Introduction

Anterior cutaneous nerve entrapment syndrome (ACNES) is a painful abdominal wall neuropathy. Throughout the twentieth century it received sporadic attention in medical practice as a non-visceral cause of abdominal pain, although the diagnosis remained controversial.[1-4] The start of the 21st century marked a surge of emerging evidence regarding etiology, epidemiology and treatment.[5-8] Less controversial, but anatomically related and of frequent incidence, surgeons have become increasingly aware of chronic post-surgical inguinal pain (CPIP) as a complication of hernia surgery. [9,10] These two neuropathic pain syndromes of the trunk are the primary focus of this thesis.

Although ACNES may seem a rare condition, its incidence in patients evaluated for acute abdominal pain in an emergency department of a large teaching hospital was approximately 2%.[11] Patients present with a localized dull anterior abdominal pain in a predictable fingertip area within the abdominal wall, often attenuated with certain activities or postures. The pain may radiate towards the flank or back and its onset is often acute without any evident cause, worsening over time. The pain is frequently located on one side although it may occur bilaterally. It is often very severe, mimicking acute visceral pathologies such as acute appendicitis or diverticulitis. Some patients experience nausea or other typically visceral complaints.

An increasing number of physicians diagnose ACNES in first- and second line practices as knowledge and schooling is currently more appropriate. These developments provide an opportunity to learn more about the syndrome by analyzing large cohorts of patients and to initiate randomized clinical trials validating the efficacy of current treatments such as trigger or tender point injection therapy and surgical neurectomy.[12,13] These investigations become ever so pressing as some ACNES patients may have a somewhat atypical presentation, may suffer from recurrent pain after an initial recovery or may demonstrate no response to therapy. These latter patients are increasingly recognized in the Netherlands and fuel the search for new treatment modalities.

Similar to ACNES, patients suffering from CPIP may also face an array of treatment challenges. Herniorrhaphies, or hernia repair surgeries, are performed 800.000 times a year in the U.S., bringing the lifetime risk for males in the industrialized world to receive this operation up to 27%.[14] It is becoming clear that 10-12% of these patients end up reporting chronic pain after the operation, and some 2% indicating that their pain level is very severe and debilitating.[15] In 30% of these CPIP patients, the pain is neuropathic due to sheer intraoperative manipulation or damage of one of the three inguinal nerves, mostly the ilioinguinal nerve.[16] Complaints can be mild or severely interfering with the patient's wellbeing and daily life. A recent study estimated that the socioeconomic costs of one CPIP patient amount up to 60.000 USD per person per year.[17] A triple or selective neurectomy luckily provides lasting pain relief in the majority of patients.[18] However, individuals with no treatment response have few options left.[19]

This scarcity of alternative treatments may change with the introduction of dorsal root ganglion (DRG) spinal cord stimulation (SCS). Neuromodulation for the treatment of chronic pain has been used for over a century.[20] The first neuromodulative use of electricity in the area of the spine aiming at pain relief was conducted by Norm Shealy in 1967 and is now used in adjusted forms in over 40,000 new patients each year.[21] Several recent systematic reviews have provided evidence that this stimulation technology is a safe and effective treatment option for patients suffering from chronic, intractable pain.[22-24] Large, prospective trials found significant reduction in pain using SCS in failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS). However, pain relief comes with a price, as the stimulation may result in paraesthesia in areas adjacent to the spinal level of SCS.[29] DRG stimulation, in contrast to traditional systems, specifically targets the DRG instead of the dorsal columns in the spinal cord.[30] This technique exists since 2011 and is the only form that can be safely used for discrete targets such as a single intercostal or inguinal nerve without interfering with vital ascending neural pathways such as bladder control. This novel tool might become an important treatment modality for CPIP as well as ACNES.

AIMS AND CONTENT OF THIS THESIS

General aim is to discuss new insights regarding etiology, epidemiology and treatment of ACNES and CPIP. Specific topics are the following:

Chapter 2 looks closely at the complex anatomy of intercostal nerves in the abdominal wall in a single cadaver study. **Chapter 3** describes the largest series of ACNES patients to date and provides major and minor criteria potentially defining the syndrome. In **chapter 4**, a hot topic in pain medicine is addressed: Do corticosteroids contribute to the therapeutic effect of peripheral nerve blocks? **Chapter 5** aims to answer this question with a randomized single-blinded controlled trial comparing multiple successive blocks of lidocaine versus lidocaine + corticosteroids in ACNES patients. In **chapter 6** we report the efficacy of such injection regimen in children with ACNES. Because of the relative low success rate of injection therapy, most ACNES patients eventually receive additional treatments in the form of a neurectomy. The success rate of this therapy is approximately 70%: **chapter 7** addresses the question whether patient characteristics may predict outcome. If a neurectomy fails, **chapter 8** explores whether dorsal root ganglion (DRG) stimulation is a viable option for treating these therapy resistant ACNES patients. **Chapter 9** includes these treatment considerations in updated Dutch Pain Guidelines that, for the first time in national history, feature a separate section about ACNES. **Chapter 10** and **11** provide a study protocol and preliminary results of a randomized clinical trial assessing the efficacy of DRG SCS in CPIP patients who were resistant to an inguinal neurectomy.

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