High-Frequency, High-Intensity Transcutaneous Electrical Nerve Stimulation for Postoperative Pain

- **Evaluating a new treatment regime and a clinical bedside prediction test in outpatient surgery**

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"Etiamsi Deus ipse cras adveniat, hodie meum malum serere velim"

attributed to Martin Luther (1483-1546)

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ABSTRACT

The incidence of postoperative pain is high, even after minor surgery, despite multimodal analgesic treatment plans. The aim of this thesis is to explore ways to improve postoperative pain in outpatient surgery.

Study I examined the ability of a clinical bedside test, the assessment of pain during peripheral venous cannula insertion, in an observational study to predict postoperative pain intensity in the post-anesthesia care unit (PACU). The findings indicate that this test is useful for predicting pain and time in the PACU. **Study II** evaluated the pain-relieving effects of high-frequency, high-intensity transcutaneous electrical nerve stimulation (HFHI TENS) compared to opioids after outpatient gynecological surgery in a systematic review and a meta-analysis. Findings revealed no difference in pain relief between HFHI TENS and opioids. HFHI TENS was opioid-sparing and reduced time in the PACU. **Study III** investigated the effects on time in the PACU and pain relief of HFHI TENS compared to opioids after laparoscopic cholecystectomy in a randomized controlled trial. The time in the PACU and pain intensity when leaving the PACU did not differ between randomized groups, but patients randomized to HFHI TENS consumed significantly less opioids than patients randomized to opioids. **Study IV** explored patients' experiences of using HFHI TENS for postoperative pain relief in a qualitative study. Results showed that patients desire alternatives to pharmaceuticals for pain relief after surgery and that HFHI TENS increased feelings of safety and autonomy. **Study V** investigated healthcare professionals' experiences of using HFHI TENS for postoperative pain relief in an interview study. Findings revealed that experiences regarding the efficacy of HFHI TENS were mixed. Opioids were considered simpler to administer than HFHI TENS, but HFHI TENS was acknowledged due to its prompt effect in responders and limited adverse effects.

Conclusion: Postoperative pain and time in the PACU can be predicted using a simple clinical preoperative test. HFHI TENS is an effective, opioid sparing

alternative for postoperative pain relief, an option that is desired by the patients.

Keywords: Prediction of postoperative pain, Transcutaneous electrical nerve stimulation, Perioperative nursing, Postoperative pain, Opioids, Outpatient surgery.

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SAMMANFATTNING PÅ SVENSKA

Postoperativ smärta är vanligt förekommande, och i många fall svår. Att förutse den enskilda individens risk att få svår postoperativ smärta är problematiskt, men vissa faktorer kan vara till hjälp vid en bedömning före operation. Sjukvården kan då anpassa den smärtlindring som ges i samband med operation efter individens behov.

Konsekvenser av postoperativ smärta inbegriper problem med rehabilitering och det finns en risk att den akuta smärtan utvecklas till en bestående, långvarig smärta. Risken för utveckling av långvarig smärta ökar om den akuta smärtan är svår eller kvarstående. Därför är det viktigt att behandla den akuta postoperativa smärtan optimalt. Opioider (till exempel morfin) utgör en hörnsten i behandlingen av svår akut smärta, men har biverkningar som kan påverka återhämtningen efter operation. På lång sikt finns en risk att utveckla ett långvarigt bruk och ett beroende av opioider, vilket medför stora hälsorisker.

Denna avhandling undersöker ett kliniskt test för prediktion av postoperativ smärta samt smärtlindrande och opioidsparande effekter av högfrekvent, högintensitets transkutan elektrisk nervstimulering (HFHI TENS), postoperativt på uppvakningsavdelningen (UVA). Avhandlingen bygger på fem delstudier.

I delstudie I undersöktes om ett kliniskt pre-operativt test kunde predicera smärta på UVA. Testet utfördes genom att man bad patienter smärtskatta insättandet av en perifer venkanyl, något alla patienter förses med före sin operation. Därefter fick patienterna skatta sin smärta på UVA, efter operation. Resultaten visade att testet kan predicera postoperativ smärta och vårdtid på UVA.

Delstudie II utgjordes av en systematisk översikt och metaanalys av HFHI TENS jämfört med opioider för smärtlindring efter dagkirurgisk gynekologisk kirurgi. Resultaten visade att det inte var någon skillnad mellan grupperna avseende smärtlindring. HFHI TENS var opioidsparande och minskade tiden på UVA.

Delstudie III var en randomiserad kontrollerad prövning, där patienter med postoperativ behandlingskrävande smärta efter laparoskopiskt borttagande av

gallblåsan lottades till olika grupper, en grupp där HFHI TENS var första behandlingsalternativ och en grupp där patienten fick opioid efter kliniska riktlinjer. Tid på UVA och smärtintensitet när man lämnade UVA skiljde sig inte åt mellan grupperna, men patienterna som lottats till HFHI TENS konsumerade signifikant mindre mängd av opioider.

I delstudie IV utforskades patienternas upplevelse av att få behandling med HFHI TENS för postoperativ smärta på UVA. Resultaten visade att patienterna önskar icke-farmakologiska alternativ för smärtlindring, och att HFHI TENS ökade trygghet och självständighet under den postoperativa tiden på sjukhuset. Däremot var upplevelsen att HFHI TENS inte fungerar som smärtlindring när den postoperativa smärtan är för svår.

I delstudie V undersöktes hur sjukvårdspersonalen upplever att använda HFHI TENS för smärtlindring på UVA. Här visade resultaten delade uppfattningar kring effektiviteten av HFHI TENS. Opioider uppfattades som lättare att administrera än HFHI TENS, men HFHI TENS var fördelaktigt utifrån snabb smärtlindrande effekt för personer som svarar på behandlingen samt till följd av frånvaron av biverkningar.

Konklusion: Postoperativ smärta och vårdtid på UVA kan prediceras med ett enkelt kliniskt pre-operativt test. HFHI TENS är ett effektivt, opioidsparande alternativ för postoperativ smärtlindring, något som patienterna önskar.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Ögren, C; Varkey, E; Angelini, E; Ögren, T; Wolf, A; Ringdal, M; Andréll, P. Assessment of pain induced by peripheral venous cannulation – a clinical bedside test for prediction of postoperative pain. Submitted.

II. Piasecki, A; **Ögren, C**; Thörn, S-E; Olausson, A; Svensson, C J; Platon, B; Wolf, A; Andréll, P. High-frequency, high-intensity transcutaneous electrical nerve stimulation compared with opioids for pain relief after gynecological surgery: a systematic review and meta-analysis. *Scand J Pain*. 2023;24: 20230068.

III. Ögren, C; Varkey, E; Wolf, A; Larsson, C; Ringdal, M; Andréll, P High-frequency, high-intensity TENS compared to standard treatment with opioids for postoperative pain relief after laparoscopic cholecystectomy: A multicenter randomized controlled trial. *Eur J Pain*. 2024; 28:1772–1784.

IV. Angelini, E; Josefsson, C; **Ögren, C**; Andréll, P; Wolf, A; Ringdal, M Patients´ experiences of TENS as a postoperative pain relief method in the post-anesthesia care unit after laparoscopic cholecystectomy: a qualitative study. *BMC Anesthesiol* 2025; 25:18.

V. Ögren, C; Angelini, E; Rehnberg, U; Andréll, P; Wolf, A; Ringdal, M Health care professionals' experiences of using TENS for postoperative pain relief after laparoscopic cholecystectomy – an interview study. Submitted.

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ABBREVIATIONS

ACC Anterior cingulate cortex

ANOVA Analysis of variance

ANCOVA Analysis of co-variance

AUC Area under curve

CAS Colored analogue scale

COX Cyclooxygenase

CPM Conditioned pain modulation

CPOT Critical care pain observation tool

DNIC Diffuse noxious inhibitory control

FAS Full analysis set

FLACC Face leg activity cry consolability scale

FPS-R Face pain scale revised

HFHI TENS High-frequency, high-intensity transcutaneous electrical nerve stimulation

HPA Hypothalamic- pituitary -adrenal axis

HR Hazard ratio

Hz Hertz

IASP International association for the study of pain

ITT Intention to treat

IV Intravenous

µs Microsecond

mA Milliampere

MCID Minimal clinically important difference

MEP Movement evoked pain

MME Morphine milligram equivalent

NRS Numerical rating scale

NSAID Non steroid anti-inflammatory drug

OIVI Opioid induced ventilatory impairment

OR Odds ratio

PCC Person-centered care

PICO Population, intervention, comparison, outcome

PO Per os, orally

PONV Postoperative nausea and vomiting

PROM Patient reported outcome measures

QST Quantitative sensory testing

ROC Receiving operating characteristic

RSS Ramsey sedation scale

(R)TA (Reflexive) thematic analysis

SAM Sympathetic-adrenal-medullary axis

TENS Transcutaneous electrical nerve stimulation

TSA Trial sequential analysis

VAS Visual Analogue Scale

VRS Verbal Rating Scale

DEFINITIONS IN SHORT

Abbey pain scale: Behavioral pain scale for adults who are cognitively challenged assessing six domains verbal and facial expressions, body language and behavior and changes in physiological and somatic parameters (1).

