression; and 29-63 severe depression[77].

d One patient scored 45 points, which is indicative of major depression. This high score was due to a major event that happened on the day of inclusion in the study.

Table 3 Socio-demographic characteristics of the current study population and eight other Dutch shoulder research study populations.

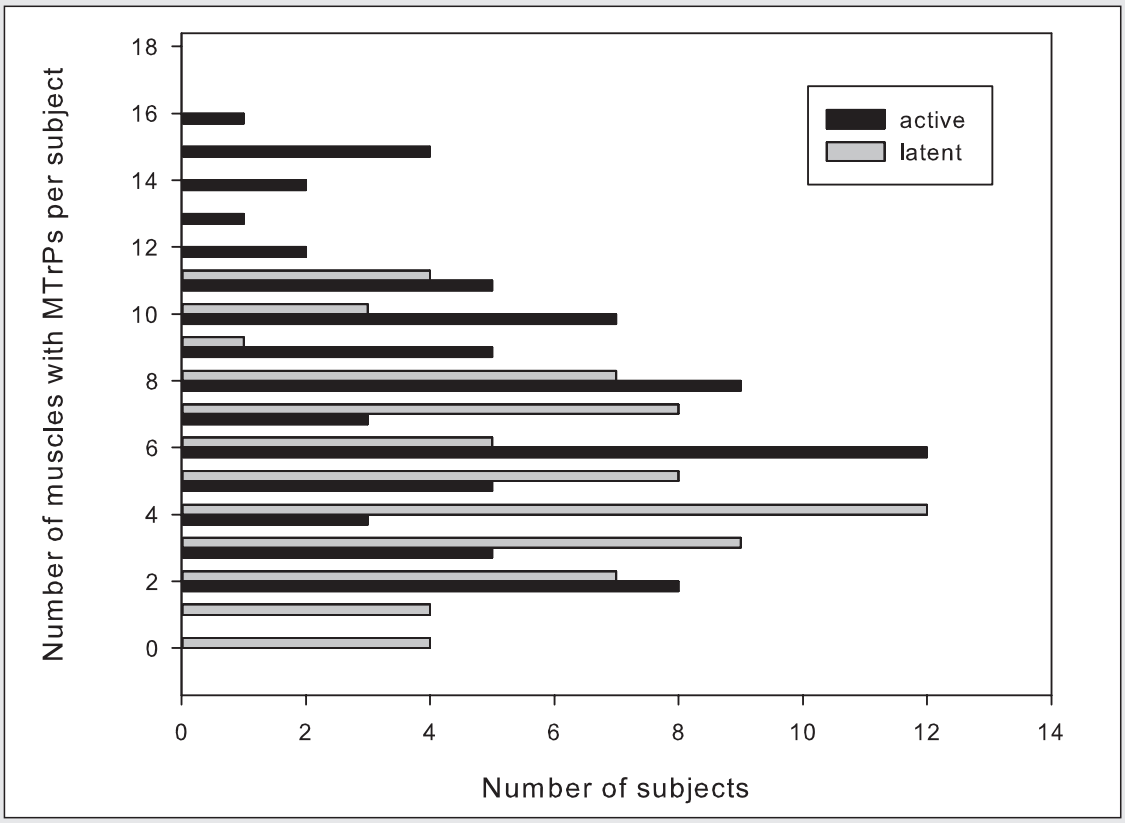
	Current study N=72	Van der Windt 1996 N=335	De Winter 1999 N=201	Winters 1999 N=101	Bot 2005 N=281	Bergman 2005 N=71	Kuijpers 2006 N=492	Feleus 2008 N=682	Reilingh 2008 N=587
Age (years,± SD)									
	43 (12.3)	49.6 (14.4)	48 (12)	47.3 (15.4)	49.2 (13.8)	47.8 (11.8)	52 (14)	45*	49.5 (14.7)† 51.9 (13.9)‡ 52.9 (13.3)¶
Gender (%)									
female	69	56	66	58	63	52	50	52	50
Education level									
low	6	NA	NA	NA	44	NA	NA	36	36
medium	47	NA	NA	NA	42	NA	NA	36	41
high	47	NA	NA	NA	14	NA	NA	28	23
Duration of shoulder pain (month)									
< 3 m	0	85	26	75	66	70	60	74	59
3-6 m			16			30	40		41
> 6 m	100	15	55	25	34		26		

* *Feleus reported the median instead of the mean age*
† *Mean age (±SD) of the acute pain group (< 6 weeks)*
‡ *Mean age (±SD) of the subacute pain group (6-12 weeks)*
¶ *Mean age (±SD) of the chronic pain group (> 3 months)*
NA (not available). It was not possible to derive these data from the papers.

Prevalence of myofascial trigger points per subject

Muscles containing active MTrPs were found in all 72 subjects. The median number of muscles with active MTrPs per subject was 6 (range 2 to 16). Muscles containing latent MTrPs were found in 67 subjects. The median number of muscles with latent MTrPs per subject was 4 (range 0 to 11). Figure 3 shows the frequency distribution of active and latent MTrPs per subject. Neither active MTrPs nor latent MTrPs were normally distributed (Shapiro W= 0.95; $p < 0.05$; W=0.96; $p < 0.05$ respectively).

Figure 3: *The number of active (black bar) and latent (grey bar) of MTrPs per subject. The X-axis shows the number of MTrPs per subject, and the Y-axis shows the number of subjects (n=72).*

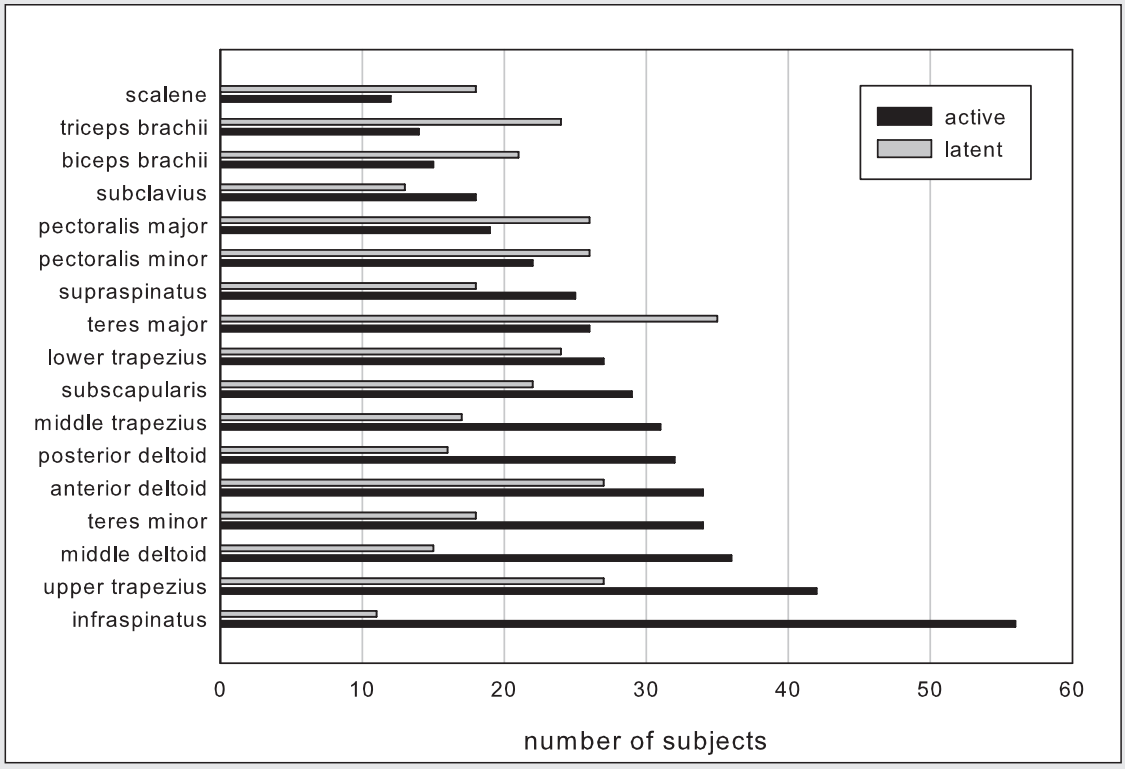


Prevalence of myofascial trigger points per muscle

Active MTrPs were found in the infraspinatus muscle in 56 subjects and in the upper trapezius muscle in 42 subjects. In addition, active MTrPs were highly prevalent in the middle trapezius (n=31), anterior deltoid (n=34), middle deltoid (n=36), posterior deltoid (32), and teres minor (n=34) muscles.

Latent MTrPs were found in the infraspinatus muscle in 11 subjects and in the upper trapezius in 27 subjects. Latent MTrPs were found in the teres major muscle in 35 subjects and in the anterior deltoid muscle in 27 subjects. *Figure 4* presents the distribution of active and latent MTrPs per muscle.

Figure 4: The number of subjects with active (black bar) or latent MTrPs (gray bar) per muscle. The X-axis shows the muscles that were examined for identification of MTrPs, and the Y-axis shows the number of subjects with MTrPs (n=72).



DASH-DLV, VAS-P, BDI-II-DLV, and PROM

The mean score on the DASH was 30.8 (SD 14.1; 95% CI 27.5 to 34.1). Mean VAS-P scores were follows: the VAS-P score for 'current pain' (VAS-P1) was 30 (SD 23.9; 95% CI 27.0 to 39.9), for 'average pain in the last seven days' (VAS-P2) was 42.1 (SD 17.7; 95% CI 37.4 to 50.0) and for 'for the most severe pain in the last seven days' (VAS-P3) was 56.6 (SD 19.8; 95% CI 51.2 to 61.9). The mean PROM score, calculated as the sum the PROM value measured for the non-affected shoulder minus the PROM value measured for the affected shoulder, was 32.4 degrees (SD 34.8; 95% CI 24.2 to 40.6), where a positive value indicates that the affected shoulder has a impaired range of motion. Both DASH and PROM scores were normally distributed ($W = 0.97$; $p < 0.05$ and $W = 0.91$; $p < 0.05$ respectively). VAS-P1, VAS-P2, and VAS-P3 scores were also considered to be normally distributed, although the Shapiro-Wilk test did present borderline results for VAS-P2 and VAS-P3.

Table 4: Correlation matrix of the current study population (n=72).

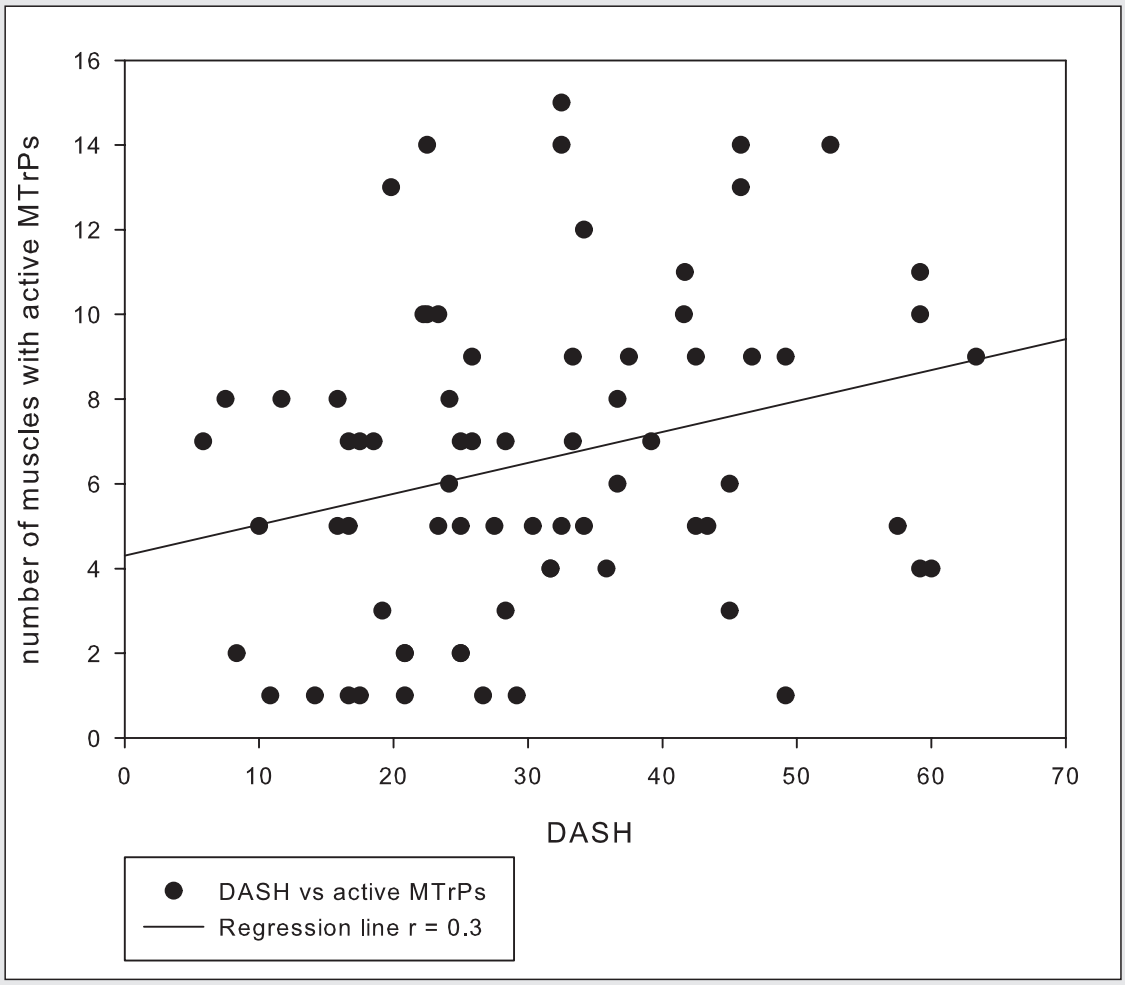
	MTrPs	Active MTrPs	Latent MTrPs	DASHDLV	BDI-II DLV	VAS P1	VAS P2	VAS P3	Duration
MTrPs	-	0.65*	0.11	0.29*	0.22	0.44*	0.31*	0.06	0.26*
AMTrPs		-	-0.64*	0.30*	0.16	0.33*	0.28*	0.01	0.12
LMTrPs			-	-0.12	0.02	-0.02	-0.06	0.04	0.04
DASH-DLV				-	0.35*	0.66*	0.58*	0.27*	0.05
BDI-II-DLV					-	0.33*	0.18	0.07	0.13
VAS-P1						-	0.68*	0.35*	0.18
VAS-P2							-	0.57*	0.18
VAS-P3								-	-0.10
Duration									-

The data represent Spearman's rank correlation coefficient. Correlation coefficients between the number of muscles with myofascial trigger points (MTrPs), the number of muscles with active MTrPs (AMTrPs) and the number of muscles with latent MTrPs (LMTrPs), the DASH (Disability of the Arm, Shoulder and Hand) outcome measure- Dutch Language Version (DASH-DLV), the Beck Depression Inventory-second version- Dutch language Version (BDI-II-DLV), the Visual Analogue Scales for current pain (VAS-P1), the average pain over the last seven days (VAS-P2), the most severe pain over the last seven days (VAS-P3) and the duration of shoulder pain (Duration), are given ($p < 0.05$).*

Correlation between the number muscles of MTrPs and pain and disability scores (DASH-DLV, VAS-P)

The number of muscles with active MTrPs only moderately correlated with the DASH-DLV (ρ= 0.30; $p < 0.05$) and VAS-P1 scores (ρ =0.33; $p < 0.05$), and poorly correlated with VAS-P2 (ρ= 0.28; $p< 0.05$) and the duration of the shoulder pain (ρ=0.26, $p < 0.05$). We were unable to detect statistically significant correlations between the number of muscles with MTrPs (either active or latent) and VAS-P3 (ρ= 0.09; $p > 0.05$) or the PROM (ρ =0.13; $p > 0.05$) scores. *Table 4* provides an overview of the correlations and *Figure 5* shows a scatterplot of DASH scores versus the number of active MTrPs.

Figure 5: Scatterplot of DASH scores versus the number of muscles with active MTrPs. The regression line shows a weak positive correlation (r = 0.3), indicating that increasing numbers of active MTrPs have only a moderate effect on DASH scores.



Discussion

Prevalence of MTrPs

All subjects with unilateral, chronic, non-traumatic shoulder pain presented with multiple shoulder muscle MTrPs. In addition, MTrPs were found in all 17 muscles examined. However, the number of shoulder muscles with MTrPs appeared to vary greatly among subjects. In particular, MTrPs were most frequently located in the infraspinatus and upper trapezius muscles, in agreement with results from Skootsky [37] and Simons [26], who found that infraspinatus muscles were frequently associated with myofascial shoulder pain. There are very few other prevalence studies in the literature, and to the best of our knowledge, this is the first extensive report on the prevalence of MTrPs in patients with chronic, non-traumatic unilateral shoulder pain.

Mean scores on DASH-DLV and VAS-P scores

The mean DASH-DLV score measured for the current study population is comparable with the mean baseline scores measured for other study populations for subjects with shoulder and arm pain [63-65]. According to Beaton [81] subjects (n=200) with DASH scores < 23.6 are still able to perform all desired daily activities, although they may experience some discomfort. For comparison, in a study population from the US (n= 1706), the mean DASH score was 10.10 (SD 14.68) and in young active and healthy adults the mean DASH score was 1.85 (SD 5.99) [66]. Importantly, the DASH-DLV score primarily reflects the level of dysfunction with less emphasis on pain and other symptoms. While 23 items refer to the ability of the subject to perform activities, only 7 items assesses the severity of symptoms. Subjects with long-standing shoulder complaints may alter the way in which they perform activities by using compensatory movements. In addition, DASH-DLV does not discriminate between activities performed using the affected or non-affected arm, which may influence the magnitude of the disability and therefore the final DASH-DLV score. In support of this, several subjects in our study commented that their DASH score would have been different if the activities in question were related to the affected arm.

Correlation between number of muscles with MTrPs, DASH-DLV scores, and VAS-P scores

The number of muscles containing active MTrPs moderately and positively correlated with DASH-DLV, VAS-P1, VAS-P2 scores, and the duration of the shoulder pain, suggesting that the number of muscles with active MTrPs explained only 10% of the variation of the outcome measures. In addition, other clinically relevant factors may have contributed to the primary and secondary outcome scores. First, although we did not measure the pain intensity at the MTrP, this may have a significant impact on pain and functioning. Hidalgo et al found that patients with shoulder pain had a larger number of both active and latent MTrPs than healthy subjects. They also found that active MTrPs were associated with greater pain intensity, and that lower Pain Pressure Thresholds (PPT) were reported for active MTrPs compared to latent and patients with shoulder pain displayed lower PPT than healthy subjects [49]. Second, in this study we did not take into consideration the number of MTrPs per muscle, which may have contributed to the moderate correlation observed between the number of muscles with MTrPs and the DASH-DLV and VAS-P scores. The total number of muscles with MTrPs was poorly but positively correlated with the duration of the complaints, indicating that the number of shoulder muscles with MTrPs may increase over time regardless of whether the MTrPs were active or latent. Finally, because one of the characteristics of the DASH-DLV score is, that it does not discriminate between the affected and the non-affected shoulder, one could speculate that patients with chronic shoulder pain may develop strategies to overcome pain and disability caused by their shoulder disorder, for instance by using the non-affected arm, resulting in decreased DASH-DLV and VAS-P scores. All these factors may have a substantial influence on the correlation coefficient. Although the number of shoulder muscles with active MTrPs correlates moderately with the various outcome measures, this does not imply that MTrPs are clinically unimportant.