Allodynia: “Pain due to a stimulus that does not normally provoke pain” (2).

Acupuncture-like TENS: Transcutaneous electrical nerve stimulation given with low frequency and high intensity.

CAS: A self-reporting pain scale for children with two sliding parts, one with a color gradient in a shape that widens towards the top. The bottom is labeled “no pain” and the top “very much pain”. The second part is a numeric ruler from zero to ten.

Conventional TENS: Transcutaneous electrical nerve stimulation given with high frequency and comfortable intensity.

CPOT: Behavioral pain scale designed for critically ill patients, consisting of four domains with special assessments for intubated patients.

FLACC: Behavioral pain scale, designed for children, mainly used with procedural pain. Five domains are assessed (face, legs, activity, cry and consolability). It is important to remember that a quiet child still can have pain.

FPS-R: Face pain scale revised, a self-reporting scale for children and adolescents using faces with different expressions, from happy to sad. Note that using face pain scales for patients that are not native speakers tend to give suboptimal assessments (3).

HFHI TENS: Transcutaneous electrical nerve stimulation given with high frequency and high intensity.

Hyperalgesia: “Increased pain from a stimulus that normally provokes pain” (2).

Neuropathic pain “Pain caused by a lesion or disease of the somatosensory nervous system” (2).

Nociceptive pain: “Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors” (2).

Nociplastic pain: “Pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain “ (2).

NRS: Numeral rating scale 0 to 10, where 0 equals no pain/no nausea/not satisfied/ not acceptable and 10 the worst imaginable pain/nausea/completely satisfied/ completely acceptable for self-reporting of pain/nausea/satisfaction (with care and treatment)/ acceptability (of treatment).

QST: measuring a person's sensory thresholds to different types of stimuli, such as temperature, pressure, and vibration.

Ramsey scale: a six-point numerical scale used to measure sedation, that categorizes patients from severe agitation to deep coma.

Sensitization: “Increased responsiveness of nociceptive neurons to their normal input, and/or recruitment of a response to normally subthreshold inputs” (2).

VAS: Visual analogue scale for self-reporting pain or nausea. The patient indicates their pain/nausea either with a cross along a 10 cm line or by moving a movable marker between the endpoints 'no pain/nausea' (0) and 'worst possible pain/nausea' (10). The indicated pain is then read using a ruler, or alternatively on the back of the VAS stick, which shows a graduated scale. Note that sometimes you state the result in mm 0-100 instead of cm.

VRS: verbal rating scale for self-reporting pain in six steps, where colloquial words are used to describe pain, from “none” to “unbearable”.

1 PREFACE

Early in my career as a nurse I observed that many patients experienced significant pain. At that time, prevailing attitudes often suggested that female patients who reported pain were not providing specific enough information and, consequently, their reports were sometimes dismissed under the assumption that they sought attention rather than pain relief. It was also conveyed to me that newborns were believed not to experience pain, with premature infants thought to be even less sensitive. Opioids were the solution for every "real" pain.

I advanced my nursing career by becoming a registered nurse anesthetist (RNA), where I applied clinical guidelines for analgesic administration to minimize the risk of patients experiencing pain upon awakening from anesthesia. Additionally, in the post-anesthesia care unit (PACU), I focused on facilitating effective pain relief for patients during their recovery. Subsequently, advancements such as epidural and spinal techniques were developed, and the approach of multimodal analgesia was implemented. Nevertheless, a significant number of patients continued to experience severe pain in the PACU.

Pain knowledge since then has made enormous progress and research indicates that opioids are not a universal solution for pain management, and even when effective, the use of them is accompanied by significant adverse effects.

To enhance my knowledge of pain, I studied the literature and began working in Pain Centers. I learned about the complexity of the phenomena of pain, well expressed by my former head, Professor Clas Mannheimer, at the Pain Center in Gothenburg: "Pain is something we do not fully understand, which we treat with methods that we don´t know how they work". During this time, I learned about transcutaneous electrical nerve stimulation, TENS. It was an intervention at that time mostly used by physiotherapists, and mostly for persistent pain, but I did not see that being a physiotherapist was a prerequisite for using TENS and why it could not be used for acute pain.

I wanted to research the effects of TENS in postoperative acute pain. Many things then came happily together: the above-mentioned Professor Clas

Mannheimer used high-frequency, high intensity transcutaneous electrical nerve stimulation (HFHI TENS), for acute angina pectoris pain and a colleague of mine, RNA Birgitta Platon, was performing research on HFHI TENS after gynecological surgery and I resumed contact with one pain physician, who also is a senior researcher, at the pain center in Gothenburg, Associated professor Paulin Andréll. She is now my primary supervisor for the thesis.

Many years of study and research have resulted in this thesis. It encompasses holistic research, starting with trying to predict the individuals´ risk of postoperative pain and incidentally confirming the high frequency of postoperative pain, searching the literature for evidence of HFHI TENS' effectiveness in the postoperative context, performing an RCT, and finally interviewing stakeholders in the HFHI TENS treatment. Thus, the thesis has merged statistical significance with patients´ and healthcare professionals' views of HFHI TENS as a method for pain relief in the PACU. This thesis aims to provide current and future colleagues with insight into postoperative pain and present suggestions on the application of HFHI TENS in postoperative care.

2 INTRODUCTION

Pain is a distressing and complex experience, a mosaic involving factors that are biological, psychological, and social in origin. Postoperative pain remains insufficiently managed, as demonstrated by both older and more recent surveys reporting comparable findings. Managing postoperative pain presents ongoing challenges for both patients and healthcare professionals, and current healthcare practices have limited ability to predict which individuals will experience moderate to severe pain following surgery.

While consensus is that younger age and female sex are risk factors for more intense postoperative pain (4-6), this knowledge is not systematically utilized in the clinical context. Adding a clinical bedside test could aid us in finding at-risk patients preoperatively and acting preventively by adding measures to their multimodal pain management plan. Likewise, the current multimodal pain management plans have been in place for decades but still leave at least 20 – 40% of postoperative patients in moderate-to-severe pain (7, 8). Opioids are a cornerstone in treating moderate-to-severe postoperative pain, but they have adverse effects, which limit their use. In the short term, this includes respiratory depression, nausea, obstipation, and sedation (9). Over the long term, approximately 6% of patients persist with opioid use following surgery (10, 11) and this has negative impacts on health and quality of life. Moreover, there is a risk of developing chronic pain after surgery, not restricted to major surgeries, which can be correlated to intense postoperative pain (12-14). Chronic pain adversely affects patients' quality of life and contributes to considerable socioeconomic costs in society (15). Therefore, it is essential for healthcare to incorporate effective, opioid-sparing approaches, such as TENS, in the multimodal peri-operative pain management plans.

TENS has existed as an option for pain relief since the 1970s. Although it may be underused in the context of postoperative pain, despite existing evidence (16), it is sometimes used to prevent and treat postoperative nausea and vomiting (PONV) (17). One stimulation regime, HFHI TENS, is of particular interest for the treatment of postoperative pain, since the pain-relieving effect can be evaluated in just minutes. TENS offers independence and autonomy, as the patient can handle the device, and thus the pain treatment, themselves.

Furthermore, the body of evidence supporting person-centered care (PCC) continues to grow, highlighting autonomy and patient participation as fundamental principles for achieving improved patient outcomes, which makes TENS especially valuable in this context. Thus, proffering TENS as a complementary and/or alternative modality to standard postoperative pain treatment with opioids could contribute to personalized care, as could the prediction of individual risk for postoperative pain intensity.

This thesis is based on research that evaluated a clinical bedside test for predicting the risk of moderate-to-severe postoperative pain (Study I), evaluated HFHI TENS in two different surgical contexts (Studies II and III), and investigated the views of patients and healthcare professionals regarding the use of HFHI TENS in postoperative pain management (Studies IV and V).

"I thought TENS worked really well, and I really hope it's a method that gets used more, so people don't have to rely on morphine and end up feeling sick." (participant in study IV)

3 BACKGROUND

3:1 POSTOPERATIVE PAIN

3:1:1 DEFINITIONS OF PAIN

The International Association for the Study of Pain (IASP; 2020) has defined pain as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage" (2).

Pain is described in different ways, as acute, persistent, and recurring chronic or cancer-related, and categorized as nociceptive, neuropathic, or nociplastic. Furthermore, there are biological, psychological, and sociological aspects of pain (18). This complexity has practical consequences, as the treatment of pain in these conditions requires different approaches.

Nociceptive pain is initiated by the activation of a nociceptor in response to tissue trauma such as heat, cold, or mechanical injury. Electrical impulses then relay the sensation along ascending pathways through the spinal cord to the brain, where several structures participate in forming the perception of pain. Thus, nociception and pain are diverse phenomena. Acute nociceptive pain caused by tissue trauma is a process to protect an individual from injury or ongoing harm and is essential for survival; however, if left untreated, it can lead to negative outcomes. Neuropathic pain is best described as a lesion, a break in the transmission of electrical impulses, because of an injury or a disease in the transmitting nervous system, which allows spontaneous pain signaling. Nociplastic pain, defined by the IASP (2017), is described as pain that arises from altered nociception (2). These categories of pain may exist simultaneously in an individual, and it is possible to have so-called mixed pain.

In the pain research community, we work with the bio-psycho-social model (19). Much clinical evidence supports the impact of psychological and sociological elements on chronic pain (defined as pain lasting > 3 months). It may seem that these aspects of the pain mosaic are less complicated in acute postoperative pain, but social and psychological factors still enter the

equation (4, 20). Yet, this receives little consideration in perioperative pain management.

Postoperative pain is primarily nociceptive, though it can encompass strands of acute neuropathic pain. It is never, by itself, nociplastic. Obviously, postoperative patients can suffer from prior neuropathic or nociplastic pain or both. This thesis is focused on acute, nociceptive, postoperative pain, particularly in the context of outpatient surgery.

3:1:2 ANATOMY AND PHYSIOLOGY

Nociception does not equal pain; it is neither sufficient nor necessary for the experience of pain. Nociception is a neural activity in which noxious stimuli are encoded. The IASP points out that "Consequences of encoding may be autonomic (e.g., elevated blood pressure) or behavioral (e.g. motor withdrawal reflex). Pain sensation is not necessarily implied." (2)

The encoding of the noxious stimuli requires transduction, which can briefly be described as a conversion of the energy from a tissue injury to an electrical impulse. It also requires transmission. Nociceptive stimuli are transmitted via lightly myelinated Aδ fibers responsible for the first sharp pain, and unmyelinated C fibers responsible for the second dull, aching pain (primary afferent neurons) to the spinal cord's dorsal horn, where they cross to the contralateral side and reach the thalamus through the ascending spinothalamic tract (secondary afferent neuron). Here it synapses with the third order neurons, that project to the somatosensory cortex which is responsible for the sensory-discriminative nature of nociception i.e. intensity and localization and makes perception of pain possible. Parallel projections reaches the hypothalamus, the limbic system, the insula, the anterior cingulate cortex (ACC) and the prefrontal cortex. The connection with the hypothalamus constitutes the foundation for the autonomic responses associated with nociceptive stimulation. The physiological stressor of nociception activates the sympathetic-adrenal-medullary (SAM) axis, acting within seconds, and the hypothalamic-pituitary-adrenal (HPA) axis, acting within minutes (21). Activation of structures in the limbic system, the insula and the ACC are responsible for the emotional-affective components of pain, e.g., anxiety and fear, while activity in the prefrontal cortex reflects the cognitive-evaluating components, such as the cause of the signaling and the meaning of it. The biochemical origin of nociceptive pain is the inflammatory

reaction due to tissue injury; thus, the immune system participates in nociceptive transmission (22). Ongoing pain causes increased responsiveness of nociceptive neurons and recruits new neurons for signaling, leading to sensitization. The area surrounding the wound becomes tender due to peripheral sensitization. Both spinal and supraspinal structures take part in developing central sensitization, creating widespread allodynia (pain after an innocuous stimulation) and hyperalgesia (increased pain sensitivity, i.e., exaggerated pain response after a painful stimulus) (23).

Nociceptive signaling is modulated by segmental inhibition in the spinal cord according to the gate control theory. The basic model for the gate control theory describes how Aβ nerve fibers that mediate touch and vibration can inhibit transmission of the nociceptive signal in the spinal cord (24), though more recent research suggests that this model is incomplete (25). Extra segmental systems, i.e., the endogenous opioid system and the descending inhibitory pain pathways, modulate nociceptive signaling together. Monoamines, such as serotonin, noradrenaline, and dopamine, in the descending pain pathways can increase or decrease pain by facilitating or suppressing nociceptive signaling (26, 27). Pain pathways show considerable plasticity, an ability to change their structure and function in different ways. Coping strategies, cognition, social factors, and emotion all play a role in modulating the pain experience. In summary, many systems and subsystems are involved in the experience of postoperative pain, and the interactions between them show a great level of complexity (28, 29).

3:1:3 PREVALENCE

Postoperative pain is universal. Many patients (20 – 40%) report severe pain after surgery, and less than 50% assess their postoperative pain relief as sufficient (30-32). Treating postoperative pain is a clinical challenge and entails achieving a balance between ensuring an adequate degree of pain relief and minimizing the adverse effects of pain-relieving drugs. Acute pain that is not sufficiently treated engenders complications, such as respiratory and cardiovascular events, and hampers recovery.

Even minor surgery can result in severe pain (32). Acute postoperative pain may develop into chronic pain, persisting months or even years after surgery. Risk factors for these events are not clearly understood, but by consensus are agreed to involve high intensity and/or prolonged duration of severe

postoperative pain, among other factors (13, 33). The prevalence of chronic pain is reported to be up to 50% after surgery, and it is severe and seriously impairs the quality of life in 2 – 10% of these patients (34). The risk of chronic pain is not restricted to major surgeries but can develop after minor procedures such as those performed in outpatient surgery (12-14).

3:1:4 PREDICTION

Predicting the intensity of postoperative pain has been the focus of many studies. Some studies have made use of quantitative sensory testing (QST), which aims to determine an individual's pain sensitivity by using modalities such as heat, cold, pressure, and/or electricity (35). Measures that are investigated include detection limit, pain threshold, and suprathreshold limits, i.e., pain tolerance limit. Different modalities essentially test different aspects of nerve fiber function. Many reviews have summarized the studies and the existing methods' potential to predict pain sensitivity in an individual (36, 37). Recent studies have incorporated the testing of more central components to QST, i.e., temporal summation of pain and conditioned pain modulation (38), and some have also investigated biomarkers and brain morphology (39, 40). These tests all can identify patients at high risk of developing moderate-to-severe postoperative pain, but they require time and resources not available in routine perioperative care, and so they are only really used in clinical research.

Several screening tools have been created using questionnaires and demographic factors, sometimes coupled with intraoperative measures (41). Regarding associated demographic factors, there exists consensus about sex and age, where female sex and younger age seem to predict heightened pain sensitivity. Also, preoperative pain, preoperative consumption of opioids, skin incision size, smoking, poor sleep, and comorbidities, such as anxiety and depression, have been demonstrated to increase the risk of moderate-to-severe postoperative pain (4, 5, 42). Some of these factors are modifiable, others are clearly not. Interestingly, patients' own expectations about postoperative pain have been demonstrated to be fairly accurate in predicting the intensity of reported postoperative pain (43, 44).

There are a few commercially available tools for discerning nociception during surgery, which are perhaps superior to routine clinical evaluation (45). These tools – by predicting the intensity of postoperative pain – could serve

as a guide for opioid dosing and the initiation of other interventions, such as clonidine and/or ketamine, before arousing the patient from anesthesia. However, these tools are obviously not usable preoperatively.

Some studies have used a clinical tool, a bedside test, to predict the intensity of postoperative pain or labor pain, such as assessing pain intensity when injecting local anesthesia before establishing spinal anesthesia or when inserting a peripheral venous cannula (46-50).

3:1:5 ASSESSMENT

The presence and the intensity of pain cannot be measured by any objective methods; therefore, only the person experiencing pain can decide whether it is present and how intense it is (51). This has been acknowledged in the pain research community for many decades (52). Thus, self-reporting of pain is considered the gold standard, the foundation of assessment, and should always be encouraged. It is important to acquire this measure repeatedly and avoid assumptions based solely on the patient's appearance (53). There exist several scales for self-reporting, e.g., Visual Analogue Scale (VAS), Numerical Rating Scale (NRS), Verbal Rating Scale (VRS), the Face-Pain Scale-Revised (FPS-R) and the colored analogue scale (CAS) (54). Recently, a digital form has been constructed, the Electronic Faces Thermometer Scale (eFTS) (55). However, it should be appreciated that not everyone can produce a pain score upon demand (56) and it should be recognized that with these scales, we only measure one dimension of pain, namely the intensity. Thus, these self-reporting scales are unidimensional, while pain itself is a multidimensional experience. They also depend on language and cultural expressions, making it intensely important that culturally skilled interpreters are used (3) when the patient is not a native speaker. However, acknowledging cultural and social factors that influence the pain experience must not preclude treating the patient as an individual, and remembering that the healthcare professional also belongs in a cultural framework (57). Another limitation of these scales is that certain vulnerable populations cannot self-report, e.g., newborns, small children, patients with dementia or otherwise cognitively impaired, and critically ill patients, but obviously, these conditions do not exclude the experience of pain (56). For these populations, behavioral scales have been developed, e.g., the Face, Legs, Activity, Cry, Consolability (FLACC), the Abbey Pain Scale, and the Critical Care Pain

Observation Tool (CPOT). However, pain measured with these tools cannot be equated to self-reported pain.