Clinical implications

To date, unilateral shoulder pain has mainly been proposed to be due to either the presence of inflammation in the subacromial tendons and bursae, or degenerative rotator cuff ruptures (diagnosed using modern imaging techniques, such as MRI or sonography). Although these pathological structures may cause pain, it is also known that similar abnormalities have been found in asymptomatic shoulders.

Active MTrPs, which are painful spots that produce familiar shoulder pain during contraction, stretching or compressing, these MTrPs may provide an alternative explanation for shoulder pain, which is independent of the presence of subacromial abnormalities. According to Simons, Travell and Simons [26], MTrPs within the infraspinatus muscle (which were most prevalent) cause pain in the anterior and middle deltoid regions which expands into the frontal upper arm, as well as referred pain and referred sensations felt in the wrist and the hand. In addition, internal rotation and cross-body adduction may be impaired, which is often the case in patients with shoulder pain. Both experimentally induced and spontaneous muscle pain lead to an aberrant motor activation pattern that is also present in patients with shoulder pain [67, 68]. Although latent MTrPs are not usually an immediate source of pain, they can elicit referred pain when mechanically stimulated, or during sustained or repeated muscle contraction. In addition, latent MTrPs may disturb normal motor recruitment patterns and movement efficiency. Lucas et al. showed that subjects who received myofascial dry needling, followed by passive muscle stretching to remove latent MTrPs, showed normalized motor activation patterns within 20 to 30 minutes following the treatment [48]. Therefore, it is reasonable to expect that treatment of MTrPs may lead to normalization of motor activation patterns and may facilitate spontaneous recovery of shoulder pain, either without exercising or by making exercise more effective.

Based on the results of this study, we propose that an alternative approach may be indicated for the assessment and management of patients with chronic, non-traumatic shoulder pain. Current treatment regimens consist primarily of pharmacological interventions, including anti-inflammatory medications, or muscle strengthening exercises. If MTrPs are one of the main reasons for shoulder pain (active MTrPs) and altered motor activation patterns (active and latent MTrPs), as several authors have proposed, then anti-inflammatory treatment [26, 48, 69] and muscle strengthening exercises should not be the treatment of first choice. Instead, the treatment should begin with MTrP inactivation. Manual techniques, including manual compression of the MTrP, known as ischemic compression or trigger point release, trigger point dry needling or injection therapy are used to inactivate MTrPs. After MTrP inactivation, muscle stretching and relaxation exercises, heat applications, dynamic exercises to improve range of motion and muscle reconditioning are instructed as appropriate. This therapy is accompanied with a gradual increase in daily activities.

If the above hypothesis is true, treatment of MTrPs could provide an innovative, promising therapy for shoulder pain. This study shows the results of patients' characteristics for a

sample of patients with chronic, unilateral non-traumatic shoulder pain, who were recruited for a randomized clinical trial to study the results of MTrPs directed interventions by physical therapists in this group. The results of this study are accepted for publication (Bron et al. BMC medicine).

General Applicability

We compared sociodemographic data from the current study population with similar data from several other Dutch shoulder pain research studies. Because none of these studies investigated MTrPs, we made this comparison to see whether there was reason to expect that the high prevalence of MTrPs we observed was unique to our population. In our study population more females were included, and the subjects were significantly younger and more highly educated than subjects from the other Dutch populations, although a specific explanation for these differences is lacking. There is no reason to suspect that educational levels correlate with the number of MTrPs and awareness of educational levels is mainly important for effectiveness studies, because they may impact the patients' motivation and compliance [70, 71]. However, increased age may also be associated with increased number of MTrPs [72]. Because the subjects of the present study were younger, and musculoskeletal complaints tend to increase with age [72], there is no reason to suspect that we overestimated the prevalence of MTrPs in our population. On the other hand, there were more females in our study population, and females may be more prone to musculoskeletal disorders in general [73]. Thus, for this reason there may be a chance that MTrPs were slightly more prevalent in our study population [74-76]. Despite the above-mentioned differences, we conclude that our subjects are comparable with other patients with chronic shoulder pain and the findings of this study can be generalized to other patients.

Strength and limitations of the present study

One of the limitations of our study is that we only examined patients with unilateral chronic shoulder pain and dysfunction, whereas MTrPs are thought to be responsible for both acute and chronic pain. It is conceivable that patients who developed chronic shoulder pain may have more MTrPs, and persistent MTrPs in the acute phase than patients who recover easily. In future research projects assessment of MTrPs in patients with acute shoulder problems should also be included. The small sample size is another limitation of this study. Before starting this study a power analysis was performed and it was calculated that 104 subjects would be needed for the clinical trial. After two years (one year more than originally planned, 72 subjects were enrolled in the study. For practical reasons, the study was completed with this smaller sample size, which may have influenced some of the results of this study. We used two observers in this study, with identical clinical experience and post-graduate training on myofascial trigger point therapy. In addition, both observers found a comparable mean number of active MTrPs. Because there was no statistically significant difference in mean DASH scores obtained by the two observers, we consider both groups to be comparable and the findings obtained by both observers to be similar.

Conclusion

This study demonstrates that MTrPs are very prevalent in patients with chronic unilateral, non-traumatic shoulder pain. In addition, the number of MTrPs is moderately correlated with DASH-DLV outcome measures and VAS-P pain measures, indicating that MTrPs contribute to the clinical picture of common shoulder pain problems. We recommend that the MTrP examination and treatment should be considered for patients with shoulder pain in both future clinical studies and clinical practice.

Authors' contributions

All authors have read, edited and approved the final manuscript. CB is the lead investigator, and developed the design of the study, carried out data-acquisition, analysis, interpretations, and prepared the manuscript as primary author. MW and RO provided advice on the study and the manuscript, and supervised the study. JD and BS provided intellectual contributions to the manuscript.

Competing interests
The authors declare that they have no competing interests.

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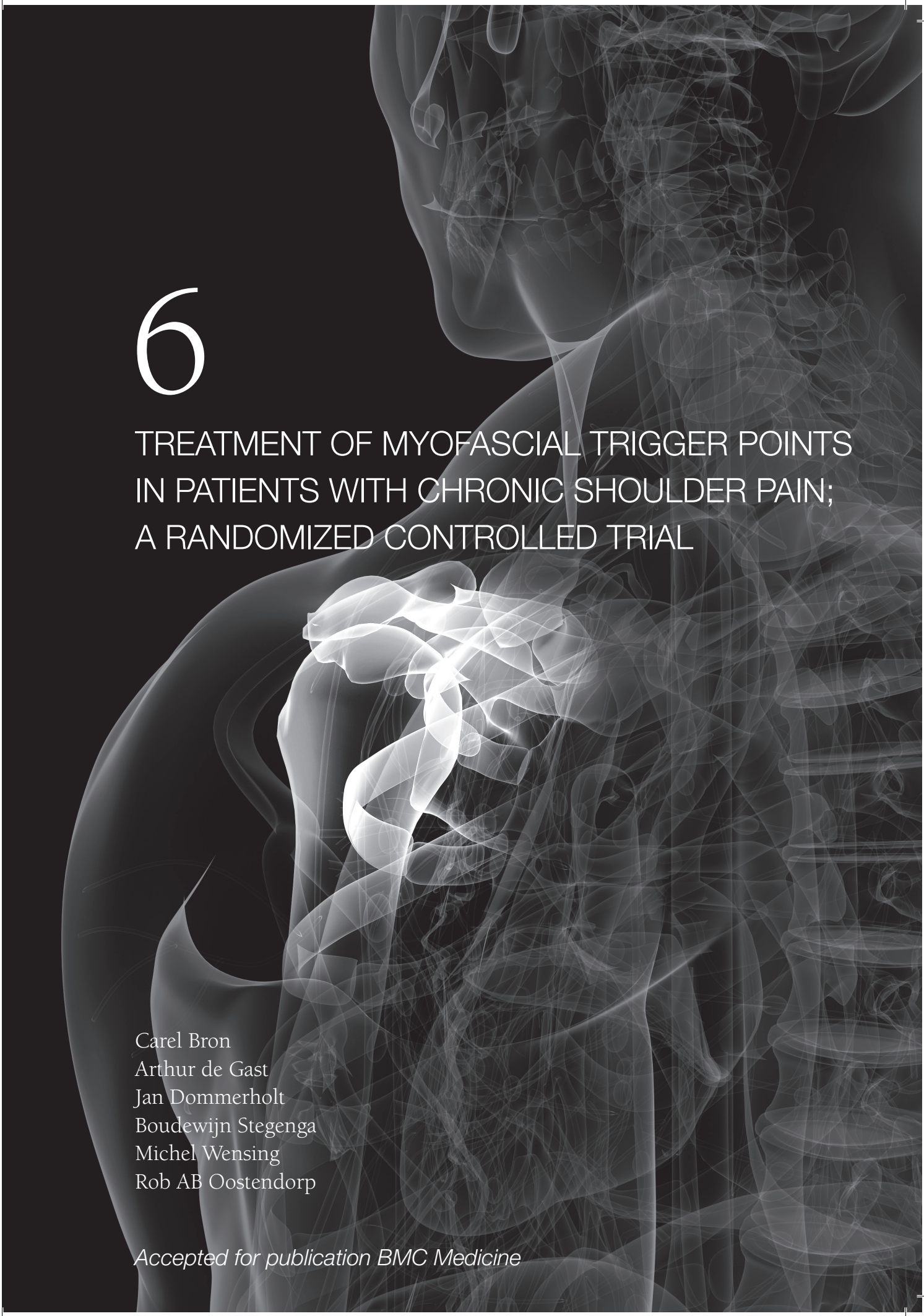

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TREATMENT OF MYOFASCIAL TRIGGER POINTS IN PATIENTS WITH CHRONIC SHOULDER PAIN; A RANDOMIZED CONTROLLED TRIAL

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TREATMENT OF MYOFASCIAL TRIGGER POINTS IN PATIENTS WITH CHRONIC SHOULDER PAIN; A RANDOMIZED CONTROLLED TRIAL

Abstract

Background Shoulder pain is a common musculoskeletal problem that is often chronic or recurrent. Myofascial trigger points (MTrPs) cause shoulder pain and are prevalent in patients with shoulder pain. However, few studies have focused on MTRP therapy. The aim of this study was to assess the effectiveness of multimodal treatment of MTrPs in patients with chronic shoulder pain.

Methods A single assessor blinded randomized controlled trial was conducted. The intervention group received a comprehensive treatment once a week, consisting of manual compression on the MTrPs, manual stretching of the muscles, and intermittent cold application with stretching. Patients were instructed to perform muscle stretching and relaxation exercises at home, received ergonomic recommendations and advises to assume and maintain "good" posture. The control group remained on the waiting list for three months. The Disability of Arm, Shoulder, and Hand outcome measure score (DASH [primary outcome]), Visual Analogue Scale for pain (VAS-P), Global Perceived Effect (GPE), and the number of muscles with MTrPs were assessed at 6 and 12 weeks in the intervention group and compared with a control group.

Results Compared to the control group the intervention group showed significant improvement ($p< 0.05$) after 12 weeks on the DASH (mean difference 7.7; 95% confidence interval [CI]: 1.2 to 14.2), VAS-P for current pain (13.8; 95% CI: 2.6 to 25.0), VAS-P for pain in the last week (10.2; 95% CI: 0.7 to 19.7), and VAS-P most severe pain in the last week (13.8; 95% CI: 0.8 to 28.4). After 12 weeks 55% of the subjects in the intervention group reported to be improved (from slightly improved to completely recovered) versus 14% in the control group. The mean number of muscles with active MTrPs decreased in the intervention group compared to the control group (mean difference 2.7; 95% CI: 1.2 to 4.2).

Conclusions The results of this study show that a 12-week comprehensive treatment of MTrPs in shoulder muscles reduces the number of muscles with active MTrPs and is effective in reducing symptoms and improving shoulder function in patients with chronic shoulder pain.

Trial Registration Current Controlled Trials [ISRCTN75722066].

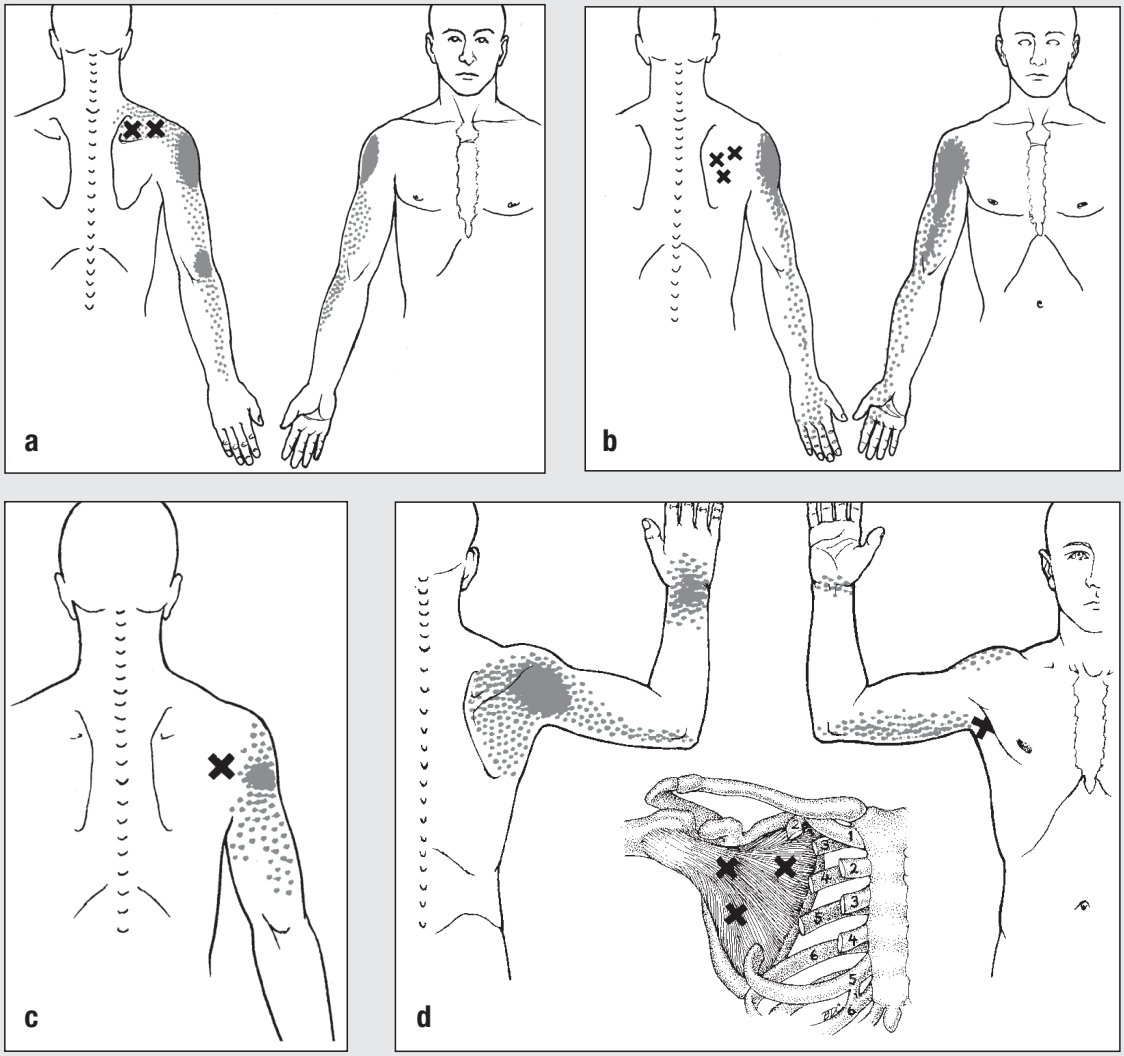
Background

Shoulder pain is a common musculoskeletal problem. In several countries the one-year prevalence is estimated to be 20% to 50% [1, 2]. The annual incidence of shoulder pain and symptoms in Dutch primary care practice ranges from 19 to 29.5 per 1000 [3, 4]. Shoulder pain is the main contributor to non-traumatic upper limb pain, in which chronicity and recurrence of symptoms are common [5, 6]. The most common cause of shoulder pain is considered to be subacromial impingement syndrome (SIS), causing inflammation and degeneration of subacromial bursae and tendons [7, 8]. SIS was first described in 1867 by French anatomist and surgeon Jarjavay and in 1972 re-introduced by Neer [9, 10]. Although the interpretation of the physical signs during shoulder examination is far from reliable, the diagnosis of SIS is based mainly on the clinical picture of pain in the shoulder as described by Neer [11-13]. The clinical picture consists of an arc of pain, crepitus and muscle weakness, and a positive impingement test, which means complete relief of pain with forced forward elevation of the upper arm after injection of a local anesthetic into the subacromial space [13]. Scientific evidence from randomized controlled trials (RCTs), meta-analyses, or systematic reviews of RCTs on the effectiveness of multimodal rehabilitation, injection therapy, medication, surgery, physical therapy, or the application of other therapies in patients with shoulder pain is conflicting or lacking [14-24], which justifies a search for an alternative explanation of shoulder pain, whether or not diagnosed as SIS.

A common cause of muscle pain is myofascial pain caused by myofascial trigger points (MTrPs) [25, 26]. MTrPs in the shoulder muscles produce symptoms similar to other shoulder pain syndromes, including pain at rest and with movement, sleep disturbances, and pain-provocation during impingement tests [27]. Clinical, histological, biochemical, and electro-physiological research have provided biological plausibility for the existence of MTrPs [28-37]. As a result, the role of MTrPs in musculoskeletal pain is increasingly accepted in the medical literature. MTrPs are defined as exquisitely tender spots in discrete taut bands of hardened muscle that produce symptoms, known as myofascial pain.

MTrPs are classified into active and latent trigger points. According to Simons et al. “an active MTrP causes a clinical pain complaint. It is always tender, prevents full lengthening of the muscle, weakens the muscle, refers a patient-recognized pain on compression, mediates a local twitch response of muscle fibers when adequately stimulated, and, when compressed within the patient’s pain tolerance, produces referred motor phenomena and often autonomic phenomena, generally in its pain reference zone, and causes tenderness in the pain reference zone”. A latent MTrP is defined as “ clinically quiescent with respect to spontaneous pain; it is painful only when palpated. A latent MTrP may have all the other clinical characteristics of an active MTrP and always has a taut band that increases muscle tension and restricts range of motion” [27]. Palpation is still considered the only reliable clinical method to diagnose MTrPs. Previous studies have shown that trained physical therapists can reliably detect MTrPs by palpation [38, 39]. Although magnetic resonance

Figure 1: *Referred pain patterns (red) from supraspinatus (a), infraspinatus (b), teres minor (c), and subscapularis (d) muscle MTrPs (Xs), according to Simons et al. Illustrations courtesy of LifeART/MEDICLIP, Manual Medicine 1, Version 1.0a, Lippincott,Williams & Wilkins, 1997*



elastography and ultrasound imaging studies have shown potential to visualize MTrPs, their clinical usefulness has yet to be established [32, 33].