Still, in clinical reality, even while healthcare professionals in the PACU ask patients to self-report, they also incorporate vital signs, body language, and facial expressions in their assessment, and their experiences of what intensity of pain to expect after a particular surgical procedure, and from these parameters, infer the intensity of the pain.

3:1:6 HOW MUCH PAIN RELIEF IS ENOUGH?

How much pain relief that is enough depends partly on what intensity of pain we are departing from. The higher the pain intensity, the larger the reduction (i.e., decrease in NRS score) is needed for the patient to experience meaningful pain relief (58).

In this regard, research has aimed to determine the so-called minimum clinically important difference (MCID). We are still talking about pain intensity, but anchoring the change in intensity, e.g., an NRS score, to a patient's feeling of improvement or deterioration in their pain, asking them if the pain is better or worse (59). The MCID is often regarded as a constant, but may need to be personalized, since the meaning of change in pain is personal, depending on the baseline pain intensity and an individual patient's opinion of sufficient improvement (60). Nevertheless, using a constant facilitates evaluation and comparisons across studies and interventions. This constant has been reported to be a reduction of pain of 1 – 2 units on the NRS, or, more recently, a 50 % reduction in pain intensity (61).

The Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (IMMPACT), requests researchers to ensure that patient perspectives are considered in clinical pain trials (62). Although the recommendations were developed for chronic pain trials, extending their application to acute pain trials appears reasonable.

3:1:7 TREATMENT

Postoperative pain is common (32), and healthcare professionals have an ethical obligation to relieve pain (63). As pain is multifactorial, pain treatment needs to employ several modalities to relieve pain efficiently. No single agent will provide complete pain relief by itself. Therefore, the concept

of multi-modal analgesia has been created (64). Multi-modal pain management plans in the postoperative context typically list paracetamol (acetaminophen) plus non-steroidal anti-inflammatory drugs (NSAIDs) or cyclooxygenase-2 (COX2) inhibitors, at set intervals, usually starting treatment prior to surgery. This is combined with local anesthesia in some form, in outpatient surgery customarily as wound infiltration, and usually a glucocorticoid steroid is administered orally (PO) before surgery or as an intravenous (IV) bolus during the surgery (65). Opioids are added as needed during and after the surgery. Despite the use of these agents, 20 – 40% of patients still experience severe pain postoperatively.

There are two clear advantages of not relying solely on one analgesic agent: 1) different agents achieve an additive or synergistic effect, and 2) the adverse effects of each agent can be kept to a minimum. Paracetamol, NSAIDs, and COX2 inhibitors all have a ceiling effect, as does local anesthesia, after which the pain-relieving effect is no longer increased, only the adverse effects. No such ceiling effect exists for the opioids used in peri-operative contexts. Still, opioids have severe adverse effects, including ventilatory impairment, nausea and vomiting, obstipation, sedation and dizziness, and opioid-induced hyperalgesia, and they contribute to neuroinflammation (9, 22, 66-69). In the longer term, there is a risk of persistent postoperative use of opioids, which has been estimated at 6% and this risk does not differ between major and minor surgery (10). Therefore, the concept of opioid-sparing analgesic regimes has been developed and has been covered in enhanced recovery after surgery, ERAS protocols (70) and also in recent guidelines for postoperative analgesia (71).

Opioid-sparing analgesia, then, is a concept commonly applied in routine pain management, using multimodal pain management plans. In some cases, ketamine (an N-methyl-D-aspartate receptor blocker) and/or clonidine (an old hypertensive medication, an α2 receptor blocker) is/are added (72, 73). Ketamine is used for dissociative anesthesia, but in small doses it can decrease the spread of hyperalgesia and has an additive effect with opioids, while clonidine has both sedative and pain-relieving effects.

Another issue that must be treated postoperatively is postoperative nausea and vomiting (PONV). Risk for PONV is higher in patients who are of female sex (74), which also constitutes a risk factor for more intense postoperative pain. Notably, nausea and vomiting are adverse effects of

opioids and of NSAID: s. PONV is treated by combining different antiemetics such as ondansetron and a glucocorticoid steroid. TENS is also effective for preventing and treating PONV (17).

As pain is a complex phenomenon, there is also a complex interindividual variation in the response to pain medication (75). For example, there is some evidence that patients of female sex need more analgesics to achieve pain relief (76). These factors complicate the process of creating postoperative pain management plans where "one size fits all" and require that adequate pain relief and the risk of adverse effects of medication be carefully weighed against each other.

What we strive for is to ensure that a patient can recover well, without bothersome adverse effects of pain or medication. In this regard, three fundamental prerequisites for enhanced recovery after surgery have been established: nutrition, mobilization, and optimized pain management (64). Further, patient education, attention to psychological comorbidities, and relevant intervention before surgery are also recommended (77), as are complementary methods for pain relief (78).

3:1:8 DOCUMENTATION

Documenting pain assessment results and pain treatment is crucial to ensure the quality of treatment and care. This is one aspect of the pain management plan that is often deficient in clinical practice (79). There are several reasons for this. Nurses in the PACU work in a busy and fast-paced environment, where acting to treat pain is prioritized over documenting it. The demands of documentation may also be seen as an administrative infliction, simply adding to the workload (54). Another reason could be that attempts to document have not achieved any visible results for the patients when physicians are presented with the documentation.

Documentation constitutes a summary of the patient's experience in the PACU and of what pain-relieving methods have been effective, which is important information for subsequent care and for any subsequent surgical procedures. Documentation also has a legal aspect; it is there to protect the healthcare professional.

3:2 SURGICAL PROCEDURES IN THE THESIS

3:2:1 GYNECOLOGICAL OUTPATIENT SURGERY

Gynecological procedures such as surgical abortion, hysteroscopy, and laparoscopic surgery for a variety of reasons, e.g., cyst enucleation and salpingo-oophorectomy, are mostly performed in an outpatient setting. These procedures are common worldwide (80). Although they are characterized as minor operations, there is evidence that patients undergoing these procedures receive insufficient analgesia (32, 81).

3:2:2 LAPAROSCOPIC CHOLECYSTECTOMY

Gallstone disease is common, affects about 6% of the global population and is typically more common in countries with a Western lifestyle (up to 15%) (82, 83). Gallstones may be silent or symptomatic. The prevalence is higher in females, about twice as common as in males, and is associated with obesity and increasing age. Clinical treatment of symptomatic gallstones is cholecystectomy, which can be performed as open surgery, or, more frequently (since 1989), using a laparoscopic approach. Approximately 18 million cholecystectomies are performed annually (84-86). Postoperative pain after laparoscopic cholecystectomy encompasses nociceptive incisional pain and nociceptive visceral pain, including referred nociceptive visceral pain. The average pain intensity on a group level is reported as > 4 on the NRS (32, 87).

3:3 TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

Transcutaneous electrical nerve stimulation (TENS) is a non-pharmacological, non-invasive neuromodulation technique that uses a mild, pulsed, alternating electrical current to alleviate pain. TENS has existed since the 1970s (88). TENS has been used for pain relief in the prehospital context, in the emergency ward, and in postoperative settings (89-95).

Before administration, electrode pads are placed on intact skin so that they surround the painful area. The TENS unit can be set to different stimulation regimes, where the most important parameters are frequency and intensity, and in some situations, pulse-width (duration of the impulse, measured in microseconds; μs). Frequency refers to the number of stimulations per second and is measured in Hertz (Hz). Low frequency is defined as 2 – 10 Hz, and high frequency as 50 – 100 Hz. Intensity refers to the strength of the electrical stimulation and is measured in milli-amperes (mA). High-frequency TENS is administered with a comfortable intensity and aims for paresthesia, which feels like a tingling sensation (conventional TENS). This regime requires about 30 minutes per session to achieve results. Low-frequency TENS is administered at a higher intensity and aims for a muscle twitch (acupuncture-like TENS). It needs to be administered for 20 – 30 minutes per session to accomplish an effect. High-frequency, high-intensity (HFHI) stimulation is a combination of these two regimes and aims to reach deeper structures than conventional TENS while keeping the advantages of the high-frequency stimulation regime. The effect of TENS is dependent on stimulation intensity (96, 97). High intensity can activate C and Aδ fibers in an antidromic manner, thereby suppressing part of the nociceptive signaling, and thus contributing to pain relief (98).

As with all treatments, TENS use is contingent upon the patient's consent, and it is important that the patient decides the intensity of the stimulation. This is especially important when using the HFHI TENS regime, since it can be experienced as uncomfortable and even painful (88, 98). Hence, the HFHI TENS treatment is not used for a duration longer than 1 minute at a time. However, after the 1-minute stimulation session, it is possible to evaluate the pain-relieving effect (99, 100).

On a segmental level, TENS activates Aβ fibers, which transmit vibration and touch, to decrease the nociceptive activity of Aδ and C fibers. This mechanism of action concurs with the gate control theory (24). Extra-segmentally, TENS activates descending inhibition by releasing endogenous opioids (101). These two effects have been shown in animal studies and are confirmed in humans. Exogenously administered opioids mostly act on mu opioid receptors, and low-frequency TENS seems to primarily activate endogenous opioids acting on mu receptors, in contrast to high-frequency TENS, which appears to primarily activate endogenous opioids acting on

delta opioid receptors. This explains why high-frequency TENS could be more effective when treating patients using opioids (102, 103). HFHI TENS may also be relevant to discussions of diffuse noxious inhibitory control (DNIC) in animals and its human analogue, conditioned pain modulation (CPM) (104). These mechanisms involve the inhibition of pain by a secondary noxious stimulus applied to a different body region—a phenomenon described as counterirritation, whereby "pain inhibits pain." It is possible that HFHI TENS could act as a counterirritant, thereby activating this endogenous pain-inhibitory pathway. This provides an additional explanatory model for the analgesic effects of HFHI TENS. (98, 105, 106).

TENS is useful for mobilization, since it is more effective for movement-evoked pain (MEP) than opioids (95, 107-110).

There exists a wealth of preclinical studies researching the effects of TENS, implying that many different neurochemicals participate in the pain-relieving effect (98). Additional effects are currently not fully understood and seem to comprise more than the peripheral, spinal, and supraspinal mechanisms induced by TENS for pain relief, such as improving wound healing, restoring impaired central inhibition, decreasing fatigue, and faster recovery of gastrointestinal function postoperatively (103, 108, 111-113). TENS has antiemetic properties, which are used to prevent and treat postoperative nausea and vomiting (PONV) in surgical settings, utilizing acupuncture points (17).

TENS is non-addictive, and it is safe and effective compared to a placebo for acute and chronic pain, irrespective of diagnosis (114). It does not interact with pharmaceuticals but has certain contraindications that must be considered: TENS should not be used when patients have electronic implants (e.g., pacemaker, implanted cardioverter defibrillator), are in the first trimester of pregnancy, have a neurological condition such as epilepsy, or have reduced sensibility over the dermatomes for pad placement.

3:4 PERSONCENTRED CARE

The concept of person-centered care (PCC) is developed to emphasize that an individual (with a disease) is just as important to consider as the biomedical markers or clinical signs of the individuals´ disease. This is accomplished by eliciting patients' narratives about what the illness and symptoms mean in

their lives, recognizing their preferences, values, resources, and experiences, and inviting them to collaborate in their care. The aim is to co-create a partnership, where the patient is an expert (in matters concerning him/herself) as well as the healthcare professional (in matters of the expertise he/she possesses). It is also crucial to document this narrative and the consequences thereof in a health management plan (115).

It is underscored by researchers that for PCC to work effectively, it must be integrated systematically at all levels, from individual healthcare professionals to culture and guidelines in the ward, and in the hospital organizational structure (116). In other words, all stakeholders need to share the vision of implementing PCC for it to work consistently in the individual context. Some national and international guidelines and recommendations exist, such as the Swedish and European Standards for patient participation in person-centered care, a WHO policy framework, and the Institute of Medicine's report "Crossing the Quality Chasm" (117-119). PCC "sits well" with the biopsychosocial positioning of pain care, in that it regards the patient as a whole being.

The leading international research center, Gothenburg Person Centered Care (GPCC), grounds its view of PCC in the philosophy of Paul Ricoeur, who promoted the view that personal identity is shaped by narrating one's story. This has led to the creation of three routines for PCC; **initiating** the partnership, **implementing** the partnership and **safeguarding** the partnership (120). PCC is also an ethical framework, requesting that one treats an individual with solicitude, dignity, and respect for his/her unique qualities by listening to their narrative. This could entail, for example, the person describing what pain means to them and what resources they use to deal with it. The studies in this thesis subscribe to this ethical framework, though admittedly PCC is not integrated into the hospitals where the studies were performed.

There is a wealth of research on PCC in long-term illness, with results showing that length of stay and cost of care can be reduced, patient outcomes can be enhanced, and healthcare professionals find it meaningful to work in this way (121-123). Although few studies describe PCC in the postoperative setting, those that do exist tell us that being recognized as a unique individual and feeling that one's wishes and apprehensions are taken seriously is crucial

to patient satisfaction and outcomes in such a vulnerable situation (124, 125). This highlights the importance of PCC in the perioperative context.

"The nice thing for me as a nurse is that there really aren't any side effects, apart from that one minute when it stings a bit. I think that's a real plus with TENS — I don't have to worry that I'm giving someone something that will cause other problems" (participant in study V)

4 AIM

This thesis aims to evaluate the ability of a preoperative bedside clinical test to predict postoperative intensity of pain in the PACU and the effects of HFHI TENS for pain relief in the PACU with the purpose of improving pain management in outpatient surgery. The specific aims were as follows.

Study I aimed to examine the ability of pain assessment at preoperative peripheral venous cannulation ("the bedside test") to predict postoperative pain intensity in the PACU in a prospective observational study in a cohort of patients undergoing laparoscopic cholecystectomy in outpatient surgery.

Study II aimed to collate studies that compared the effects of conventional pain treatment, i.e., opioids, and HFHI TENS after gynecological outpatient surgery in a systematic review and meta-analysis to scope the research field.

Study III aimed to compare the effects of conventional pain treatment, i.e., opioids, and HFHI TENS after laparoscopic cholecystectomy in outpatient surgery in an RCT, investigating the effects on time in the PACU, pain relief, opioid consumption and patient satisfaction.

Study IV aimed to describe patients' experiences of using HFHI TENS as a pain-relieving method in the PACU.

Study V aimed to explore healthcare professionals' experiences of using HFHI TENS as a pain-relieving method in the PACU.

"TENS has been amazing! Partly because it's so incredibly simple, you can control it yourself, it's super handy, and for me it started working right away." (Participant in study IV)

5 METHODS

5:1 OVERVIEW OF STUDIES

This thesis examines methods to improve postoperative pain relief in outpatient surgery. Towards this goal, five studies were conducted between 2019 – 2023. The thesis comprises one prospective observational study, one systematic review and meta-analysis, one RCT, and two interview studies. Using multiple methodological methods, Study I gives insights into the prediction of postoperative pain intensity, and Studies II – V provide a comprehensive understanding of HFHI TENS in the postoperative context. An overview of the studies is presented in Table 1.

Table 1, Overview of studies

Study	Design	Data collection	Material/participants	Data analysis
Study I	Prospective observational study	Case report forms and medical records	258 patients scheduled for elective laparoscopic cholecystectomy	Parametric tests for significance, logistic regression, receiver operating characteristic (ROC) with area under the curve (AUC) analysis, Spearman correlation and effectplots
Study II	Systematic review (SR) and meta-analysis (MA)	Bibliographic search of Embase, Medline, Web of Science, Amed, Cochrane Library, and Cinahl databases, and trial registers (WHO and ClinicalTrials.gov)	3 randomized controlled trials (RCT: s), including 362 patients	Meta-analysis using a random-effects model and trial sequential analysis (TSA)
Study III	Multicentre randomized controlled trial (RCT)	Case report forms and medical records	166 patients, randomized to either HFHI TENS or standard treatment with opioids .	Non-parametric tests for significance, univariable logistic regression test for prediction of TENS response, Cox regression for time-to-event analyses
Study IV	Qualitative interview	Individual interviews	Semi structured interview guide, 20 patients randomized to HFHI TENS	Thematic analysis with an inductive approach
Study V	Qualitative interview	Individual interviews	Semi structured interview guide, 13 health care professionals who had cared for patients randomized to HFHI TENS	Reflexive thematic analysis with an inductive approach

HFHI TENS = high-frequency, high-intensity transcutaneous electrical nerve stimulation

5:2 PARTICIPANTS

This thesis involved the participation of 258 patients (Studies I, III, and IV) and 13 healthcare professionals (Study V). The 258 patients recruited for Study I, an observational study, were simultaneously recruited for Study III, an RCT, and 166 of them were randomized in accordance with the study protocol. Since one participant withdrew consent, and two were incorrectly randomized, 163 patients were analyzed. Of the patients randomized to HFHI TENS (n= 85), 20 patients were interviewed in Study IV. The meta-analysis

in Study II included 3 trials with a total of 362 patients; these trials were performed between 2010 – 2020 (figure 1).