Manual techniques, spray-and-stretch, and trigger point needling can inactivate MTrPs. MTrP inactivation may be combined with ergonomic advice, active exercises, postural correction, and relaxation if and when appropriate [27, 40-46]. Treatment of MTrPs is rarely included in systematic reviews of the effectiveness of conservative interventions in patients with shoulder pain. However, several case studies suggest that the treatment of MTrPs in patients with shoulder pain may be beneficial, although well-designed controlled studies

are still lacking [47-52]. Recently, Hains et al compared ischemic compression of relevant MTrPs (intervention) with ischemic compression of irrelevant MTrPs (sham treatment). The results of this study suggest that ischemic compression on MTrPs in shoulder muscles may reduce the symptoms of patients experiencing chronic shoulder pain [53].

The aim of the current study was to assess the effectiveness of a comprehensive treatment program of MTrPs in shoulder muscles on symptoms and functioning of the shoulder in patients with chronic non-traumatic shoulder pain compared to a wait-and-see approach.

Methods and Subjects

A single-blinded randomized controlled trial (RCT) was conducted, which was approved by the Medical Ethics Committee of the Radboud University Nijmegen Medical Centre, the Netherlands [CMO 2007/022]. This RCT is registered at Current Controlled Trials [ISRCTN75722066] and the study protocol was published [54].

Participants/Study sample

Between September 2007 and December 2009, all consecutive patients with shoulder pain referred to a primary care practice for physical therapy, were potential study participants. The patients were self-referred or referred by general practitioners, orthopedic surgeons, neurologists, or physiatrists. Patients were eligible if they had unilateral non-traumatic shoulder pain for at least six months and were aged between 18 and 65 years old, and whose clinical presentation did not warrant referral for further diagnostic screening. Patients who previously had been diagnosed with shoulder instability, shoulder fractures, systemic diseases, such as rheumatoid arthritis, Reiter's syndrome, or diabetes, or whose medical history or physical examination suggested neurological diseases, or other severe medical or psychiatric disorders were excluded from the study. Patients with signs and symptoms of a primary frozen shoulder were also excluded. Because the questionnaires were in the Dutch language, subjects had to understand written and verbal Dutch. The lead investigator (CB) checked all available information from referral letters and additional information from the patients. All eligible patients were invited to participate in the study. The patients were informed of the study before the first assessment and signed a written informed consent.

Data assessment

Two research assistants (MO and MB, see acknowledgements), each with 30 years of clinical experience in primary care practice and more than 5 years experience in identifying and treating MTrPs, performed the physical examination, including the assessment of passive range of motion (PROM) of the shoulder and the MTrPs palpation of the shoulder muscles. The total number of shoulder muscles with active and latent MTrPs was counted. The research assistants were blinded to the treatment allocation during the entire study period. The assessments were at intake, prior to the randomization, and at 6 and 12 weeks. For

every single patient only one observer was active. A detailed medical history was completed, which included demographic variables and potential prognostic factors [55, 56], and a set of self-administered questionnaires for outcome measurements, including the Disabilities of Arm, Shoulder and Hand questionnaire (DASH), Visual Analogue scales for Pain (VAS-P), RAND-36, and the Beck depression Inventory-II (BDI-II). A third research assistant (IS, see acknowledgements) transferred the collected data to a worksheet. After transferring the data from the worksheet into a statistical software package the lead investigator (CB), who was blinded to the treatment allocation until all statistical tests were performed, analyzed the data. Blinding of the patients or the treating physical therapists was impossible due to the treatment characteristics.

Sample size

The planned sample size was based on an assumed mean improvement of the primary outcome, DASH questionnaire score of 15 points (SD 22), which implies an effect size of 0.68 [57]. To test the null hypothesis at α = .05 with 90% power and assuming a uniform dropout rate of 5%, it was calculated that 52 patients in each group would be required.

Randomization

After collection of patient's data at baseline, the included patients were randomly assigned to either the intervention group or the "wait and see" group. A research assistant (IS) performed the randomization by generating random numbers using computer software (Research Randomizer on www.socialpsychology.org). These numbers were stored on a computer and were only accessible to the assistant. No stratification or blocking strategies were used.

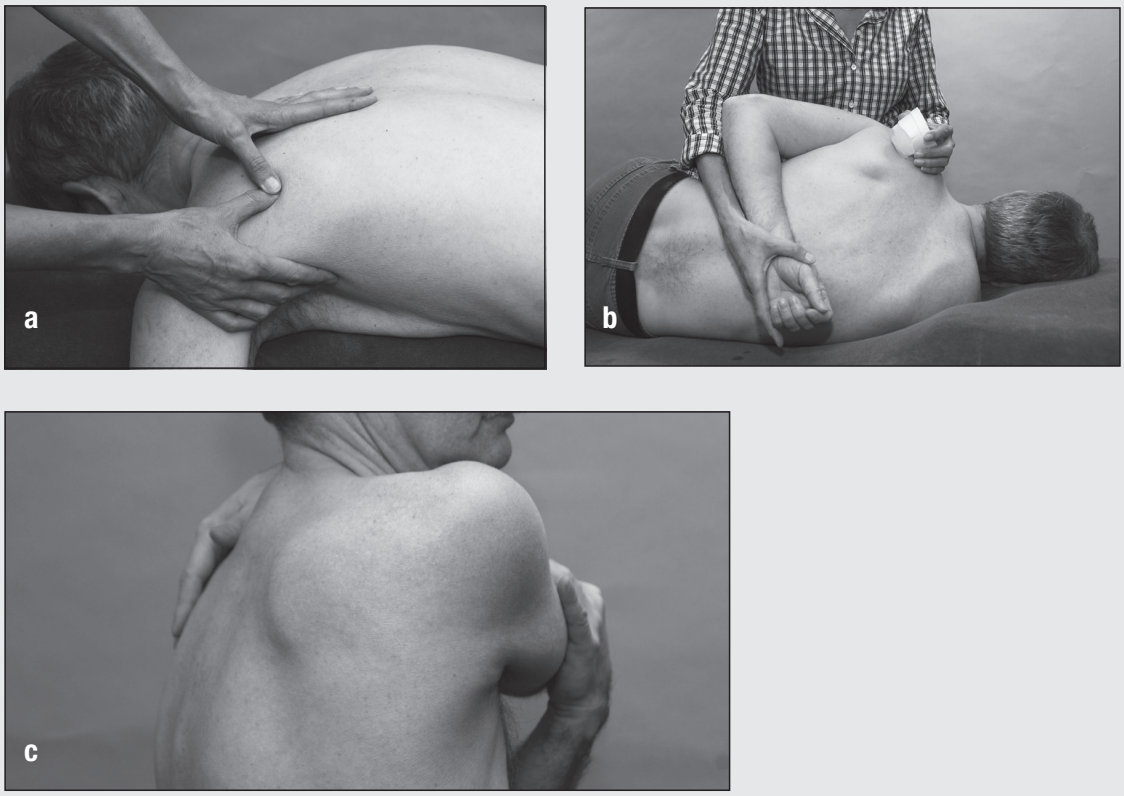
Interventions

The patients in the intervention group were treated by a physical therapist once a week for a maximum period of 12 weeks. Five physical therapists were involved in the treatment of the patients. All participating physical therapists were experienced in treating patients with persistent shoulder pain and MTrPs. They were trained and skilled in the identification and treatment of MTrPs and had successfully completed a certification-training program in trigger point therapy.

The treatment started with inactivation of active, pain-producing MTrPs by manual compression. The physical therapist applied gentle, gradually increasing pressure on the MTrP until the finger encountered a definite increase in tissue resistance. At that point the patient commonly would feel a certain degree of discomfort or pain. The pressure was maintained until the therapist sensed relief of tension under the palpating finger or the patient experienced a considerable decline of pain. At that point the therapist could repeat this procedure several times until pressure on the MTrP would only provoke little discomfort without pain. This technique was combined with other manual techniques, such as deep stroking (pressure directed along the length of the taut band) or strumming (pressure

perpendicularly across the muscle fibers). Both techniques can manually stretch the trigger point area and the taut band. These manual techniques could be preceded or followed by "intermittent cold application by using ice-cubes followed by stretching the muscle" according to Simons et al [27]. The effectiveness of muscle stretching exercises was enhanced by including short isometric contractions and relaxation (hold-relax). Patients were instructed to perform at home simple gentle static stretching and relaxation exercises several times during the day. When appropriate, the relaxation exercises were augmented by using a portable myofeedback device (Myotrac I, Thought Technology, Quebec, Canada). Furthermore patients were instructed to apply heat, such as a hot shower or hot packs, for muscle relaxation and pain relieve at least twice every day. All patients received ergonomic advice and instructions to assume and maintain "good" posture [58, 59]. The content and aim of each session varied based on the specific findings from the initial evaluations and patients' responses to previous treatment sessions. All individual treatments however, were consistent with the limits of the treatment protocol [54].

Figure 2: *Manual compression on the MTrP in the infraspinatus muscle of the left shoulder (a), stroking with ice (in a polystyrene cup) in unidirectional parallel strokes combined with gentle muscle stretching applied for the infraspinatus muscle of the left shoulder in side lying (b), and cross-body muscle stretching exercise for posterior shoulder muscles, including the infraspinatus muscle (c).*



Stop rule
Treatments were discontinued when patients were completely free of symptoms or when a patient and physical therapist agreed that treatment would not further benefit the patient. Participation in the study continued, unless patients decided to stop participation in the study. Subjects were free to withdraw from the study at any time without consequences for their treatment.

Treatment integrity
To enhance the integrity of the interventions, all participating physical therapists were allowed to discuss the content of each therapy session with the lead investigator (CB) without releasing names or any other information that could jeopardize the blinding of the lead investigator. After 6 and 12 weeks, the lead investigator interviewed the patients of the intervention group to assure that the received treatments had been consistent with the study protocol.

Wait and See
Patients in the control group remained on a waiting list and were informed that they would receive the same physical therapy treatment after 3 months had passed. They were instructed not to change their self-management of their shoulder pain. If they were using either prescribed or over-the-counter medication they were encouraged to continue the medication at the patient's discretion, because of their participation in the study. In addition, they were requested to report any other intervention or other relevant change during the study period. Every six weeks they visited the physical therapy practice and provided research data similar to the patients from the intervention group. After 12 weeks they started the physical therapy treatment.

Outcome measures

Primary Outcome Measure
The DASH is an internationally widely used multidimensional 30-item self-report measure focusing on physical function, pain, emotional, and social parameters [60]. The score ranges from 0 to 100 whereby a higher score indicates greater disability. The Minimal Clinically Important Difference (MCID) is approximately a 10-point difference between pre- and post treatment [57, 61, 62]. The DASH is a reliable and valid questionnaire and considered to be one of the best questionnaires for patients with shoulder symptoms [61, 63.]

Secondary Outcome Measures
The Visual Analogue Scale for Pain (VAS-P) is a self-report scale consisting of a horizontal line, 100 mm in length, anchored by the words "no pain" at left side (score 0) and "worst pain imaginable" at the right side (score 100) [64-66]. The VAS-P was used to measure pain at

the current moment (VAS-P1), the average pain during the last seven days (VAS-P2), and the most severe pain during the last seven days (VAS-P3). A 14 mm change is considered to be a MCID in patients with rotator cuff disease [67-70].

To assess Global Perceived Effect (GPE) the subjects rated the effect of treatment on an ordinal 8-point scale with categories ranging from "1 = much worse" to "8 = completely recovered". GPE was then dichotomized into the number of improved (from slightly improved to completely recovered) versus not improved (from unchanged to much worse) patients. GPE has good test-retest reliability and correlated well with changes in pain and disability [71].

Passive range of motion (PROM) of the shoulder was measured by a handheld digital inclinometer (The Saunders group Inc, Chaska, MN) and recorded in degrees. Forward elevation of the shoulder, external rotation, and cross-body adduction were measured in the supine position, internal rotation in prone position, and glenohumeral abduction in the upright position. The range of motion of the non-painful shoulder was used as a reference. A detailed description of the goniometric measurement of the PROM is published in the design of the study [54].

Table 1. List of muscles examined for MTrPs

upper trapezius muscle	middle trapezius muscle	lower trapezius muscle
infraspinatus muscle	supraspinatus muscle	subscapularis muscle
teres minor muscle	teres major muscle	anterior deltoid muscle
middle deltoid muscle	posterior deltoid muscle	pectoralis major muscle
pectoralis minor muscle	biceps brachii muscle	triceps brachii muscle
scalene muscles	subclavius muscle	

The total number of shoulder muscles with MTrPs was counted using the same methods as at baseline and then compared to the baseline measurements. While the patient was in supine or in prone position, depending on the muscle that was examined, seventeen muscles were palpated bilaterally for the presence of a taut band, spot tenderness, the presence of a nodule, local twitch response, and local and referred pain *(table 1)*. When the patient recognized the pain from compression on the tender spot, the MTrPs were considered to be active. When the pain was only local and not familiar, MTrPs were considered to be latent [27, 38, 54].

At 6 and 12 weeks, participants were asked to complete a self-assessment form, which included questions regarding whether they had changed their self-management, or had received any medical treatment that could have influenced their shoulder pain.

Table 2. Characteristics of participants at baseline.

	Intervention (n=34)	Control (n=31)
Age (years; mean; SD; 95% CI)	42.8 (11.7; 38.7-46.9)	45.0 (13.2; 40.2-49.9)
Female (n; %)	21 (62)	23 (74)
Level of education* (n; %)		
Low	2 (6)	2 (7)
Intermediate	13 (38)	17 (55)
High	19 (56)	12 (38)
Right-handed (n; %)	33 (97)	29 (94)
Pain dominant side (n; %)	24 (70)	19 (61)
Duration of complaints (n; %)		
6-9 months	10 (29)	5 (16)
9-12 months	4 (12)	8 (26)
1-2 years	8 (23)	6 (19)
2-5 years	6 (18)	5 (16)
>5 years	6 (18)	7 (23)
Episode (n; %)		
first	13 (38)	11 (35)
second	8 (24)	8 (26)
third or more	13 (38)	12 (39)
DASH-DLV (mean; SD; 95% CI)†	30.3 (16.6; 24.5–36.1)	30.8 (11.9; 26.5–35.2)
VAS-P1 (mean; SD; 95% CI)§	31.9 (24.3; 21.9–41.9)	35.2 (25.7; 25.7–43.0)
VAS-P2 (mean; SD; 95% CI)§	41.3 (19.7; 33.2–49.4)	43.4 (17.0; 37.2–50.0)
VAS-P3 (mean; SD; 95% CI)§	54.9 (21.9; 45.8–63.9)	59.5 (18.2; 52.8–66.2)
BDI-II-DLV (mean; SD: 95% CI)¶	6.3 (4.0; 4.9–7.8)	5.8 (8.2; 2.8–8.8)
RAND-36-DLV (mean; SD; 95% CI)**		
social functioning	78.7 (20.3; 71.6 – 85.8)	81.1 (18.5; 74.3 – 87.8)
limitations due to physical problems	47.7 (43.0; 32.5 – 63.0)	49.5 (37.2; 35.8 – 63.1)
vitality	59.3 (17.0; 53.3 – 65.1)	62.6 (17.9; 56.0 – 69.1)
bodily pain	51.6 (16.0; 45.7 – 57.6)	52.7 (12.3; 48.2 – 57.2)
general health perception	52.9 (8.5; 50.0 – 55.9)	56.6 (7.0; 54.1 – 59.2)
PROM (mean; SD;95% CI)‡	28.4 (34.8; 16.1 – 40.7)	39.0 (34.9; 26.2 - 51.8)
Muscles with MTrPs (mean; 95% CI)‡‡		
active MTrPs	7.4 (3.6; 6.1 - 8.7)	6.1 (3.5; 4.8 – 7.4)
latent MTrPs	4.2 (2.7; 3.2 – 5.1)	5.9 (3.0; 4.8 – 7.0)

* *High education (university and higher vocational school), medium education (middle vocational school and higher or middle general secondary school), and low education (lower vocational school, lower general secondary school, primary school, or no education).*

† *Higher Dash-DLV (Disabilities of the Arm, Shoulder and Hand outcome measure- Dutch Language Version) scores indicate more disability with a maximum of 100 (range 0 to 100).*

§ *Higher scores on the VAS-P (Visual Analogue Scales for Pain) indicate more pain with a maximum of 100 (range 0 to 100). VAS-P1: current pain score, VAS-P2: average pain score of the past seven days, and VAS-P3: most severe pain score of the past seven days.*

¶ *Higher scores on the BDI-II-DLV (Beck Depression Inventory-second edition- Dutch Language Version) indicate more symptoms of depression (range 0-63).*

** *Only the subscales of the nine subscales of the RAND-36 that differ significantly from a normal Dutch population are presented here [89]. Higher scores indicate a better quality of life (range 0-100).*

‡ *A positive number (degrees) of the mean score of PROM (Passive Range Of Motion) indicates impairment of the PROM of the affected shoulder.*

‡‡ *Number of Muscles with active, resp. latent MTrPs (range 0-17 muscles)*

Statistical Analysis

Analyses were performed according to the intention-to-treat principle. Both groups were compared for baseline characteristics using t-test and Chi-square for binominal variables. For the DASH, VAS-P, and the number of muscles with MTrPs the t-test for normally distributed data was used to assess the difference between the two groups at week 6 and week 12. We considered a mean difference of more than 10 points on the DASH as clinically important (MCID). Effect sizes Cohen's d were calculated to examine the average impact of the intervention [72]. According to Cohen, $d \approx 0.2$ indicates small effect, negligible clinical importance, $d \approx 0.5$ indicates medium effect, moderate clinical importance, and $d \approx 0.8$ indicates a large effect, crucial clinical importance [73]. To compare patients who improved more than 10 points on the DASH with patients who improved less than 10 points we calculated relative risk (RR) and their 95% confidence intervals (95% CI). To examine the impact on individual patients in more detail, we dichotomized participants' measures of GPE into improved versus not improved. The proportions of patients who had clinically improved between groups were compared by calculating RR and the 95% CI at 6 weeks and 12 weeks. Pearson correlation coefficients were used to relate the variables of the number of muscles with active MTrPs and the DASH score.