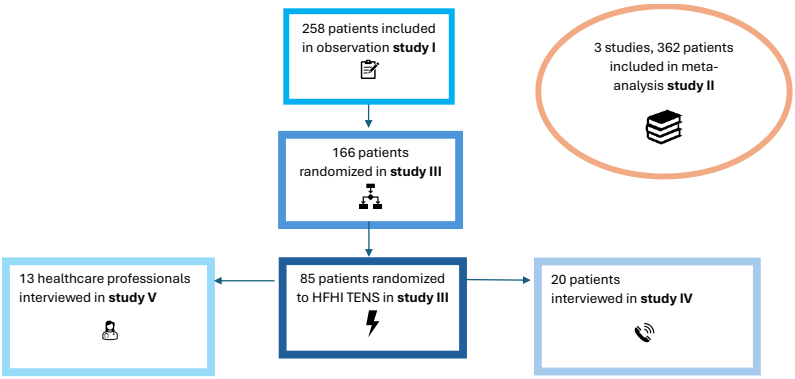


Figure 1. *Connection between studies.*

5:3 SETTINGS AND PROCEDURES

Studies I, III, IV and V were set in the same two hospitals in the southwest of Sweden. The same anesthetic procedure was used in Studies I and III. Study II was a systematic review and meta-analysis.

5:3:1 STUDY I

Recruitment was carried out in conjunction with that of Study III. Therefore, the exclusion criteria were the same as in Study III. The inclusion criterion was being due for an elective laparoscopic cholecystectomy. A total of 258 patients were included. Prior to surgery, a peripheral venous cannula was inserted, and the experienced pain from this procedure was reported as peripheral venous cannulation pain (PVCP) on the NRS. Postoperatively, patients were asked to assess their pain in the PACU on the NRS, prior to any postoperative pain treatment. Data were collected from medical records and case report forms.

5:3:2 STUDY II

This systematic review and meta-analysis explored the effects of HFHI TENS in gynecological outpatient surgery. A literature search was

undertaken, with a Population, Intervention, Comparison, Outcome (PICO) frame, on six databases and two trial registers (Table 2).

Table 2. *PICO framework (92).*

P-Population	Inclusion	Adult (≥18 years old) female patients who had undergone elective gynecological surgery reporting postoperative pain requiring treatı PACU
	Exclusion	Patients undergoing acute surgery and/or cancer-related surgery
I-Intervention		high-frequency, high-intensity TENS
C-Comparison		conventional opioid-based pharmacological pain treatment
O-Outcomes	Primary	O1 pain intensity (NRS/VAS) in PACU
		O2 pain intensity (NRS/VAS) at discharge from PACU
	Secondary	O3 time in PACU (minutes)
		O4 number of patients with NRS/VAS 0 during stay in PACU
		O5 number of patients with NRS/VAS 0 at discharge from PACU
		O6 number of patients treated with opioids in PACU
		O7 number of patients required rescue opioids in TENS group
		O8 opioid consumption for patients in O6 and O7
		O9 side effects in PACU (sedation, nausea, respiratory depression)

The software application Rayyan was used for screening eligible articles (126).
Quality of included RCT: s was assessed using risk of bias (127).
Risk of bias (RoB) is a tool from Cochrane for evaluating the risk of bias in randomized controlled trials when assessing the studies before including them in a meta-analysis (Figure 2). It appraises the quality of the individual study in different domains.

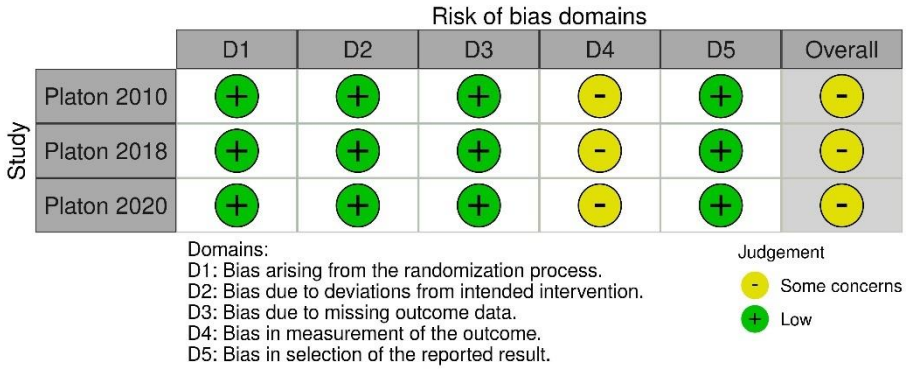


Figure 2. *Risk of bias in the included studies (92).*

After appraising the risk of bias, the meta-analysis was performed using Review Manager (128).
Grading of Recommendations Assessment, Development and Evaluation (GRADE) was used to assess the quality of evidence for each outcome (129). GRADE assesses the quality of evidence in the meta-analysis, referring not to the individual studies but to what is called a body of evidence, i.e. a collation of studies. GRADE evaluates factors such as imprecision, indirectness and other aspects that may affect the confidence in effect estimates. This is compiled in a summary of findings table for each outcome you want to GRADE. It concludes by assigning a rating of the overall certainty of evidence as very low, low, moderate or high (130). Subsequently, trial sequential analysis (TSA) was performed on certain outcomes such as time in the PACU and opioid consumption (131).

5:3:3 STUDY III

In this study, patients due for laparoscopic cholecystectomy in outpatient surgery were invited consecutively to participate. Primary screening was carried out at the preoperative visit, and secondary and final screening for inclusion was performed on the morning of the surgery. Inclusion criteria were elective surgery and assessing postoperative pain as ≥ 3 on NRS in the PACU. Exclusion criteria were not consenting to participate, needing an interpreter, having electronic implants (e.g., pacemaker, implanted cardioverter defibrillator), preoperative habitual use of opioids, chronic pain,

known substance abuse, reduced sensibility over the potential site for applying TENS pads, and inhalation anesthesia.

A total of 492 patients were screened, and 166 patients were randomized. Subsequently, three of the randomized patients were excluded and intervention discontinued – one was a request from the patient, and two were found not to fulfill the inclusion criteria upon closer scrutiny.

Randomization in this study was done in the PACU. Thus, healthcare professionals in the operating theatre had no knowledge of which group the patient would belong to. The cut-off point for randomization was patient-reported postoperative pain ≥ 3 on the NRS. Patients were then randomized 1:1 to either standard treatment with IV opioids or HFHI TENS, in a web-based software with optimal allocation based on sex and age. The maximum allowed intra-site difference in the number of participants between the arms was four. Data were collected from medical records and case report forms. If HFHI TENS did not sufficiently alleviate pain, the treatment strategy was to be changed to standard treatment with IV opioids. Patients who so desired could be taught how to manage the TENS device themselves, choosing intensity and stimulation regime (high-frequency with set or constantly changing pulse-width, which would be 80 µs or shifting between 70 and 180 µs).

5:3:4 STUDY IV

In this interview study, data were collected from telephone interviews with patients who had been randomized to HFHI TENS in the RCT (Study III). The inclusion criterion was randomization to HFHI TENS in the RCT. Patients were invited consecutively. A semi-structured interview guide was used. The first question was: “How have you experienced the treatment with TENS?” The interview guide can be found in the supplementary material of Study IV. Interviews were recorded and transcribed verbatim. A total of 20 patients were included.

5:3:5 STUDY V

In this interview study, healthcare professionals, nurses and assistant nurses, working at the two PACUs during the RCT (Study III) were asked to participate. Exclusion criteria were working as a study manager, declining to participate, and not having the experience of caring for patients randomized to HFHI TENS. Three healthcare professionals were excluded in accordance with these criteria. A total of 13 participants (of 16 possible) were included. A semi-structured interview guide was used. The first question was: "How did you experience working with TENS as a pain relief method?" The interview guide can be found in the supplementary material of Study V. Data collection was performed with individual interviews conducted face-to-face in the ward during working hours, or, in one case, by telephone.

5:4 OUTCOME MEASURES

While outcome measures differed between Studies I – III, they were overall focused on pain intensity in the PACU, time in the PACU and pain relief with HFHI TENS compared to that of opioids (table 3). Outcome measures were not specified in Studies IV and V since the aim was to unconditionally explore the experiences of patients and healthcare professionals without measuring or classifying responses.

Table 3. *Outcome measures in study I – III.*

Outcome measure	Definition	Collected as	Study I	Study II	Study III
Postoperative pain	Postoperative pain intensity	NRS or VAS	x	x	x
Opioid consumption	Consumption of opioids in the PACU	MME	x	x	x
Time in the PACU	Time from arrival to departure	minutes	x	x	x
Pain relief with opioids	Patient assessment of pain relief using IV or PO opioids	NRS or VAS		x	x
Pain relief with HFHI TENS	Patient assessment of pain relief using high-frequency, high-intensity TENS	NRS or VAS		x	x
Time to pain relief	Minutes from intervention to NRS < 3	minutes			x
PVCP	Pain at insertion of peripheral venous catheter	NRS	x		
Nausea	Patient reported nausea at baseline, at 15 and 30 minutes after intervention	NRS		x	x
Sedation	Healthcare professional assessment of sedation	Ramsey scale		x	x
Satisfaction with care and treatment	Patient satisfaction when leaving the PACU	NRS			x
Acceptability of treatment	How acceptable is the treatment received	NRS			x
Predictors for TENS response	Which variables predict response to TENS treatment	OR			x

MME = Morphine Milligram Equivalents; NRS = Numerical Rating Scale: OR = Odds Ratio; PVCP = Peripheral Venous Cannulation Pain; TENS = Transcutaneous Electrical Nerve Stimulation; VAS = Visual Analogue Scale

5:4:1 STUDY I

Study I The primary outcome was maximum postoperative pain intensity rated as NRS ≥ 3 in the PACU, in relation to PVCP ≤ 2 or PVCP > 2. This cutoff was chosen according to the local clinical routine at the sites involved in the study, where NRS ≥ 3 constituted the cutoff for pain relieving intervention. Nevertheless, a cut-off has in previous studies been set at VAS/NRS ≥ 4 (46, 49), thus secondary outcomes were postoperative pain intensity rated as NRS ≥ 4 and maximum pain during the PACU stay. Tertiary outcomes were opioid consumption in the PACU and the length of stay in the PACU.

5:4:2 STUDY II

The primary outcome was pain intensity measured with the VAS or the NRS in the PACU and at discharge from the PACU. Secondary outcomes included time in the PACU, measured as time from admission to discharge from the PACU, number of patients requiring rescue opioids in the TENS group, and total opioid consumption during the stay in the PACU.

5:4:3 STUDY III

The primary outcome in this study was time in the PACU, measured as time from admission to discharge from the PACU, chosen because three previous studies performed at our pain center showed that HFHI TENS decreased time in the PACU compared to opioids after gynecological outpatient surgery (99, 132, 133). Secondary outcomes were pain relief (maximum pain in the PACU and change in pain from baseline to discharge from the PACU), analgesic consumption in the PACU, nausea and sedation in the PACU, and patient satisfaction with care and treatment, following IMMPACT recommendations (62). Exploratory outcomes was time to pain relief NRS < 3 in the PACU, this since the cut-off point for randomization was postoperative pain NRS ≥ 3. Follow-up questions on postoperative day 1 and 7 regarding pain, use of analgesics, and satisfaction with postoperative care, and whether participants would have desired to loan a TENS unit for home use, as well as predictors for responding to TENS treatment were also exploratory outcomes.

5:5 STATISTICS

5:5:1 OVERALL

Studies I – III were statistically analyzed. Both SAS® v9.4 (Cary, NC) software and IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp were used. Descriptive and inferential statistics were used (table 4).

Table 4. *Overview of statistics.*

Overview Statistical Descriptives and Analysis used in Studies I-III	I	II	III
Descriptive Statistics			
Mean and SD	X	X	X
Median (Min; Max)	X		X
Statistical Analysis			
Comparison between two groups:			
T-test for continuous variables	X		
Fisher's non-parametric permutation test for continuous variables			X
Pearson's Chi-Square test for dichotomous variables	X		
Fisher's exact test for dichotomous variables			X
ANCOVA - continuous variables adjustment for confounders	X		X
Comparison between three groups: ANOVA – Continuous variables	X		X
Logistic regression, Odds ratio (OR) with 95% Confidence Intervals	X		X
Roc-curves, AUC, Nagelkerke R-Square and effect plots	X		
Spearman correlation coefficient	X		
Cox regression analysis of time to event data			X
Review Manager		X	
Random effects model		X	
Inverse variance method for continuous outcome variables		X	
Mantel Haenszel method for dichotomous outcome variables)		X	
Forest plots, I^2 statistics and Chi^2 test		X	
Risk of Bias Cochran tool and certainty of evidence with the GRADE System		X	
Trial Sequential Analysis (TSA)		X	

5:5:2 STATISTICAL ANALYSIS IN STUDY I

The sample size was established based on a prior study by Persson et al., 2016 (46), where a total of 151 patients was required to reach 95% statistical probability and 80% power to discover a difference (with a confidence interval [CI] of ≥ 8%) in the proportion of patients with maximum

postoperative pain intensity VAS < 4, between patients assessing PVCP as VAS ≤ 2 and > 2. Patients were recruited from the comprehensive project, encompassing the RCT, and thus the number of included patients in the observational cohort study surpassed the estimated sample size for postoperative pain NRS ≥ 4. However, no power analysis was performed for postoperative pain NRS ≥ 3.

Between groups, Pearson's chi-square test was used to compare dichotomous variables. Student´s t-test and analysis of variance (ANOVA) were used to compare continuous variables between two and three groups, respectively. Analysis of covariance (ANCOVA) was used for adjusting time in the PACU for duration of surgery. Given the sample size of 258 patients, the application of the central limit theorem justified the use of parametric tests. NRS-scores of > 2 for PVCP was analyzed for the predictive ability regarding maximum pain intensity NRS ≥ 3 postoperatively. Furthermore, PVCP was also analyzed as a continuous variable in a logistic regression, with the result presented as an effect plot. For correlation analysis Spearman correlation coefficient was used. Predictors of maximum pain intensity NRS ≥ 3 postoperatively were identified using univariable and multivariable logistic regression analysis. Only the variables showing statistical significance in the univariable analysis (PVCP, age and sex) were included in the multivariable analysis. Area under ROC-curve (AUC-statistics) was calculated for description of goodness of predictors. Nagelkerke R-square was also calculated. A cross-tabulation table with PVCP ≤ 2 / >2 vs maximum postoperative pain NRS <3 /≥3 were set up to calculate sensitivity, specificity and positive predictive value. Subsequently, all tests were repeated on maximum postoperative pain ≥ 4.

All significance tests were two-sided and conducted at the 5% significance level.

5:5:3 STATISTICAL ANALYSIS IN STUDY II

The software Review-manager version 5.3 was used to perform meta-analysis, applying a random-effects model and using the Mantel-Haenszel method for dichotomous outcomes and the inverse variance method for continuous outcomes. P-values ≤ 0.05 were deemed statistically significant. The studies were assessed for heterogeneity using the Higgins I square test. Subsequently, TSA was executed to explore if sample sizes were sufficient.

A random-effects model, using the Der Simonian-Laird method was used for the TSA, and performed for several outcomes including time in the PACU and total opioid consumption in the PACU.

5:5:4 STATISTICAL ANALYSIS IN STUDY III

Sample size was calculated by an external statistician, showing that a sample size of 75 participants was needed in each randomized group to find a difference of at least 15 min between the two groups for time spent in the PACU, since time in the PACU was the primary outcome. This sample size provided 80% power with a two-sided Fisher's non-parametric permutation test for the comparison of two independent means with standard deviation (30.7 vs. 34.3 min) and a significance level of 0.05. To protect for dropouts, 10% additional participants were added, yielding a need of 166 study participants. The primary outcome analysis was performed on a modified intention-to-treat (m-ITT) population, since three patients were excluded after randomization; one withdrew consent and two were incorrectly randomized when scrutinizing anesthesia, leading to analysis being performed on 163 randomized individuals.

Sensitivity analysis was executed, adjusting for age, sex, preop pain, PVCP, duration of surgery, taken analgesia at home, previous abdominal surgery as well as per-operatively administrated paracetamol, parecoxib and oxycodone, using ANCOVA.

For categorical variables data was shown as number and percent, for the continuous variables mean and median were presented. The secondary and exploratory endpoints were analyzed on the Full Analysis Set (FAS) population. All NRS variables were analyzed as continuous variables. Fisher's exact test was used for dichotomous variables, and Fisher's non-parametric permutation test for continuous variables, for the unadjusted comparison between randomized groups. For the adjusted comparison for continuous variables between the two groups, ANCOVA was used. The results from ANCOVA were mean adjusted differences, reported with 95% CIs and p-values. Adjustments were performed using the following confounders: age, sex, preoperative pain, duration of surgery, previous abdominal surgery, and analgesics during surgery.

Tests for prediction of TENS response were executed with univariable logistic regression and were reported as odds ratios (ORs) with 95% CIs and p-values. Cox regression was used for time-to-event analyses, in this study time to pain NRS < 3.