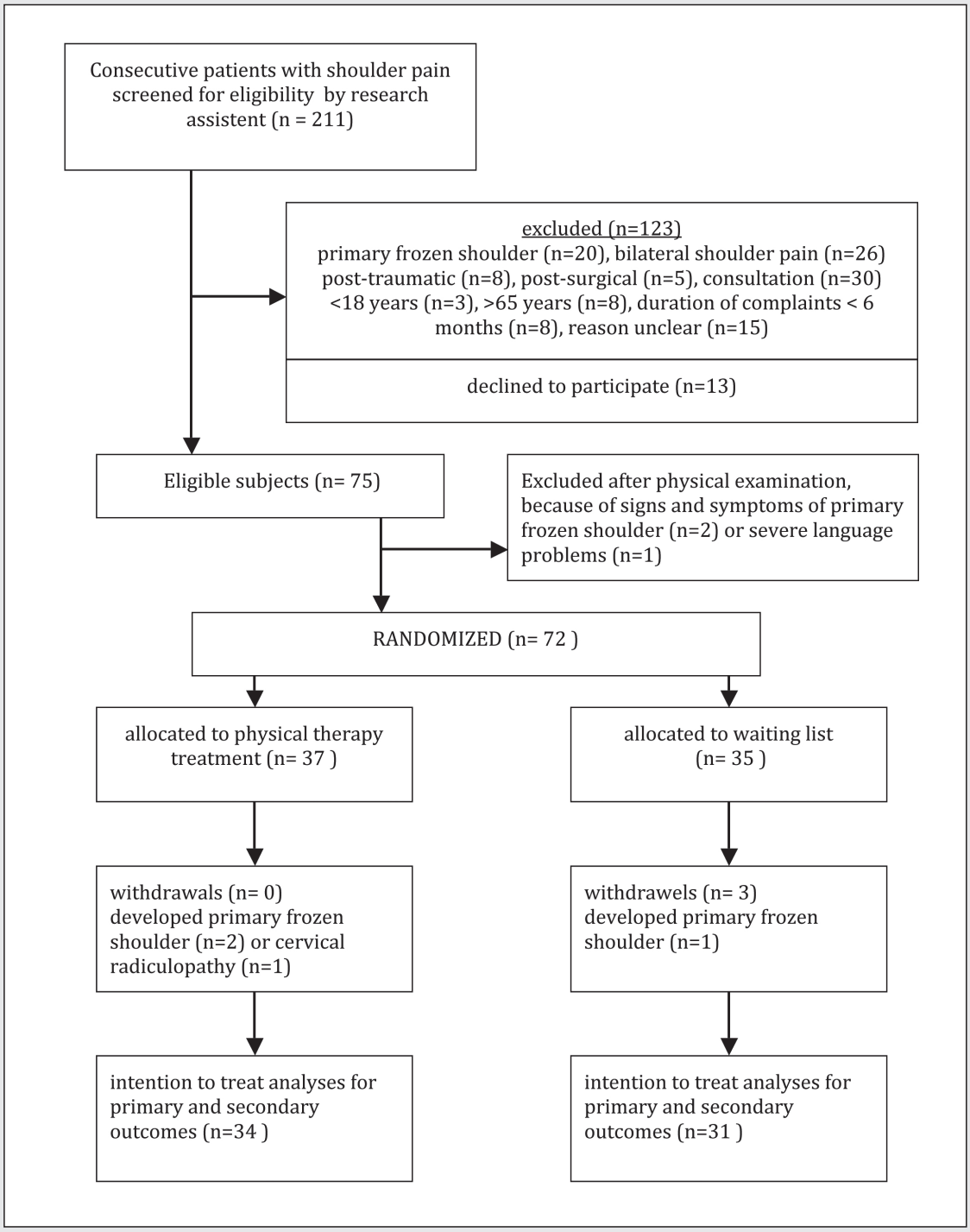
In addition, the effect of the intervention was evaluated in a regression analysis. The DASH score at 12 weeks was the dependent variable; the group variable, the DASH score at baseline, the number of muscles with active MTrPs at intake, the number of muscles with latent MTrPs at intake, and PROM included as covariates in this multiple linear regression model.

To evaluate the successfulness of the blinding procedure, both observers were asked to identify the treatment allocation. A goodness-of-fit $\chi 2$ test was used to determine that the number of correctly and incorrectly identified cases fitted a probability of 50%. For all comparisons, $p < 0.05$ was considered statistically significant (two-tailed). If the 95% confidence interval (95% CI) of the difference does not include the value 0, the difference is statistically significant (at $\alpha = 0.05$). Systat 12, Sigmaplot 11, and Sigmastat 3.11 (Systat Inc. Richmond, California, USA) for Windows were used for the statistical analysis.

Results

Between September 2007 and September 2009, 72 patients were randomly assigned to either the intervention group or the control group. See *figure 3* for the schematic summary of the patient participation and *table 2* for the patients' characteristics at baseline. At baseline, both groups were comparable for all variables with no statistical or clinical relevant differences, except for the number of muscles with latent MTrPs and the level of education.

Figure 3: Flow diagram showing the schematic summary of the patient participation.



Primary outcome

DASH

The difference between the intervention group and the control group was not significant after 6 weeks (4.1; 95% CI -2.8 to 11.1), and significant after 12 weeks (7.7; 95% CI: 1.2 to 14.2). The graphical presentation of the mean DASH scores at intake, after 6 and 12 weeks is shown in *figure 4*.

Seventeen subjects (50%) in the intervention group and seven (22%) in the control group improved more than 10 points (MCID) on the DASH outcome measurement (relative risk 2.3; 95% CI 1.1 to 4.7) *(figure 4)*. The effect size (Cohen's d) was 0.60 *(table 3)*.

The multiple linear regression analysis with the baseline score as a covariate demonstrated a significantly higher DASH score at 12 weeks of 7.447 (95% CI: 2.14 to 12.75) in the intervention group compared with the control group. Adjustment for the covariates had no influence on this result.

Secondary outcomes

VAS-P1, VAS-P2, and VAS-P3

The intervention group showed on average significantly lower scores on all VAS-P scales compared to the control group after 12 weeks (VAS-P1; 13.8; 95% CI: 2.6 to 25.0), VAS-P2; 10.2; 95% CI: 0.7 to 19.7), and VAS-P3; 13.8; 95% CI: 0.8 to 28.4). The differences after 6 weeks were not significant, except for VAS-P3 (15.6; 95% CI: 2.3 to 28.8). The difference between baseline and after 12 weeks in the intervention group reached the MCID for all three VAS-P scales, while changes in the control group did not reach the MCID. The effect sizes on the three VAS-P scales varied from 0.5 to 0.7 *(table 3)*.

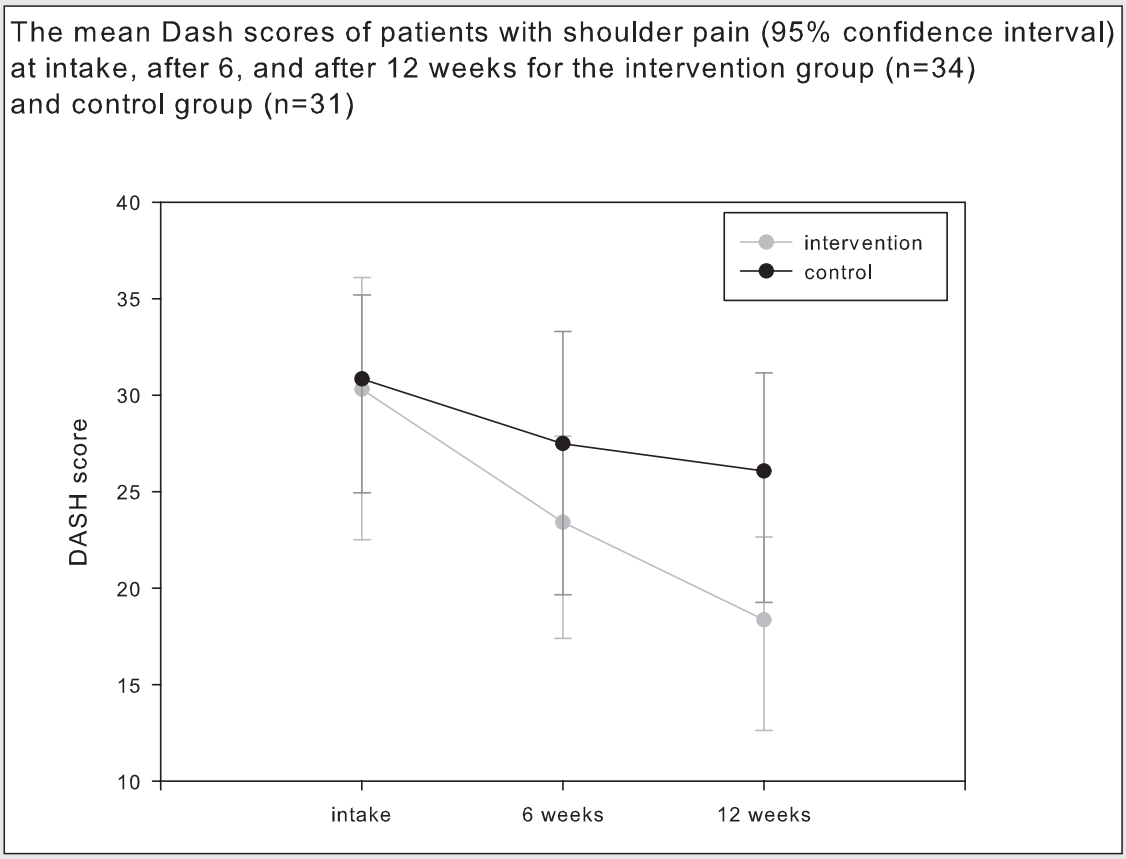
GPE

After 6 weeks, improvement was reported by 49% (16/33) of the patients in the intervention group versus 17% (5/30) patients in the control group (relative risk 2.9; 95% CI: 1.2 to 7.0). After 12 weeks, 55% (18/33) of the patients in the intervention group reported to be improved versus 14% (4/28) of the patients in the control group (relative risk 3.8; 95% CI: 1.46 to10.0) *(table 3)*.

Number of muscles with trigger points

The number of muscles with active MTrPs was significantly lower in the intervention group compared to the control group after 12 weeks (mean difference 2.7; 95% CI: 1.2 to 4.2). The change in the number of muscles with latent MTrPs was non-significant versus control group (mean difference 0.4; 95% CI: -0.7 to 1.5) *(table 3)*. Effect size (Cohen's d) for active MTrPs after 12 weeks was 0.89, a large effect and for latent MTrPs 0.13.

Figure 4: *The mean DASH scores (error bars present 95% confidence interval) at intake, after 6, and after 12 weeks for the intervention group (n=34) and control group (n=31).*



Correlation between the number of muscles with active MTrPs and the DASH outcome at 12 weeks
The number of shoulder muscles with active MTrPs was positively correlated with the DASH outcome at 12 weeks (r = 0.49; regression coefficient = 2.13; p = 0.000; ANOVA F = 9.6; p = 0.000), when corrected for muscles with active MTrPs at intake). This implies that the number of muscles with active MTrPs was associated with 24% of the variation in DASH outcome. Two cases were identified as significant outliers during the multiple linear regression analysis (both in the intervention group) and were removed before further analysis.

PROM
The PROM difference between the groups did not change significantly during the measurements at 6 weeks (mean difference 8.8; t= 1.14; p > .05) and 12 weeks (mean difference 8.2; t= 1.19; p >.05).

Table 3. Primary and secondary outcomes in intervention group and control group after 6 and 12 weeks

outcome	intervention (n=34)	control (n=31)	mean difference (95% CI)	p-value	Effect Size (Cohen's d)
DASH (mean; SD)†					
baseline	30.3 (16.6)	30.8 (11.9)	0.5 (-6.7 to 7.7)	NS	
after 6 weeks	23.4 (12.6)	27.5 (15.5)	4.1 (-2.8 to 11.1)	NS	
after 12 weeks	18.4 (12.3)	26.1 (13.8)	7.7 (1.2 to 14.2)	<.05	0.60
VAS-P1 (mean; SD)§					
baseline	31.9 (24.3)	35.2 (25.7)	3.3 (-9.1 to 15.7)	NS	
after 6 weeks	29.0 (18.4)	37.8 (17.9)	8.8 (-0.2 to 17.8)	NS	
after 12 weeks	17.2 (19.5)	31.0 (21.0)	13.8 (2.6 to 25.0)	<.05	0.69
VAS-P2 (mean; SD)§					
baseline	41.3 (19.7)	43.4 (17.0)	2.0 (-7.1 to 11.1)	NS	
after 6 weeks	32.9 (19.3)	40.0 (20.7)	6.7 (-3.6 to 17.0)	NS	
after 12 weeks	22.5 (16.4)	33.2 (23.3)	10.2 (0.7 to 19.7)	<.05	0.54
VAS-P3 (mean; SD)§					
baseline	54.9 (21.9)	59.5 (18.2)	4.6 (-14.6 to 5.4)	NS	
after 6 weeks	41.0 (25.1)	56.6 (28.3)	15.6 (2.3 to 28.8)	<.05	
after 12 weeks	34.0 (21.9)	47.8 (27.3)	13.8 (0.8 to 28.4)	<.05	0.57
GPE (proportion; %)*				**RR (95% CI)**	
Improved					
after 6 weeks	16/33 (49%)	5/30 (17%)		< .05	2.9 (1.2-7.0)
after 12 weeks	18/33 (55%)	4/28 (14%)		< .05	3.8 (1.5-10.0)
Number of muscles with active trigger points (mean; SD)					
baseline	7.4 (3.7))	6.1 (3.5)	1.3 (-0.5 – 3.1)	NS	
after 6 weeks	6.2 (3.5)	6.8 (3.6)	0.6 (-1.2 – 2.4)	NS	
after 12 weeks	4.8 (3.0))	7.5 (3.2)	2.7 (1.2 – 4.2)	< .05	0.89
Number of muscles with latent trigger points (mean; SD)					
baseline	4.2 (2.7)	5.9 (3.0)	1.7 (-0.3 – 3.1)	< .05	
after 6 weeks	3.8 (2.1)	4.8 (2.8)	1.0 (-2.3 - 0.2)	NS	
after 12 weeks	4.7 (2.3)	4.4 (2.3)	0.4 (-0.7 – 1.5)	NS	0.13

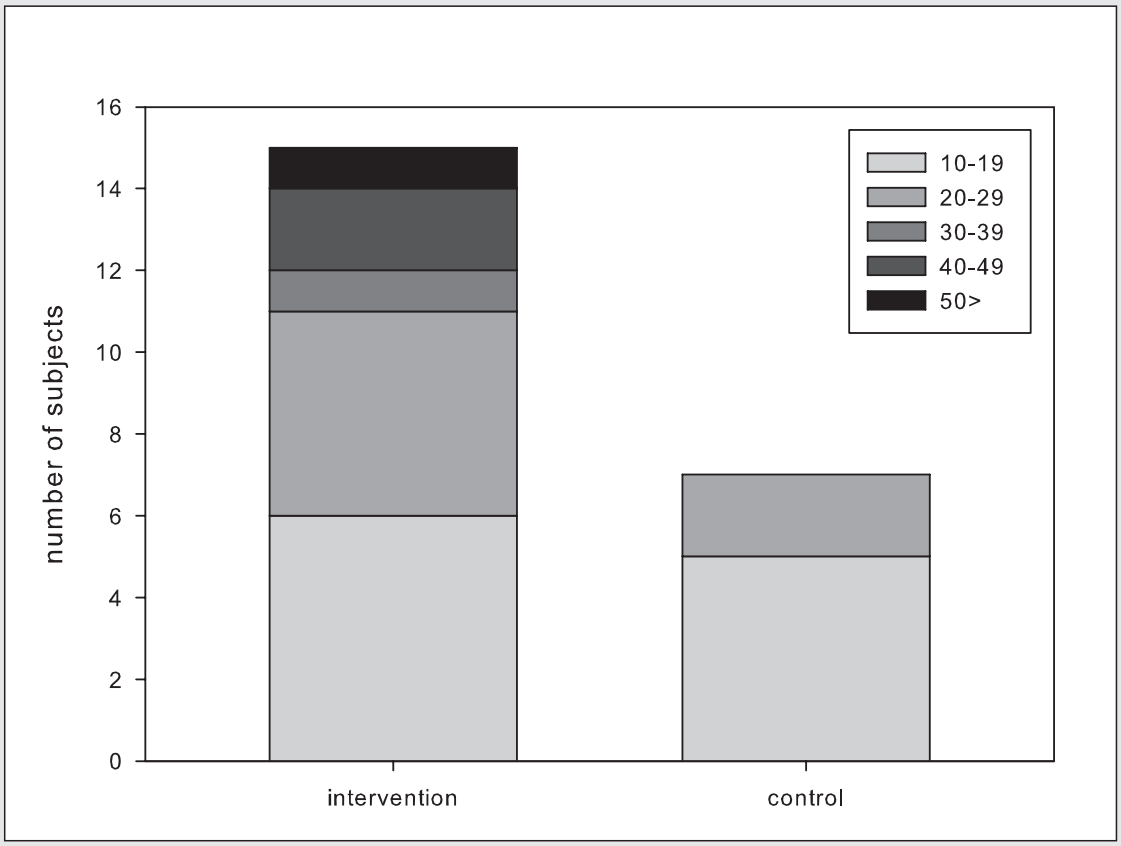
ES = effect size. NS = not significant.

† *Higher Dash-DLV (Disabilities of the Arm, Shoulder and Hand outcome measure- Dutch Language Version) scores, more disability with a maximum of 100 (range from 0 to 100).*

§ *Higher scores on the VAS-P (Visual Analogue Scales for Pain) indicate more pain with a maximum of 100 (range from 0 to 100). VAS-P1 represents the current pain score, VAS-P2 represents the average pain score of the past seven days, and VAS-P3 the most severe pain score of the past seven days.*

* *GPE; Global Perceived Effect*

Figure 5: *Number of subjects that improved more than 10 points (minimal clinically important difference) on the DASH outcome measure after 12 weeks for the intervention (n=34) and control group (n=31).*



Evaluation of Blinding

After 6 weeks, the observers identified the treatment allocation correctly in 62% ($\chi 2$ =4.70, p = 0.03) and after 12 weeks in 71% ($\chi 2$ =13.86, p = 0.00) of the patients after completing the physical examination and MTrP count.

Co-interventions

We checked whether the participants in either group had received other interventions other than those described in the treatment protocol. During the first 6 weeks of the study, one subject in each group received an injection administered by a general practitioner. After 6 weeks no co-interventions were reported in either group.

Discussion

Summary of main findings

This single blinded randomized controlled trial evaluated the effectiveness of a 12-week comprehensive MTrP physical therapy treatment program in patients with chronic non-traumatic unilateral shoulder pain when compared to a wait-and-see strategy. After 12 weeks the intervention group showed statistically as well as clinically significant differences compared to the control group on the primary and secondary outcome measures. The effect sizes were considered to be medium and consistent with the hypothesized effect size. The number of shoulder muscles with active MTrPs was significantly lower in the intervention group than in the control group), supporting the assumed biomedical mechanism underlying MTrP therapy.

Explaining the results/ comparing with other studies

To our knowledge, this is the first study of the effectiveness of a comprehensive MTrP therapy program in patients with shoulder pain. The difference of the DASH scores between groups was smaller than the MCID. However, the mean of the baseline DASH score was smaller than was expected based on results from other studies [57, 74, 75]. With a smaller mean value, it is less likely to get great differences between baseline and follow up at 12 weeks. However, the effect size was 0.6, which is considered to be a medium effect that is clinically relevant. When considering the number of subjects improving more than 10 points, there is a clinically relevant result. Furthermore, many more subjects in the intervention group reported improvement (GPE) than in the control group.

Previous trials have investigated various types of physical, manual or exercise therapy. The treatments in these studies included interventions showing similarities to components of the treatment program of this study, but were not specifically aimed at treating MTrPs. For example, exercise therapy or manual therapy interventions included soft tissue massage and muscle stretching exercises, which generally are performed for anterior and posterior muscle tightness [76-79]. These interventions may have an unintentional effect on MTrPs in shoulder muscles, as MTrPs seem to be prevalent in patients with shoulder pain, which may have contributed to the results of other studies [25, 26]. However, as these studies did not focus on MTrPs, there is no direct evidence that these interventions did have or did not have effect on MTrPs.

Recently, Hains published the first report on the effectiveness of ischemic compression therapy of MTrPs in shoulder muscles in chronic shoulder conditions compared to sham compression. The intervention group received 15 sessions (comprising of 15 second compression of MTrPs in up to four muscles, including the supraspinatus, infraspinatus, deltoid, and biceps muscles) three times a week without taking any other therapeutic measures. The control group received sham therapy (15 seconds compression of MTrPs in shoulder muscles, considered irrelevant for the shoulder pain). The intervention group

showed a significant improvement on the Shoulder Pain and Dysfunction Index (SPADI) when compared to the sham group [53]. The authors did not report any change in the number of MTrPs in the shoulder muscles or in the number of shoulder muscle with MTrPs. The current study showed that a decrease of the numbers of shoulder muscles with active MTrPs is correlated with better outcome. While the number of muscles with active MTrPs decreased in the intervention group, the number of muscles with latent MTrPs tended to increase slightly. One explanation can be that the state of MTrPs is more or less dynamic and changes from active to latent and vice versa occur, depending on the degree of irritability [80].

One of the clinical features of active MTrPs is spontaneous pain, in rest or during activity, which is felt at a distant from the MTrP side and, by definition, has to be recognized by the patients as their familiar pain. According to Mense, "the current concept of the referral of muscle pain is based on the observation that the efficacy of synaptic connections of central dorsal horn neurons can change, particularly under the influence of a nociceptive input. The important point is that ineffective synaptic connections can become effective under pathological circumstances. This means that a neuron can acquire new receptive fields in the presence of nociceptive input" [81]. This process is called central sensitization. By expanding receptive fields, non-nociceptive input, originating from a location other than the originally painful location, may be perceived as painful. In patients with shoulder pain, MTrPs in, for example, the infraspinatus, supraspinatus, teres minor, or subscapularis muscle may cause local and referred pain, which can be felt deep in the shoulder. In other words, MTrPs may mimic pain interpreted as pain arising from subacromial bursitis, tendonitis or tendonopathy, which may explain why often treatment of inflammation is so ineffective.

Furthermore, MTrPs can cause particular motor effects as well. MTrPs can lead to muscle weakness of the involved painful muscle and reorganization of motor activation patterns. Restricted range of motion may be observed secondary to a contracted taut band [80, 82, 83]. A changed motor activation pattern is often reported in the shoulder pain literature [84]. Since MTrPs can alter such patterns, MTrP inactivation should be considered prior to any form of muscle strengthening exercises. When muscle weakness persists, it may alter a patient's shoulder kinematics and eventually causes humeral head migration, rotator cuff degeneration and formation of bony spurs in the subacromial space. Early recognition and treatment of MTrPs may prevent patients from developing chronic shoulder pain and early degeneration.

As we did not examine the effects of single components of the intervention we cannot conclude whether a single component or a combination of components attributed more to the treatment effect than others. Others have examined the effect of single ischemic compression or a combination of ischemic compression and stretching and concluded that both interventions had positive effects on the recovery [45]. The management of MTrPs is not restricted to MTrP inactivation, but needs correction of perpetuating factors, that are clinically apparent, but not yet necessarily scientifically established [27, 42, 85]. Further research is needed to clarify the importance of perpetuating factors in shoulder patients, such as mechanical factors [86].

Limitations of the study

The power analysis indicated that 104 subjects were needed for this clinical trial. Partly because of an overestimation of the number of eligible subjects and partly because of the unwillingness of patients to enter the trial, the study was completed with a smaller sample size. This study took two years to complete, which is one more year than originally was planned. However, the results were significant and clinically relevant, although the study population was smaller than the initially calculated sample size. A greater sample size is unlikely to have altered the direction of the results.

In the intervention group the participants had a higher level of education than in the control group. Awareness of educational levels is important, as it may impact the patients' motivation and compliance [87, 88], but adding the level of education as covariate in a multiple linear regression analysis did not alter the results.

Evaluation of the blinding of the independent observers, who performed the physical examination and counting of MTrPs, revealed that after 12 weeks the observers were able to identify to which group a patient belonged. It is likely that the changes in physical findings and decrease in the number of MTrPs improved the observers' accuracy of group identification. Since the blinding only influenced the observer, who performed the MTrP identification, this finding had no effect on the reliability of the other outcomes scores.

The subjects in the control group were instructed to maintain their self-management of their shoulder pain and to report any management deviation. While this may pose a potential threat for the comparability of the groups, no significant changes were reported. As all patients were suffering from chronic shoulder pain and likely had explored various self-management strategies before entering into the study, we did not anticipate that they would change their self-management strategy during the study period.

Although the observers did not intend to give some "good" advise during the physical examination, they may have unintentionally instructed the subjects to avoid provocative activities. When the subjects in the control group followed the instructions and acted more carefully during daily live, their symptoms may have reduced, while they were still suffering from MTrPs. This may explain the improvement in the control group.

Implications for research and clinical practice

This study showed that patients with chronic unilateral non-traumatic shoulder pain had better outcome after a treatment for MTrPs than those without treatment and this outcome was correlated with a decrease of the number of muscles with active MTrPs.

Treatment of MTrPs can be considered as a promising approach for the treatment of patients with shoulder pain. Future clinical trials should be directed to establishing the effectiveness of MTrP treatment in patients with varying underlying pathology of the shoulder and in a wider context than a specialized physical therapy practice. It would be worthwhile to identify predictors for successful MTrP treatment, and to investigate whether MTrPs treatment is more successful when combined with supportive interventions, such as

exercises and manual therapy. Observational follow-up studies are needed to investigate the long-term effects of treatment of MTrPs in patients with chronic shoulder pain.

Given the high number of patients with shoulder pain, this will require a substantial effort and financial investment. Studies on the cost-effectiveness of treatment of patients with MTrPs in the shoulder muscles are therefore needed.

Conclusions

Participants in the intervention group had better outcome on all outcome measures after 12 weeks of comprehensive MTrP treatment program than those on the waiting list. Clinically relevant improvements were achieved in 55% of the patients with shoulder pain and the number of muscles with active MTrPs was significantly decreased.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

All authors have read, edited and approved the final manuscript. CB is the lead investigator, and developed the design of the study, carried out data-acquisition, analysis, interpretations, and prepared as primary author the manuscript. MW and RO supervised the study and helped to prepare the manuscript. JD, BS, and AdG provided intellectual contributions to the manuscript.

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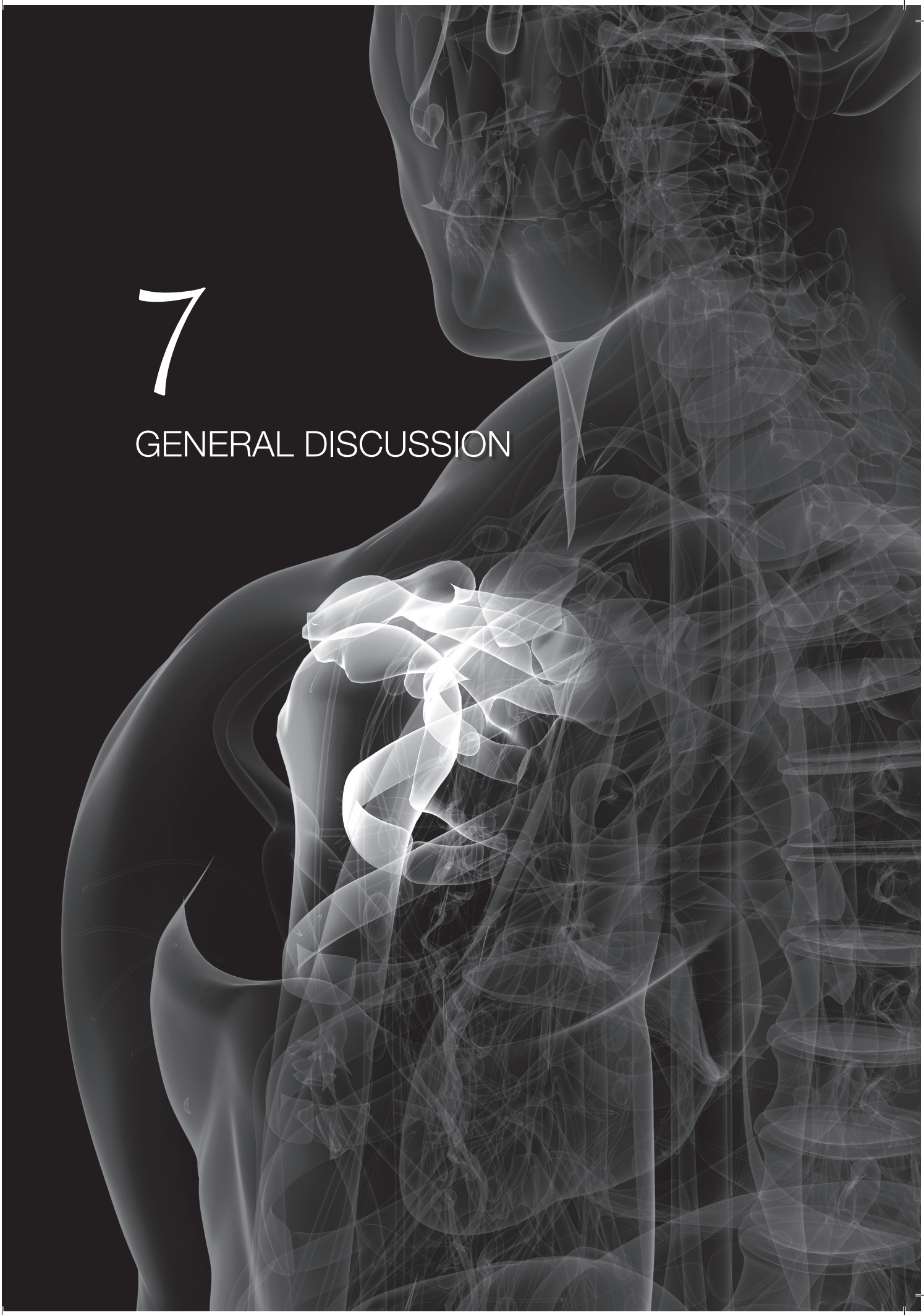
7

GENERAL DISCUSSION



7

GENERAL DISCUSSION

The central aim of this thesis was to describe the impact of myofascial trigger points (MTrPs) on pain and functioning in patients with chronic unilateral non-traumatic shoulder pain.

Background

Non-traumatic shoulder pain is often called non-specific shoulder pain, which means that a specific medical diagnosis is not provided. Specific shoulder pain diagnoses include, among others, glenohumeral labral lesions, fractures, tendon tears, dislocations, glenohumeral instability, osteoarthritis, infections and rheumatoid arthritis.

Shoulder pain is highly prevalent in the population. Together with low back pain and neck pain, it is the most common among musculoskeletal disorders. Furthermore, shoulder pain is persistent and recurrent, even with medical treatment. Most non-traumatic shoulder pain is explained as being the result of inflammation, degeneration or impingement of the soft tissues in the subacromial space, usually referred to as subacromial impingement syndrome (SIS). Medical treatment usually consists of anti-inflammatory drugs, muscle strengthening exercises for the rotator cuff muscles or surgery for decompression of the impinged tendons and bursa.

However, there is no evidence that any of these therapeutic interventions are effective in patients with non-traumatic shoulder pain, with a few exceptions [1-4]. These exceptions are subacromial corticosteroid injections for rotator cuff disease and intra-articular injection for adhesive capsulitis. They may be beneficial although the effect may be small and not well-maintained [2]. Exercises combined with mobilization, including soft tissue massage, shoulder muscle strengthening and stretching exercises, are beneficial for patients with rotator cuff disorders (SIS) [3, 5-7].

Shoulder diagnostics are hampered by the fact that physical examination tests have only limited diagnostic validity due to low specificity, and abnormalities revealed by medical imaging are not necessarily pathognomonic [8-10].

Research studies on shoulder pain have rarely mentioned MTrPs, and the effect of MTrP therapy in patients with shoulder pain remains unclear. In this thesis, a comprehensive MTrP therapy program administered by specifically-trained physical therapists over three months was compared to a wait-and-see strategy in patients with chronic (duration more than six months) unilateral non-traumatic shoulder pain.

In **Chapter 2** we presented an evidence-informed review on MTrPs with the current knowledge of aetiology, pathophysiology and clinical implications. This chapter offers a conceptual framework which helps to explain why MTrPs develop, why they are sustained,

and what mechanism explains the therapeutic effects. MTrPs are determined by manual palpation and together with information from the patients' medical history and findings from the physical examination, the assessment of myofascial shoulder pain caused by MTrPs can be made. Gerwin and Sciotti have confirmed the reliability of manual MTrP palpation [11, 12]. Simons et al. have recommended 'clearly, a clinical or experimental research study of human MTrPs, to obtain the most meaningful results, should employ both experienced and trained examiners who have been tested for interrater reliability before the study is conducted' [13].

In **Chapter 3**, we presented the results of an interrater reliability study. This study compared the palpation findings of three different observers, examining bilaterally six MTrP locations in three shoulder muscles (infraspinatus, anterior deltoid and biceps brachii muscles) in 40 subjects. Thirty subjects had unilateral shoulder pain, and 10 subjects had no current shoulder pain. The raters were blinded to the pain status of the subjects. All subjects were examined for the characteristic features of MTrPs, including a hard nodule in a taut band, referred pain, the local twitch response and the jump sign. In this study, we found a high prevalence of latent MTrPs in the unaffected shoulder of the patients with unilateral shoulder pain as well as in the shoulders of pain-free shoulder subjects. Latent MTrPs are described as "clinically quiescent with respect to spontaneous pain; it is painful only when palpated. A latent MTrP may have all other clinical characteristics of an active MTrP and always has a taut band that increases muscle tension and restricts range of motion". Since all raters were blinded for the status of the subjects (shoulder pain or non-shoulder pain) they were not able to distinguish active from latent MTrPs. In reliability studies, the Cohen's kappa is most often used as a statistical measure for agreement. The unexpected high number of MTrPs had an unintentional influence on the Cohen's kappa. Therefore, we also provided the prevalence index (P_i), which expresses the ratio between the presence and absence of certain features. In other words, when the P_i is high, the Cohen's kappa will be low, although the percentage of agreement is high. It has been reported that latent MTrPs are highly prevalent in the shoulder muscles of asymptomatic healthy subjects [14], and in future studies, it is recommended to check control subjects for latent MTrPs before entering the study. In clinical practice, the patient provides the clinician with information about the sensitivity of the MTrP and the recognizable sensations, including pain and paresthesia, caused by compression on the MTrP. This extra information is likely to increase the reliability of MTrP palpation. Objective criteria, confirming the assessment of MTrPs by palpation, are provided by needle EMG, microdialysis, magnetic resonance elastography and ultrasonography, but these facilities are not available in primary care [15-23].

In **Chapter 4**, the study protocol of the clinical randomized trial was presented. This study was conducted in one physical therapy practice. All participating physical therapists were specialized in the treatment of patients with musculoskeletal disorders of the neck, shoulder and arm. They were experienced in diagnosing and treating of patients with MTrPs. Thus, the results of this trial may apply only to experienced physiotherapists. In this trial, we compared a comprehensive MTrP therapy protocol with a waiting list. The various elements of this MTrP

approach were according to the guidelines of Simons et al. [13]. Due to the design of the study, we were only able to make conclusions on this MTrP therapy and not on its single elements. In general, treatment followed the principles of inactivation of MTrPs, restoration of muscle function and correction of the factors that precipitated and perpetuated the MTrPs [24]. A combination of treatment elements may be more effective than a single element [13, 25-27].

For example, myofeedback or MTrP compression alone is probably not effective, but an effective combination employs MTrP compression, which decreases the sensitivity of the muscle and therefore makes it easier to relax, and myofeedback, which helps to relax and thereby decreases sustained muscle overloading. Applying heat as a single modality seems to be ineffective, but applying it after MTrP compression followed by muscle stretching exercises may improve blood circulation within the muscle. Normalizing blood circulation seems to be a key factor in the physiological response after MTrP therapy [19, 23, 28].

Since the prevalence of MTrPs in patients with shoulder pain was unclear, we collected data on the presence of MTrPs in our study sample at baseline. The results of this observational study are presented in **Chapter 5**. We found active MTrPs in all patients, indicating that MTrPs are responsible for at least a part of the shoulder pain in all patients. The median number of active MTrPs was six, but varied greatly per subject. If multiple MTrPs contribute to shoulder pain, then elimination of only one MTrP will probably not improve the patients' pain and functioning. Conversely, some or probably all active MTrPs have to be treated adequately before the patient improves. Most active MTrPs were found in the infraspinatus and the upper trapezius muscle. According to Simons et al., the infraspinatus muscle refers pain to the frontal and lateral side of the shoulder and the pain is felt as 'deep shoulder pain'. The upper trapezius muscle refers to the top of the shoulder and eventually to the neck, and even to the temporal region of the head [13]. When (ipsilateral) headache accompanies shoulder pain, this may also have a myofascial origin [29-33]. We looked at the association between the number of active and latent MTrPs, the DASH and the VAS-P. There was a significant positive, but only moderate, correlation between active MTrPs and the DASH or VAS-P1 scores. This may have several reasons:

1. We counted the number of muscles with active MTrPs and not the total number of active MTrPs. It is likely that the number of active MTrPs is more correlated to the outcome scores than the number of muscles with active MTrPs.
2. We did not determine the sensitivity of the MTrPs, which can be measured by the Pain Pressure Threshold (PPT). According to Hidalgo, 'active MTrPs in some muscles are associated to greater pain intensity and lower PPTs when compared to those with latent TrPs in the same muscles', and 'significant negative correlations between pain intensity and PPT levels are found'. Therefore, we assume that a higher sensitivity of MTrPs could result in higher outcome scores.
3. The mean DASH score was 30.8 (95% CI 27.5 to 34.1; minimum 0 and maximum 100). This relatively low score happens to be common in other shoulder research investigating chronic shoulder pain. In studies examining the effects of conventional

therapy in patients with chronic shoulder pain, the DASH at baseline ranged from 31.3 to 35.0 [34-36]. In studies examining the effects of surgical interventions, the DASH score was slightly higher, ranging from 42.0 to 43.0 [34, 37, 38]. There may be several reasons for generally low outcome scores at baseline in patients with chronic musculoskeletal pain, including shoulder pain. First, this may be explained by the fact that chronic shoulder patients may have learned to cope with their shoulder pain and the limitations in functioning and therefore, have a lower score on the DASH. Second, as patients with higher DASH scores have more pain and more disability, they are less willing to participate in a study because of the chance of being allocated in the control group, which means that they have to wait another three months before therapy starts. Therefore, it is conceivable that selection bias has led to a relatively low DASH score. For the same reasons, this also holds true for VAS-P1 (mean 30.0; 95% CI 27.0 to 39.9), VAS-P2 (mean 42.1; 95% CI 37.4 to 50.0) and VAS-P3 (mean 56.6; 95% CI 51.2 to 61.9).

In **Chapter 6**, we presented the results of the RCT. We had calculated that we needed 104 patients (52 in each arm) to detect a clinically relevant improvement. Partly because of an overestimation of the number of eligible subjects and partly because of the unwillingness of patients to enter the trial, the study was completed with a smaller sample size. The study took two years to complete, which is one more year than was originally planned. The reason for the declined patient flow remained unclear. Despite the smaller sample size, we found significant and clinically relevant differences between the intervention group and the control group. While the study stopped after three months, it is unclear whether the improvement will continue or stop after this time. A follow up study is needed to assess this, but this was not part of this thesis. As previously mentioned, the functional status of included patients at baseline was relatively good. This implies that it is difficult to achieve significant improvement; even a 50% improvement is still only 15 points on the DASH. Nevertheless, small improvements may have important clinical implications, although they are close to or even smaller than the Minimal Clinical Important Difference (MCID). In this study, all patients were treated once a week for 12 weeks. The duration of each session was 30 minutes. It is unclear whether this is the most optimal frequency and the most optimal duration of the session. In this study, we used manual techniques for inactivation of MTrPs. There were two major reasons for this choice. First, not all participating physical therapists had attended courses in addition to manual MTrP therapy. Second, manual techniques can easily be administered by general physical therapists without any additional extensive educational course. In recent years, new techniques have become available for physical therapists in several countries, including the Netherlands. Especially, trigger point dry needling (TPDN) is one of the innovations in MTrP therapy [39]. TPDN might be more effective than manual techniques, but requires additional training, since physical therapists are not allowed to treat invasively without additional training [40-42].

Recommendations

Clinical practice

We recommend to use the clinical diagnostic term 'shoulder pain caused by MTrPs', when the presence of MTrPs is confirmed by physical examination, including palpation and provocation by firm digital pressure, instead of using the generally accepted term 'non-specific shoulder pain'. We further recommend examining patients who have already been diagnosed with subdeltoid or subacromial bursitis, rotator cuff disorder, tendonitis, tendinopathy or subacromial impingement for the presence of MTrPs, since MTrPs may accompany other diseases or disorders of the shoulder.

While a substantial number of patients benefitted from the MTRP therapy, it is important to note that some patients did not benefit. It remains unclear whether continued treatment or innovative types of MTrP treatment would be beneficial in this group. Future observational studies can help to elucidate these ambiguities.

For the moment, we recommend evaluating patient progress carefully and stopping MTrP treatment when no improvement occurs. Based on the results of the RCT, we are not able to define a clear stop rule, but based on clinical experience, it is conceivable that patients with chronic shoulder pain need more treatment sessions over a longer period of time than the three months period of the RCT.

Other authors have suggested that it may take more than 11 weeks for patients with chronic shoulder pain to fully enjoy the benefits of an active exercise program [43].

Implementation

Nationwide implementation of MTrP treatment is a new challenge, which was not considered in our clinical studies. Nevertheless, these studies give some clues about possible barriers for implementation. Most implementation experts recommend identifying the most relevant barriers for change and tailoring implementation interventions to those barriers. However, even carefully developed and well-applied implementation programs have mixed and moderate effects. The uptake of biomedical knowledge in clinical practice is a slow and haphazard process [44, 45]. Regarding MTrP therapy, we suggest that the following factors may be associated with its implementation:

1. Knowledge and skills of physiotherapists regarding MTrP assessment and management
2. Motivation to apply this assessment and management among physiotherapists
3. Knowledge and motivation among physicians to refer patients for MTrP treatment
4. Preferences, concerns and expectations of patients with shoulder pain
5. Strength of evidence related to MTrP treatment
6. Availability of alternative, effective treatments for shoulder pain
7. Reimbursement for the treatment (insurance and/or co-payment)
8. Annual number of patients needed for optimally effective and efficient delivery

Organizational, legal or economic factors may be underlying barriers for change in clinical practice. The knowledge and skills of physical therapists regarding MTrP treatment are obviously important, as in almost all situations of implementation. Physicians and therapists can reliably identify MTrPs in shoulder muscles, provided that they are trained well and have enough clinical experience. Dutch physical therapists should be able to provide manual therapy interventions, including various massage techniques and muscle stretching exercises, as it is part of their undergraduate education. In addition, continued education has to be provided and followed to keep up with new developments. In many countries, post-graduate manual trigger point therapy and trigger point dry needling courses are offered. Trigger point dry needling (TPDN) is an invasive procedure in which a solid filament needle (acupuncture needle) is inserted into the skin (superficial dry needling) and muscle (deep dry needling). As the name implies, TPDN is directed at MTrPs and its aim is to inactivate them. TPDN falls within the scope of physical therapy practice in many countries including Canada, Spain, Ireland, South Africa, Australia, the Netherlands, Switzerland, and in a growing number of states in the United States [39].

Generally, physical therapists have to get motivated to apply the clinical aspects of MTrPs, among clinical signs and symptoms by means of research evidence on the effectiveness of their intervention, the satisfaction of their patients and financial viability of providing the treatment. Because MTrPs are highly prevalent in patients with shoulder pain, health insurance companies may also be interested when MTrP therapy is shown to be capable of decreasing the overall costs for shoulder pain interventions, for example by preventing unnecessary shoulder surgery. Cost-effectiveness studies can help to convince decision makers to reimburse MTrP treatment.

Physicians should consider MTrP therapy for patients with shoulder pain and refer to physical therapists with or without in combination with other interventions, such as steroid injections or NSAIDs. With persistent shoulder pain, MTrP therapy can be considered prior to resorting to surgical interventions.

Since direct access to physical therapy was introduced in 2006, the number of patients who contacted physical therapists without consulting a general practitioner gradually increased from 21% (2006) to 38% (2009) (from www.nivel.nl/lipz). Since 7% of these patients receiving physical therapy in 2009 had shoulder pain, there is a need for undergraduate and post-graduate physical therapy and medical education to include training in MTrP assessment and management to assure that patients may be treated accordingly.

Clinical guidelines

The authors of clinical guidelines should include the assessment and management options of MTrPs when revising the guidelines, since MTrPs are highly prevalent, easily diagnosed and effectively treated by relatively simple interventions, including physical therapy. We also recommend the introduction of the concept of MTrP, and teaching the diagnostic and therapeutic tools at schools for physical therapy and medical schools, and further

implementation of assessment and treatment of MTrPs in the daily practice of physicians and physical therapists. MTrP therapy may be helpful in recovering from shoulder pain, especially in those cases which seem resistant to other interventions such as steroid injections or exercise therapy.

Future research

We recommend that in future clinical studies on the assessment and management of MTrPs should be considered in patients with shoulder pain. The effectiveness of MTrP therapy should be compared with other interventions, and combinations of MTrP therapy with other interventions should also be explored. For example, the combination of a single steroid injection for short-term relief (up to six weeks) combined with MTrP therapy for long-term relief may be beneficial for the patient and may help to decrease the recurrence rate. Such combination therapies may be more effective than single intervention approaches, and may eventually help to lower the costs for society. Other MTrP interventions, such as TPDN may be even more effective than manual soft tissue massage or mobilization techniques. Therefore, these interventions should be investigated as well as other interventions. The optimal dose, duration and intensity of interventions in physical therapy practice are still unknown and this has to be established as well. In future studies, PPT and counting the number of active MTrPs should be included, instead of the number of muscles with active MTrPs, and in addition to subjective patient self-reported outcomes, more objective tests to measure function, for instance lifting a heavy weight or carrying a shopping bag, can be used as well.

In recent decades, several articles have contributed to explain the aetiology and pathophysiology of myofascial pain and myofascial trigger points [20, 46-49]. However, there is still a need for more fundamental research in this field. For example, there is evidence for a central role for acetylcholine in the integrated trigger point hypothesis, although evidence collected by analyzing its concentrations in the vicinity of the neuromuscular junction by microdialysis is still lacking.

Furthermore, some studies have shown that experimental and clinical shoulder muscle pain can induce abnormal motor activation patterns, but only one study has shown an association between latent MTrPs and abnormal motor activation patterns [50]. Studies using objective parameters, including electromyography, can help to explain the association between MTrPs and muscle function. In clinical studies, using physical therapy modalities, it is not possible to blind the therapist and the patient, which means that it is impossible to exclude the placebo effect. Therefore, the magnitude of the placebo effect remains unclear in physical therapy. However, pragmatic controlled studies comparing several interventions can help us to find the most effective intervention.

Conclusions

From the studies in this thesis, we may conclude that MTrPs in patients with shoulder pain are highly prevalent and are at least partly responsible for shoulder pain. Physical examination, including palpation according to the guidelines of Simons et al., is a reliable method to diagnose MTrPs, which may increase when patients guide the physician or therapist during physical examination, in terms of recognizable pain [13]. Our study shows that comprehensive treatment of MTrPs was effective in patients with chronic shoulder pain within 12 weeks.

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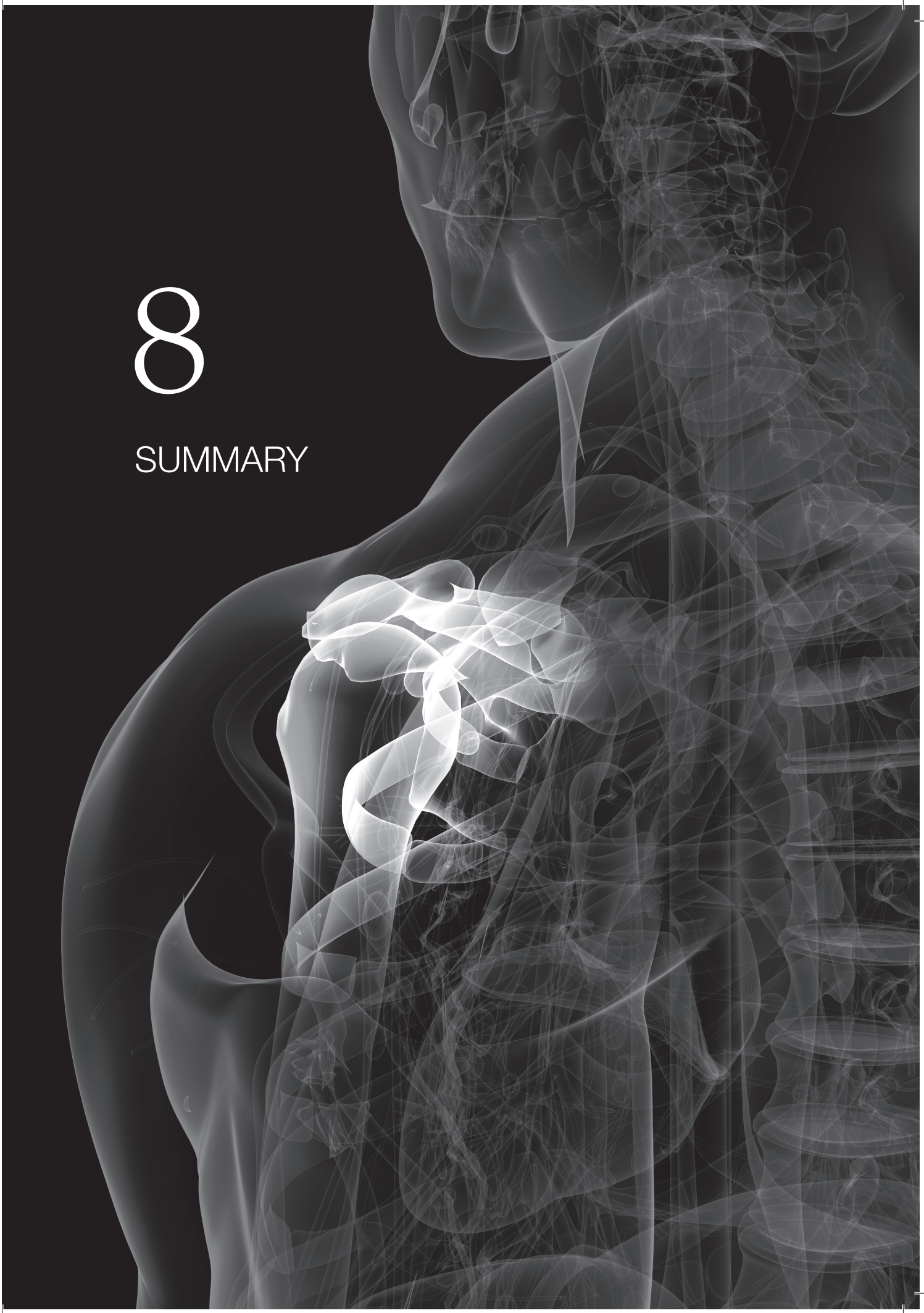
8

SUMMARY



8

SUMMARY

Shoulder pain is, after low back pain and neck pain, the most common complaint of the musculoskeletal system. In The Netherlands and other countries, the percentage of individuals with shoulder pain in the population is estimated to be around 20% to 50% per year. Shoulder pain has an important influence on the daily functioning of the individual patient. About half of all patients with shoulder pain seek medical help. Patients with shoulder pain have difficulties in recovering from shoulder pain so that it is often recurrent, despite medical treatment. Shoulder pain affects not only the patient but also the whole of society through direct and indirect costs and sick leave.

The terms "shoulder pain", "shoulder complaint", and "shoulder disorder" are often used interchangeably. In this thesis, we use the term "shoulder pain", as pain was the main complaint of the patients when consulting a physician or therapist. Shoulder pain caused by trauma is beyond the scope of this thesis.

The clinical picture, which the patient presents with, consists of pain at the frontal or lateral side of the shoulder, often radiating to the upper arm and sometimes even into the forearm and hand. The pain is often present at rest and almost always provoked or aggravated by posture or (repeated) movements of the arm. The patient sleeps poorly because of the inability to lie on either shoulder. The pain often leads to limitations in daily life and problems with participation in work, sporting and leisure activities.

Non-traumatic shoulder pain is mostly explained by local pathological changes in the subacromial space [1], including inflammation of the rotator cuff tendons or the subacromial bursa, or degenerative changes in the subacromial space, such as tendon degeneration. However, there is growing scientific evidence to indicate that local inflammation is not the (only) causal explanation for shoulder pain, and degenerative changes in rotator cuff tendons are seen as often in people without shoulder pain as patients with shoulder complaints. Therefore, it remains unclear as to whether or not the abnormal findings of additional imaging techniques, including ultrasound and magnetic resonance imaging (MRI), can explain the existence or occurrence of shoulder pain.

The main etiological explanation for shoulder pain was described by Dr Charles Neer, who in 1972 argued that the so-called subacromial space in these patients was too small. Because of this insufficient space, impingement of the subacromial bursa and the rotator cuff tendons may occur. The constant and repetitive encroachment of these structures could lead to acute bursitis, or, when persistent, to chronic bursitis, and finally, to degenerative rotator tendon tears. This is called subacromial impingement syndrome (SIS) and up until today it has been the main explanation for non-traumatic shoulder pain. Because the physical examination of patients with shoulder pain and additional imaging are of limited diagnostic value, and since there is only a small amount of scientific evidence for the effectiveness of various interventions aimed at the treatment of SIS, the question of whether or not there might be another possible explanation for non-traumatic shoulder pain is justified.

To date, there has been little or no attention paid to the role of myofascial trigger points (MTrPs) in shoulder muscles in the scientific literature on the emergence or persistence of shoulder pain. MTrPs are local changes in skeletal muscles that may result in sensory, motor and autonomic symptoms. An MTrP is defined as a hyperirritable spot in skeletal muscle that is associated with a hypersensitive palpable nodule (muscle hardening) in a taut band. MTrPs are divided into active and latent trigger points. Active MTrPs cause spontaneous pain and latent MTrPs only cause pain and other sensations when directly stimulated by mechanical compression, muscle contraction, or muscle stretching. Both active and latent MTrPs can decrease the mobility of the shoulder and may cause muscle weakness.

The aim of the research described in this thesis was to gain more insight into the role of MTrPs in patients with shoulder pain.

Before examining the influence of MTrPs on the pain in patients with shoulder pain, **Chapter 2** describes what is known about the etiology, pathophysiology and clinical implications of MTrPs for physiotherapy treatment.

In particular, Dr Janet Travell (1901-1997) and Dr David Simons (1922-2010) are generally credited with bringing MTrPs to the attention of medical and other healthcare providers.

The comprehensive "expanded integrated hypothesis" describes the complex interactions that can help explain the emergence and persistence of MTrPs. It is assumed that various mechanisms can cause MTrPs, such as sustained or frequently repeated muscle contractions and unusual eccentric or concentric muscle contractions, leading to higher intramuscular pressure, and direct (muscle bruising) or indirect (sprain or strain) muscle trauma. In all of these cases, the repeated or sustained loading of the muscle goes beyond the properties of the tissue, which may lead to muscle overload in the end. During muscle overload, biochemical changes in and around the muscle fibers occur, leading to an increased and sustained contracture (contraction due to high concentrations of Ca^{2+} in the muscle fiber, without depolarization) and to the release of various sensitizing and other pain-related substances. Under this condition, there is no motor neuron activity that leads to sustained contraction. As a result, this muscle overload creates a lack of adenosine triphosphate (ATP), which is an energy-rich substance needed for the release of large amounts of Ca^{2+} from the myosin-actin-complex and for its re-uptake into the sarcoplasmic reticulum, where it is stored.

The lack of ATP results in prolonged linking of the proteins actin and myosin, causing a shortened and thickened muscle fiber. It is assumed that the thickening of multiple muscles fibers obstructs blood flow through the smallest capillaries, resulting in ischemia and hypoxia of the muscle tissue. For the synthesis of ATP, large amounts of oxygen are needed, which can only be obtained through the capillary blood flow.
As the thickened muscle fiber cells prevent a sufficient blood flow, a self-perpetuating situation develops.

Chapter 3 describes an inter-rater reliability study of the palpation of MTrPs in three shoulder muscles, i.e. the infraspinatus, anterior deltoid, and biceps brachii muscles. A total of 6 MTrP locations on both shoulders in 40 subjects were studied.

Thirty subjects had unilateral shoulder pain and ten subjects were symptom-free at the time of investigation. The observers did not know whether one of the shoulders was painful or not, and if so, which one it was. The muscles were palpated to determine the presence or absence of a noticeable hardening in a taut band, to determine whether or not firm compression during palpation could generate referred pain [2] (RP), and to determine whether snapping palpation could elicit a local twitch response [3] (LTR) or cause a "jump sign" [4] (JS). The palpation findings were subjected to a pairwise comparison. Finally, based on the combination of these findings, the presence or absence of an MTrP was scored.

The most reliable characteristics of the MTrPs were RP and JS, followed by the localization of a local hardening (nodule) in a taut band and the LTR. The highest degree of reliability for the presence or absence of an MTrP was found in the infraspinatus muscle.

One of the three observers had 2 years of experience in MTrP therapy and the other two investigators had 16 and 21 years of experience in MTrP therapy, respectively.

No difference was found in the degree of agreement between the different pairs of observers.

Based on this study, it was concluded that palpation of MTrPs in shoulder muscles is reliable and, therefore, a potentially useful diagnostic tool in the diagnosis of myofascial pain in patients with non-traumatic shoulder pain. It also appears that 2 years of experience is sufficient.

Chapter 4 describes the research protocol for a randomized controlled trial (RCT) of the effectiveness of MTrP therapy in patients with chronic, unilateral, and non-traumatic shoulder pain. This study took place between September 2007 and December 2009.

The treatment consisted of physical therapy (aimed at eliminating MTrPs in shoulder muscles) for three months, compared with expectant management.

The primary outcome measure used was the Disabilities of Arm, Neck and Hand questionnaire (DASH). The secondary outcome measures used were the Visual Analogue Scale for pain for current pain (VAS-P1), the average pain in the last week (VAS-P2), the worst pain in the last week (VAS -P3), the global perceived effect (GPE), and the number of muscles with active or latent MTrPs. Prior to the study, it was calculated that in order to show a clinically relevant difference on the DASH, 104 patients would be needed (52 patients per group).

Chapter 5 describes the prevalence of MTrPs in 17 shoulder muscles in patients with unilateral shoulder pain. Mainly because of logistical reasons, this study was completed with a smaller sample size than was originally calculated. All patients (n = 72), who were included in the RCT, were examined prior to randomization for the presence of active or latent MTrPs [5]. The number of muscle MTrPs was counted.

Muscles containing active or latent MTrPs were found in all 72 subjects. The median number of muscles with active MTrPs was 6 (ranging from 2 to 16). The median number

of muscles with latent MTrPs was 4 (ranging from 0 to 11). Active MTrPs were most prevalent in the infraspinatus, upper trapezius, and middle deltoid muscles. Latent MTrPs were most prevalent in the teres major, anterior deltoid, and upper trapezius muscles. The number of muscles with active MTrPs only moderately correlated with the DASH score (Spearman's $\rho = 0.3$). The number of muscles with active MTrPs only explained 10% of the variation of the DASH outcome measure. Other factors were the degree of sensitivity of the individual MTrPs, alone or in combination with the number MTrPs per muscle. In addition, there may have been other relevant factors that were not included in this study.

Based on these prevalence data, examination for the presence of MTrPs in patients with shoulder pain is recommended.

Chapter 6 describes the results of physical therapy in patients with chronic, unilateral non-traumatic shoulder pain. In the period from September 2007 to December 2009, 65 patients were included in this study. Patients in the intervention group were treated by one of five experienced physical therapists from the same physical therapy practice, specialized in the management of patients with musculoskeletal disorders of the neck, shoulder and arm, once a week for a 3-month period. Patients in the control group remained on the waiting list. They were instructed not to change their self-management regarding their shoulder pain or to report any changes. At intake, relevant patient characteristics were recorded and several questionnaires were completed. The passive range of shoulder motion was measured and the number of muscles with MTrPs was counted. The treatment consisted of inactivating the MTrPs by sustained compression of the MTrP, followed by stretching the muscle, including the "taut band", and a combination of muscle stretching exercises and a cold application (which was a variant of the spray-and-stretch method originally described by Dr Janet Travell).

Subsequently, the patients were instructed to perform muscle stretching and relaxation exercises several times a day. When appropriate, these relaxation exercises were augmented by the use of a (portable) myofeedback device. Finally, all patients received ergonomic advice and instructions to assume and maintain "good posture".

In this study, we chose an intervention strategy aimed at treating MTrPs that best reflects daily physical therapy practice. The idea behind this was that the different parts might have no (permanent) or little effect separately, whereas their combination may have an effect as the various components reinforce each other. The disadvantage of this approach is that the influence of the various components of the final outcome remains unknown.

Compared to the control group, after 12 weeks the intervention group scored significantly better on the primary and secondary outcome measures (DASH, VAS P1, P2 and VAS VAS-P3). The differences were all clinically relevant.

After 12 weeks, 55% of the patients in the intervention group were reported to have improved versus 14% in the control group. Also, the extent to which the patients improved was significantly greater in the intervention group than in the control group. The average number of muscles with active MTrPs decreased significantly in the intervention group, whereas this number increased in the control group. The number of muscles with latent

MTrPs did not change significantly in the intervention group and was significantly decreased in the control group. The number of muscles with active MTrPs moderately correlated with the improvement in the DASH score (Pearson's r = 0.49). All of the abovementioned effects were achieved after 12 weeks.

Although after 6 weeks a slight trend was seen in the improvement of the outcomes in favor of the intervention group, the difference between the two groups after 6 weeks was not significant. Because the study ended after 3 months, no conclusions can be drawn concerning the effects of the treatment beyond this period, but it is conceivable that a longer-term treatment may lead to a better result.

Chapter 7 presents the general discussion and the main conclusions of this thesis.

The main conclusions of this thesis were:

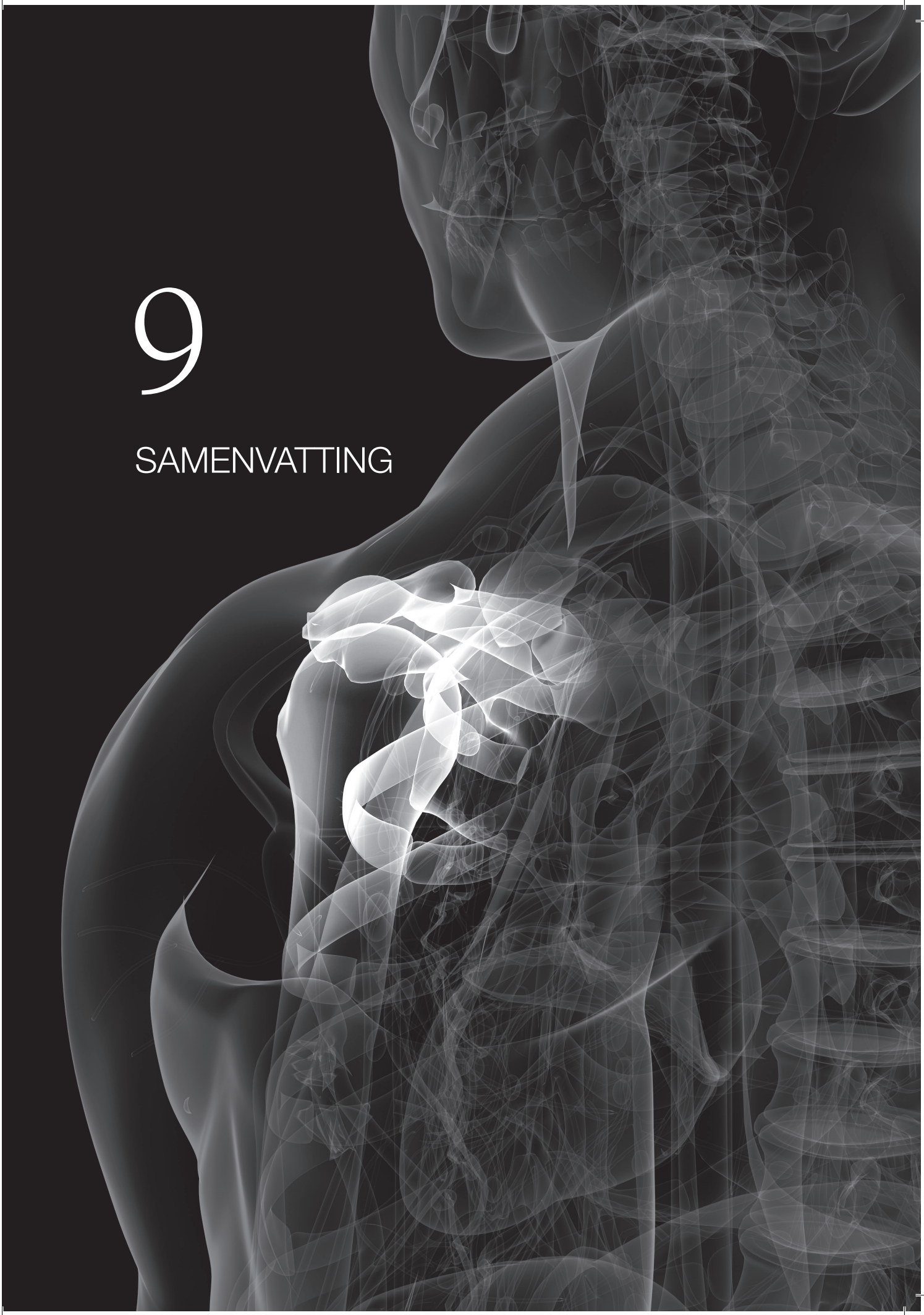
- MTrPs provide a promising new explanation and treatment target for shoulder pain, which is well grounded in pathophysiological knowledge.
- MTrPs in the shoulder muscles can be reliably determined by palpation and are an important addition to the physical examination.
- MTrPs are highly prevalent in shoulder muscles in patients with chronic, unilateral, non-traumatic shoulder pain.
- Most active MTrPs were found in the infraspinatus, the upper trapezius, and the middle deltoid muscles. Most latent MTrPs were found in the teres major, anterior deltoid, and the upper trapezius muscles.
- The multimodal treatment of MTrPs in shoulder muscles in patients with chronic, unilateral, non-traumatic shoulder pain is effective.
- The multimodal treatment of MTrPs in shoulder muscles in patients with chronic, unilateral, non-traumatic shoulder pain takes 12 weeks to complete at a frequency of one treatment per week.

References

1 The subacromial space lies underneath the acromion, the coraco-acromial ligament, and the coracoid process and above the humeral head, the upper margin of the glenoid fossa and the superior labrum.
2 Referred pain (RP) is not felt at the site of a tissue lesion but is felt at some distance from it, often entirely remote from its source. It is often described as radiating pain.
3 A local twitch response (LTR) is a transient contraction of a group of tense muscle fibers (taut band) that traverse an MTrP. The LTR can be elicited by snapping palpation of the taut band or by needling the MTrP.
4 The jump sign is a general pain response of the patient, who winces, may cry out, and may withdraw in response to pressure applied to an MTrP.
5 Active MTrPs cause spontaneous pain in rest or during (repeated) movement. The pain that arises from firm digital palpation is recognized as the patients' familiar pain. Latent MTrPs have the same characteristics as active MTrPs, but they are clinically silent.

9

SAMENVATTING



9

SAMENVATTING

Schouderpijn is na lage-rugpijn en nekpijn, de meest voorkomende klacht van het musculoskeletale systeem. Zowel in Nederland, als in diverse andere landen, wordt het percentage personen met schouderpijn in de bevolking geschat op zo'n 20 tot 50% per jaar. Schouderpijn heeft een belangrijke invloed op het dagelijks functioneren van de individuele patiënt. Ongeveer de helft van alle patiënten met schouderpijn zoekt medische hulp. Verder blijkt dat patiënten moeilijk herstellen van schouderpijn en dat deze klacht, ondanks medische behandeling, gemakkelijk recidiveert. Schouderpijn heeft niet alleen invloed op de individuele patiënt, maar ook op de totale samenleving door ziekteverzuim en directe en indirecte kosten.

De begrippen 'schouderpijn' (shoulder pain), 'schouderklachten' (shoulder complaints) en `schouderaandoening' (shoulder disorder) worden vaak door elkaar gebruikt. In dit proefschrift gebruiken we zoveel mogelijk de term schouderpijn (shoulder pain), omdat pijn één van de belangrijkste klachten is waarmee de patiënt bij de dokter of fysiotherapeut komt. Schouderpijn door traumata valt buiten het bestek van dit proefschrift. Het klinische beeld, waarmee de patiënt zich presenteert, bestaat uit pijn aan de voor- of zijkant van de schouder, vaak uitstralend naar halverwege de bovenarm en soms zelfs tot in de onderarm en hand. De pijn is vaak in rust aanwezig en wordt vrijwel altijd uitgelokt of verergerd door (herhaalde) bewegingen of houdingen van de arm. De patiënt slaapt vaak slecht, omdat hij/zij noch op de aangedane schouder, noch op de niet-aangedane schouder kan liggen. De pijn leidt regelmatig tot beperkingen in het dagelijks leven en participatieproblemen in werk, sport en hobby's.

De verklaring voor niet-traumatische schouderpijn wordt gezocht in veronderstelde locale pathologische veranderingen in de subacromiale ruimte[1], bestaande uit een ontsteking van de pezen van de rotator cuff of de subacromiale bursa of degeneratieve veranderingen in de subacromiale ruimte, zoals degeneratieve scheuren van de rotator cuff. Er zijn in toenemende mate wetenschappelijke aanwijzingen dat deze lokale ontstekingen niet de causale verklaring bieden voor schouderpijn. Degeneratieve veranderingen van de rotator cuff worden net zo vaak gezien bij personen zónder schouderklachten als bij patiënten mét schouderklachten. Het is dan ook onduidelijk of afwijkende bevindingen van aanvullend beeldvormend onderzoek, waaronder echografie en magnetic resonance imaging (MRI), verklarend zijn voor het bestaan of ontstaan van schouderpijn.

De belangrijkste etiologische verklaring voor deze schouderpijn is beschreven door dr. Charles Neer, die in 1972 stelde, dat de zogenaamde subacromiale ruimte bij deze patiënten te gering was. Door deze te geringe ruimte ontstaat er inklemming van de bursa en de pezen van de rotator cuff. Het voortdurend repeterend inklemmen van deze structuren zou kunnen leiden tot acute of, bij voortduring, tot chronische bursitis en degeneratieve

scheuren in de pezen van de rotator cuff. Dit wordt het subacromiale impingement syndroom (SIS) genoemd en wordt tot op heden als belangrijkste verklaring voor niet-traumatische schouderpijn gehanteerd. Hoewel het lichamelijk onderzoek bij patiënten met schouderpijn en het aanvullend beeldvormend onderzoek weinig diagnostisch valide zijn en er weinig overtuigend bewijs voor de effectiviteit van de verschillende interventies, gericht op de behandeling van de gevolgen van het SIS, bestaat, is de vraag gerechtvaardigd of er niet een andere mogelijke verklaring is voor de schouderpijn.

Tot op heden is er in de wetenschappelijke literatuur over het ontstaan of voortbestaan van schouderpijn niet of nauwelijks aandacht voor de rol van myofasciale triggerpoints (MTrPs) in schouderspieren. MTrPs zijn lokale veranderingen in skeletspieren, die sensorische, motorische en autonome verschijnselen kunnen geven. Een MTrP is gedefinieerd als een sterk prikkelbare plaats in de skeletspier, die samenvalt met een overgevoelige palpabele spierverharding ('nodule') in een strakke band. MTrPs worden ingedeeld in actieve en latente trigger points. Actieve MTrPs geven spontane pijnklachten en latente MTrPs geven alleen pijn en andere sensaties bij directe stimulatie door mechanische druk of door aanspanning of rek van de spier. Zowel actieve als latente MTrPs kunnen verminderde beweeglijkheid van de schouder en krachtsverlies van de schouderspieren tot gevolg hebben. Het doel van het onderzoek, dat beschreven is in dit proefschrift, is om meer inzicht te verkrijgen in de rol van de MTrPs bij patiënten met schouderpijn.

Alvorens in te gaan op de invloed van MTrPs op de klacht bij patiënten met schouderpijn, wordt in **hoofdstuk 2** beschreven wat er bekend is over de etiologie, de pathofysiologie van MTrPs en de klinische implicaties voor de fysiotherapeutische behandeling. Het zijn met name dr. Janet Travell (1901-1997) en dr. David Simons (1922-2010) geweest, die MTrPs onder de aandacht hebben gebracht van (para-)medici.

De uitgebreide, geïntegreerde hypothese beschrijft de complexe interactie, die het ontstaan en het persisteren van MTrPs kan helpen verklaren. Er wordt daarin aangenomen, dat er diverse mechanismen zijn die MTrPs kunnen veroorzaken, zoals langdurig aangehouden of veelvuldig herhaalde contracties, ongewone excentrische of concentrische contracties, waarbij hoge intramusculaire druk ontstaat, en direct (spierkneuzing) of indirect (overrekkingsletsel) spiertrauma. In alle gevallen gaat het om situaties, waarbij de belasting van de spier als anatomische structuur de belastbaarheid kortdurend, herhaaldelijk of langdurig overstijgt. Gedurende deze situaties ontstaan biochemische veranderingen in en om de spiervezels, die enerzijds leiden tot een toegenomen en aanhoudende contractuur (contractie, als gevolg van hoge concentraties Ca^{2+} in de spiervezel, zonder depolarisaties) en anderzijds tot het vrijkomen van talrijke aan nocisensoriek en pijn gerelateerde stoffen. Er is in deze conditie geen sprake van een activiteit vanuit de motorische zenuwvezel die tot deze aanhoudende contractie leidt. Als gevolg van deze spieroverbelasting ontstaat een tekort aan adenosinetrifosfaat (ATP). Deze energierijke stof is nodig om de grote hoeveelheid aan myosine en actine gebonden Ca^{2+} vrij te maken en terug op te nemen in het

sarcoplasmatisch reticulum. Door dit tekort blijven de myosine en actine eiwitten gekoppeld, waardoor de spiercel verkort en verdikt. Deze verdikking, zo wordt aangenomen, zorgt voor obstructie van de bloedtoevoer via de allerkleinste weefselcapillairen, waardoor ischemie en hypoxie van de spier ontstaat. Voor de vorming van ATP zijn grote hoeveelheden zuurstof nodig, die via de capillaire aanvoer moet worden verkregen. De verdikte spiercellen verhinderen deze aanvoer en een zich zelf in standhoudende situatie is ontstaan.

Hoofdstuk 3 beschrijft het onderzoek naar de interbeoordelaarsbetrouwbaarheid van palpatie naar het voorkomen van MTrPs in drie schouderspieren, namelijk de M. infraspinatus, de M. deltoideus pars anterior en de M. biceps brachii. Bij 40 proefpersonen werden aan beide schouders in totaal 6 MTrP locaties onderzocht. Van deze proefpersonen hadden 30 enkelzijdige schouderklachten en 10 hadden op het moment van onderzoek geen schouderklachten. Elke proefpersoon werd door drie verschillende onderzoekers onderzocht. De onderzoekers wisten niet of de schouder pijnlijk was en zo ja, welke schouder pijnlijk was. Er werd gescoord op de aan- of afwezigheid van een voelbare verharding in een strakke streng, het opwekken van 'referred pain[2]' (RP), en de mogelijkheid tot het opwekken van een 'local twitch response[3]' (LTR) of het veroorzaken van een 'jump sign[4]'. De zo verkregen gegevens werden tussen de drie beoordelaars paarsgewijs vergeleken. Op basis van de combinatie van bevindingen werd gescoord op de aan- of afwezigheid van een MTrP. De meest betrouwbare kenmerken van MTrPs waren het opwekken van RP en een 'jump sign' , gevolgd door de lokalisatie van een lokale verharding (nodule) in een strakke streng (taut band) en de LTR. De hoogste mate van betrouwbaarheid voor de aan- of afwezigheid van een MTrP werd gevonden in de M. infraspinatus. Een van de drie onderzoekers had twee jaar ervaring in MTrP-therapie en de andere twee onderzoekers hadden respectievelijk 21 en 16 jaar ervaring met MTrP-therapie. Er werd daarbij geen verschil gevonden in de mate van overeenkomst tussen de verschillende combinaties van onderzoekers. Op basis van dit onderzoek werd geconcludeerd dat de palpatie van MTrPs in deze schouderspieren betrouwbaar was en een goede aanvulling was op het lichamelijk onderzoek bij patiënten met niet-traumatische schouderpijn. Verder blijkt dat twee jaar ervaring voldoende was om dit even betrouwbaar te doen als iemand met langere ervaring.

Hoofdstuk 4 beschrijft het onderzoeksprotocol voor een gerandomiseerd, gecontroleerd onderzoek (Randomized Controlled Trial [RCT]) naar de effectiviteit van MTrP therapie bij patiënten met chronische, enkelzijdige, niet-traumatische schouderpijn. Dit onderzoek heeft plaatsgevonden tussen september 2007 en december 2009. De behandeling bestond uit fysiotherapeutische behandeling (gericht op het opheffen van MTrPs in schouderspieren) gedurende drie maanden, vergeleken met een afwachtend beleid. De primaire uitkomstmaat was de score op Disabilities of Arm, Hand and Neck questionnaire (DASH). De secundaire uitkomstmaten waren de scores op Visual Analogue Scale voor pijn (VAS-P) voor de huidige pijn (VAS-P1), voor de gemiddelde pijn in de laatste week (VAS-P2), de hevigste pijn van de afgelopen week (VAS-P3), op het globaal ervaren effect (GPE), het aantal spieren met actieve of latente MTrPs. Voorafgaande aan het onderzoek werd berekend, dat voor een relevant klinisch verschil op de DASH, 104 patiënten nodig waren (52 patiënten per groep).

Hoofdstuk 5 beschrijft de prevalentie van MTrPs in 17 schouderspieren bij patiënten met unilaterale schouderpijn. Door vooral logistieke problemen is het niet gelukt om het gewenste aantal patiënten te includeren.

Alle patiënten (n=72), die werden geïncludeerd voor de RCT, werden voorafgaande aan de randomisatie, onderzocht op de aanwezigheid van actieve en/of latente MTrPs[5]. Daarbij werd het aantal spieren geteld met MTrPs.

Alle onderzochte patiënten hadden meerdere actieve en latente MTrPs. De mediaan van het aantal spieren met actieve MTrPs bedroeg 6 (variërend van 2 tot 16) en met latente MTrPs 4 (variërend van 0 tot 11). De spieren met de meeste actieve MTrPs waren de M. infraspinatus, de M. trapezius (pars descendens) en de M. deltoideus (pars medius). De spieren met de meeste latente MTrPs waren de M. teres major, de M. deltoideus (pars anterior) en de M. trapezius (pars descendens). Er was een geringe correlatie tussen het aantal spieren met actieve MTrPs en de DASH score (spearman's $\rho = 0.3$). De hoogte van de DASH score wordt voor ongeveer 10% verklaard door het aantal spieren met actieve MTrPs. Andere factoren zijn de mate van gevoeligheid van de afzonderlijke MTrPs, al of niet in combinatie met het aantal MTrPs per spier. Daarnaast zijn er wellicht ook andere relevante factoren, die in dit onderzoek niet zijn meegenomen. Op basis van deze prevalentiegegevens wordt het onderzoeken van de patiënt met schouderpijn op de aanwezigheid van MTrPs aanbevolen.

Hoofdstuk 6 beschrijft de resultaten van de fysiotherapeutische behandeling van patiënten met langdurige, enkelzijdige niet-traumatische schouderpijn. In de periode van september 2007 tot december 2009 werden 65 patiënten geïncludeerd. De patiënten in de interventiegroep werden door 5 ervaren fysiotherapeuten uit dezelfde gespecialiseerde fysiotherapie praktijk behandeld gedurende maximaal 3 maanden één keer per week. De patiënten in de controlegroep bleven op de wachtlijst staan en werden gevraagd hun zelf-management/attitude ten aanzien van hun schouderpijn niet te veranderen of veranderingen tijdens de meetsessies te rapporteren. Bij de intake werden de relevant geachte patiënt-kenmerken vastgelegd, diverse vragenlijsten ingevuld, passieve bewegingsuitslagen van de schouder gemeten en het aantal spieren met MTrPs geteld. De behandeling bestond uit het inactiveren van MTrPs door aanhoudende druk op het MTrP, gevolgd door het rekken van de spier inclusief de 'taut band', en een combinatie van spierrekkingsoefeningen met ijsapplicatie (een variant van de door Janet Travell omschreven "spray and stretch'- methode). Vervolgens werden de patiënten geïnstrueerd meerdere keren per dag spierrekkings- en ontspannings-oefeningen te doen. Indien gewenst, kon het leren ontspannen worden ondersteund met een (portable) myofeedbackapparaat. Tenslotte kregen alle patiënten adviezen over hun houding, en ergonomische adviezen. In dit onderzoek is er voor gekozen om een behandeling gericht op MTrPs te geven, die overeenkomt met een fysiotherapeutische behandeling uit de dagelijkse praktijk. De gedachte hierachter is dat de verschillende onderdelen afzonderlijk geen of weinig (blijvend) effect hebben, maar dat de verschillende componenten elkaar versterken. Het nadeel van een dergelijke aanpak is, dat de invloed van de verschillende onderdelen op het eindresultaat onbekend blijft.

Vergeleken met de controlegroep scoorde de interventie groep na 12 weken op de primaire en secundaire uitkomstmaten (DASH, VAS-P1, VAS-P2 en VAS-P3) significant beter. De verschillen werden allen klinisch relevant beschouwd. Na 12 weken gaf 55% van de patiënten uit de interventiegroep aan te zijn verbeterd tegen 14% uit de controlegroep. Ook de mate waarin de patiënten verbeterden was groter in de interventiegroep dan in de controlegroep. Het gemiddelde aantal spieren met actieve MTrPs nam af in de interventiegroep, terwijl dit aantal toenam in de controlegroep. Het aantal spieren met latente MTrPs veranderde in de interventiegroep niet-significant en nam significant af in de controlegroep. Er werd een positieve correlatie gevonden tussen de afname van het aantal spieren met actieve MTrPs en de verbetering van de DASH-score ($r = 0.49$). Alle bovengenoemde effecten werden bereikt na 12 weken. Hoewel er na 6 weken een lichte trend was te zien in de verbetering op de uitkomstmaten in het voordeel van de interventiegroep, was het verschil tussen beide groepen na 6 weken niet significant. Omdat het onderzoek na 3 maanden eindigde kunnen geen uitspraken worden gedaan over het effect van een behandeling die langer duurt dan drie maanden, maar het is niet ondenkbaar dat een langer durende behandeling wellicht tot een beter resultaat leidt.

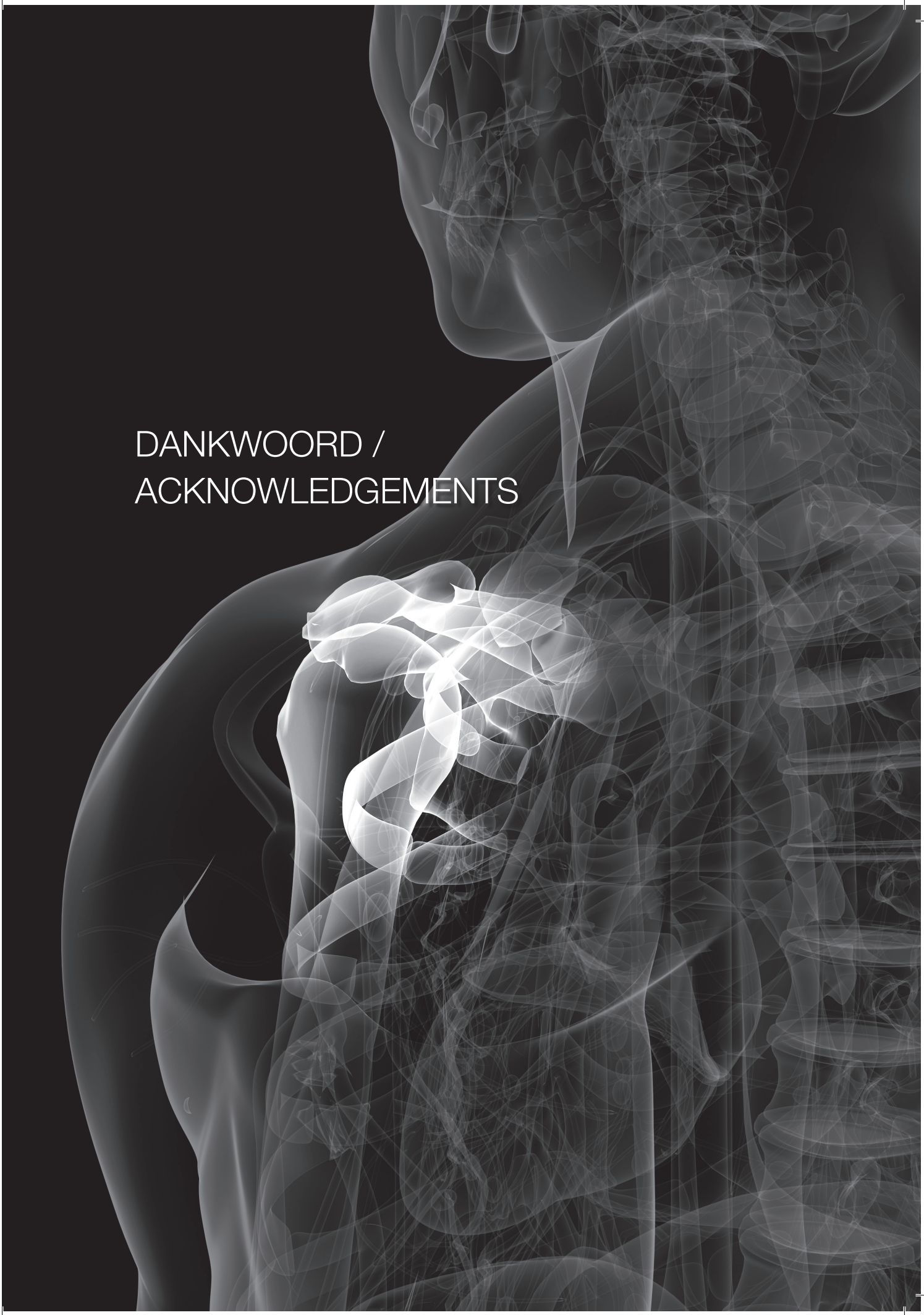
In **hoofdstuk 7** worden de discussie en belangrijkste conclusies van dit proefschrift gepresenteerd.

De belangrijkste conclusies van dit proefschrift zijn:

- MTrPs leveren een veelbelovende verklaring en nieuwe behandelmogelijkheden voor schouderpijn, gebaseerd op pathofysiologische inzichten.
- MTrPs in schouderspieren kunnen voldoende betrouwbaar worden vastgesteld door palpatie en zijn een belangrijke aanvulling op het lichamelijk onderzoek.
- MTrPs komen veelvuldig voor in schouderspieren bij patiënten met chronische, enkelzijdige, niet-traumatische schouderpijn.
- De meeste actieve MTrPs werden gevonden in de M. infraspinatus, de M. trapezius (pars descendens) en de M. deltoideus (pars medius). De meeste latente MTrPs werden gevonden in de M. teres major, M. deltoideus (pars anterior) en de M. trapezius (pars ascendens).
- De behandeling van MTrPs in schouderspieren bij patiënten met chronische, enkelzijdige, niet-traumatische schouderpijn is effectief.
- De effectieve behandeling van MTrPs in schouderspieren bij patiënten met chronische, enkelzijdige, niet-traumatische schouderpijn neemt 12 weken in beslag bij een frequentie van één behandeling per week.

Voetnoten

1 De subacromiale ruimte is aan de bovenzijde begrensd door het acromion, het ligamentum coraco-acromiale en het processus coracoideus en aan de onderzijde door de bovenrand van de cavitas glenoidale, het labrum glenoidale en het caput humeri.
2 Referred pain is pijn die niet gevoeld wordt op de plek van de weefselbeschadiging, maar die gevoeld wordt op enige afstand van die plek. Dit wordt vaak omschreven als uitstralende pijn of irradiatie.
3 Local twitch response (LTR) is een korte contractie van een groep spiervezels in de strakke streng (taut band). Deze LTR ontstaat als gevolg van een korte dwarse manipulatie van de strakke streng of door het aanprikken van het MTrP met een (injectie, emg of acupunctuur) naald.
4 Jump sign is een algemene respons van de patiënt in de vorm van grimassen, kreunen, terugtrekreactie als reactie op de palpatie van een MTrP.
5 Actieve MTrPs veroorzaken spontane pijn in rust of bij (herhaald) bewegen. De pijn die ontstaat als gevolg van palpatie wordt door de patiënt herkend als de 'bekende' pijn. Latente MTrPs hebben alle karakteristieken van een MTrP, zijn ook drukpijnlijk, maar geven bij palpatie geen herkenbare pijn.



DANKWOORD / ACKNOWLEDGEMENTS

DANKWOORD

Het schrijven van een proefschrift voelt als het lopen van een marathon. Des te verder men komt, des te moeilijker wordt het. Alle aanmoedigingen, die vanaf de zijkant worden toe geroepen maken het lopen niet gemakkelijker, maar zorgen dat opgeven geen optie meer is.

Dit proefschrift was niet tot stand gekomen zonder de hulp en aanmoedigingen van heel veel mensen, zoals familie, vrienden, kennissen en collega's.

Speciaal wil ik ook alle patiënten noemen, die in de afgelopen jaren mij hun vertrouwen hebben geschonken en mij ontzettend veel geleerd hebben. Een groot aantal patiënten en proefpersonen hebben meegewerkt aan de verschillende onderzoeken. Voor hen een speciaal woord van dank.

Verder wil ik in het bijzonder nog noemen:

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De manuscriptcommissie bestaande uit prof. dr. C. van Weel, prof. dr. P.L.C.M. van Riel, prof. dr. L.A.L.M. Kiemeney, prof. dr. P.U. Dijkstra en prof. dr. R.L. Diercks dank ik hartelijk voor de snelle beoordeling van het manuscript.

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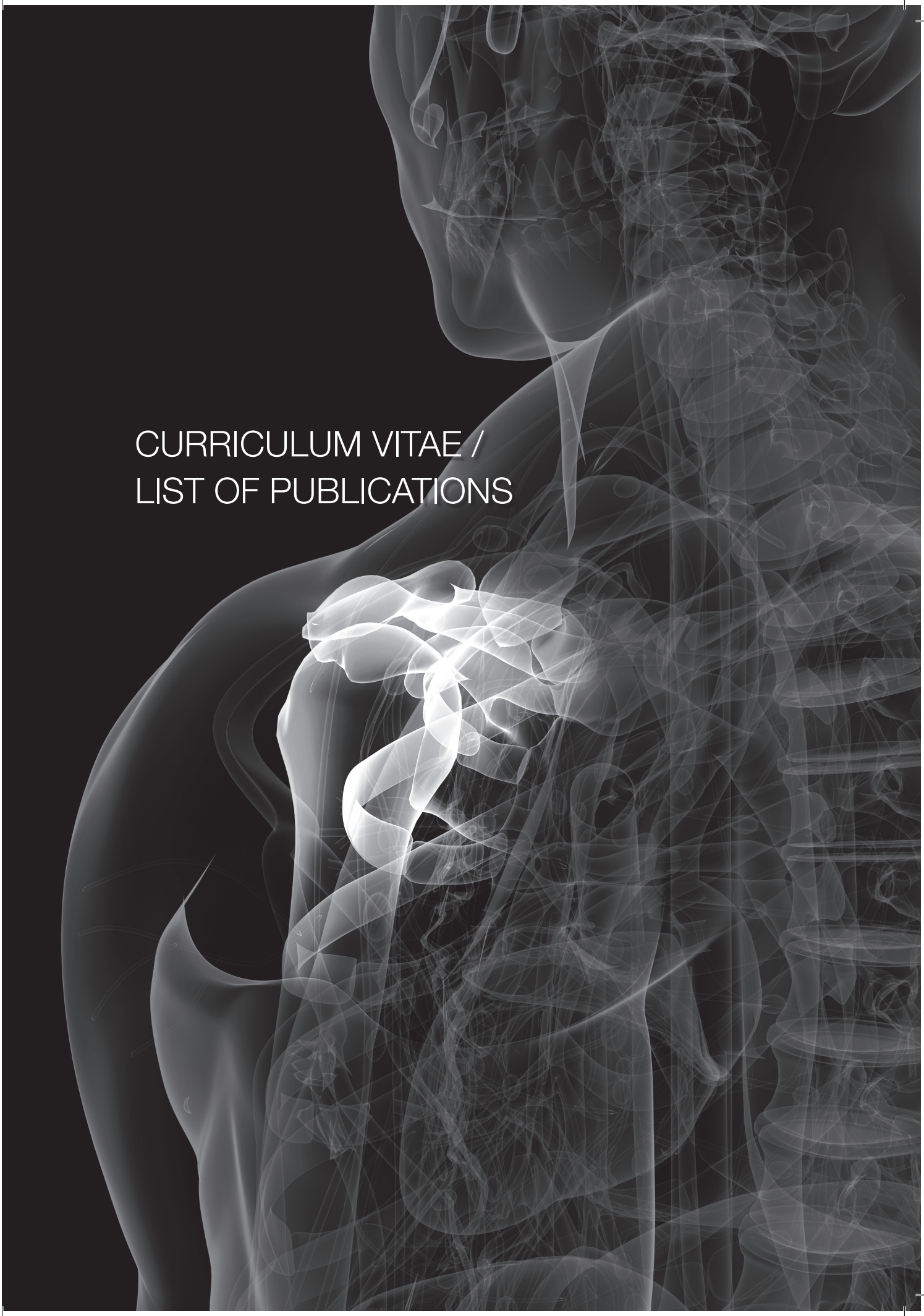
Dennis, Jasper, Annick en Maria. Jullie zijn het mooiste wat er is. Vele malen belangrijker nog dan een proefschrift.



CURRICULUM VITAE / LIST OF PUBLICATIONS

CURRICULUM VITAE

Carel Bron is a manual physical therapist. He is co-owner of the Physical Therapy Practice for Neck, Shoulder, and Upper Extremity Disorders in Groningen, The Netherlands and co-founder of the Myofascial Pain Seminars Groningen.

Carel Bron was born on December 13th 1956, in Winschoten, the Netherlands. Upon graduating from the Wessel Gansfort College in Groningen, he studied physical therapy between 1975 and 1979 at the Academie voor Fysiotherapie in Groningen. After his graduation he worked as physical therapist at the University Medical Center Groningen (formerly known as Academic Hospital Groningen) until 1991. In 1983, he commenced his manual therapy studies at the Stichting Opleidingen Manuele Therapie (Foundation of Manual Therapy Education) in Eindhoven and Amersfoort, the Netherlands and graduated in 1988.

In November 2002, he started his PhD-studies at the Scientific Institute for Quality of Healthcare (IQ-healthcare, department Chair: Prof. dr. R. Grol) at that time known as the Centre for Quality of Care Research, Radboud University Nijmegen Medical Centre.

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