5:6 QUALITATIVE ANALYSIS IN STUDIES IV AND V

In **study IV**, data was collected from telephone interviews with patients who had been randomized to HFHI TENS in the RCT. A total of 20 patients were included. In **study V**, all healthcare professionals working in the PACU: s involved were invited to participate. A total of 13 respondents (of 16 possible) participated. Semi-structured interview guides were used in both studies. The interviews were audio recorded and transcribed verbatim. NVivo version 14 was used for data management and data was analyzed using a thematic analysis and reflexive thematic analysis respectively according to Braun and Clark (134, 135)

Note on Thematic Analysis: In 2006, Braun & Clarke described thematic analysis (TA) as a seldom acknowledged but often used qualitative analysis method. Two decades later, it has been boosted both in use and acknowledgement, and the method has evolved to become reflexive thematic analysis (RTA). In RTA, the unique perspectives of the researcher, the ontology and epistemology the researcher holds to be true, and the iterative, creative work involved during the analysis are even more emphasized than in traditional TA.

RTA consists of six phases, like TA. The first phase entails familiarizing oneself with data in an immersive way. In phase two, meaningful units are extracted from the data, and code labels are applied. In phase three, one searches for and creates themes, constantly moving back and forth between codes and potential themes. Phases four and five comprise continued work with tentative themes, reviewing and defining them, making sure they are internally homogeneous and externally heterogeneous. In phase six, one decides how to present the analysis findings.

Notably, TA and RTA are analysis methods not originally tied to ontological or epistemological theories but can flexibly accommodate the theory on which the research is based. Methodologically they are used to find patterns or themes in the data, and can be used inductively (bottom-up, i.e., creating codes and themes directly from the data) or deductively (top-down, i.e., taking a readymade frame to the data and searching for codes and themes that fit into the frame). There can be different levels of abstraction as well, if one searches the data for semantic or latent meanings.

5:7 ETHICAL CONSIDERATIONS

In healthcare, action and interventions take their cue from the concept of "primum non nocere"; the first duty of healthcare professionals is to do no harm. In clinical research, this implies that the risk-benefit ratio for participants must be weighted in favor of benefits. It is also important to design clinical research studies so that the results will contribute to improved clinical treatment, scientific knowledge, and overall gains for society. Further, research waste should be considered, since resources are limited.

As a patient, one is in a vulnerable situation. It is conceivable that one feels greater pressure to participate when informed about a study and asked to participate if one is a patient, than in another context. Individuals asked to participate in clinical studies must be allowed to make their own decision about participation after receiving written and oral information about the purpose, risks, and potential benefits, and not consent because of being persuaded by eager researchers or because of fearing that their care would be less adequate if they decline. Information, both oral and written, should underscore these points and make it clear that a participant has the right to withdraw consent at any moment without questions or negative consequences. Finally, after participants give oral consent, this should be confirmed by a signed consent form, which also constitutes a stage where consent may be withdrawn.

All studies in this thesis complied with the Helsinki Declaration of 1975, as revised in 2013 (136). Study II was a systematic review and meta-analysis, which was registered at PROSPERO (PROSPERO CRD42021231048); the included studies had received ethical approval. Studies I and III – V were granted ethical approval by the Regional Ethics Review Board in Gothenburg

and the Swedish Ethical Review Authority: registration number 954 – 18, supplementary applications registration numbers 2021 – 03306 and 2023 01979 – 02. Studies I and III were registered at ClinicalTrials.gov (NCT 04114149).

Studies I and III recruited patients scheduled for elective laparoscopic cholecystectomy. During the preoperative visit to the surgical clinic, patients were informed about the study and provided written information. This information included a detailed description of HFHI TENS and the possibility that the stimulation regime might be perceived as uncomfortable. It also clarified that if HFHI TENS did not provide adequate analgesia, there might be a brief delay before administering opioids; however, opioids would always be administered if HFHI TENS proved insufficient pain relief. A potential benefit of HFHI TENS was highlighted as the reduction of opioid-related adverse effects, contingent upon successful pain relief with HFHI TENS. On the morning of surgery, patients were screened for exclusion criteria, and additional oral information was provided. It was emphasized that participation was voluntary, that the standard of care would not be affected by the decision to participate or not, and that consent could be withdrawn at any time. All participants signed a written consent.

Study IV recruited patients who had been randomized to HFHI TENS in the RCT (Study III). The possibility of being asked to participate in this interview study was mentioned in the recruiting information for the RCT. Postoperatively, before discharge from the hospital, patients who had been randomized to HFHI TENS received further information, emphasizing that this study was separate from the RCT and completely voluntary. Patients were asked if they would like to participate. If so, they were contacted by the interviewer some days postoperatively by phone, who, after receiving oral consent, sent the patient a document for obtaining written consent. The date and time for the phone interview were agreed upon. The author of this thesis did not take part in the interviews, since she had cared for some of the patients in the hospital.

Study V recruited healthcare professionals who had cared for patients randomized to HFHI TENS in the RCT (Study III). The staff were informed by the researchers during a ward meeting at one of the two hospitals. In the other hospital, the healthcare manager informed the staff about the study. All participants in the study also received written information and then gave oral

and written consent to participate. Most interviews were done face-to-face during working hours, though one was carried out over a telephone call. The author of this thesis did not participate in the interviews, since she had a working relationship with the interviewees.

In Studies I – III, an NRS score of < 3 (NRS < 3) was chosen as a point where patients would be discharged from the PACU, implying that they would not need any more pain-relief that requires intense observation, i.e., opioids. However, this was primarily due to clinical resources (space in the PACU), and not necessarily how the patients felt. This ethical problem can partly be solved by using TENS, which does not need surveillance of ventilation, as a part of the multimodal postoperative pain management plan.

In Study III, at postoperative follow-up day 7, there were patients in both randomized groups who reported pain, ranging from NRS 4 to 10 (n = 3 in the TENS group and n = 7 in the opioid group). These patients were referred to their surgeon for advice and help. This implies a need to routinely follow up patients after outpatient surgery.

We learned from Studies III and IV that patients desired to borrow a TENS unit for at-home use during the first postoperative week. This was new knowledge and implies a need to establish some kind of lending system, or a recommendation that patients invest in a TENS unit to bring along before surgery. Since not all patients have the economic resources to buy such a device, and some will not be responders to TENS, letting patients borrow a TENS device (contingent upon the effect) seems to be the most pragmatic way to solve this problem. Simply put, it would be unreasonable to expect that postoperative patients, on their way home after discharge from outpatient surgery, take a detour to buy a TENS unit. As this new knowledge was acquired by asking patients participating in studies III and IV, it cannot be regarded as unethical not to have provided this service in Study III. However, it would be unethical not to consider this finding when designing further studies.

Another ethical issue was brought up by participants in Study V during the interviews with healthcare professionals. Participants described that they experienced that many patients find the HFHI TENS regime uncomfortable, and sometimes even as hurting. This was foreseen because of prior evidence (88, 99, 132, 133). Therefore, the protocol instructions were clear that the

patients were the ones to decide the intensity of the stimulation and if it should be discontinued. Consistent with this, in Study III, the stimulation intensity ranged between 14 and 60 mA. For the future, we recommend that the healthcare professionals applying HFHI TENS to patients have tried out this treatment regime on themselves.

"TENS is fantastic when it works. When you see how it just sort of releases — like, they've had this pain right in the middle of the abdomen, and then you connect TENS and within a minute … suddenly, the pain is just gone." (Participant in study V)

7 RESULTS

This chapter presents high-level findings in Studies I – V.

7:1 RESULTS IN STUDY I

Results confirmed that PVCP can be used for prediction and a correlation plot showed that each one-point increase in PVCP was associated with a successively higher risk of postoperative pain. Patients reporting PVCP rated NRS > 2 reported significantly higher maximal pain postoperatively (PVCP rated > 2 NRS 4.80 [SD 2.65] versus PVCP rated as ≤ 2, NRS 3.65 [SD 2.56], $p < 0.001$; MD −1.16 [95% CI −1.80; −0.51]) and required a significantly longer stay in the PACU (144 min [SD 94.9] versus 114 min [SD 47.2], $p = 0.002$, MD −30.2 [95% CI −49.6; −10.8]). When adjusted for duration of surgery, time in the PACU was 145 min (PVCP > 2) versus 113 min (PVCP ≤ 2) ($p < 0.001$).

PVCP rated as NRS > 2 was a significant predictor (OR 2.00, 95% CI 1.15 – 3.51, $P = 0.015$) of maximum postoperative pain intensity NRS ≥ 3 in the univariable logistic regression. Despite this, in the multivariable regression analysis adjusting for age and sex, significance was not reached ($P = 0.089$). The multivariable regression demonstrated that age was the factor with the most significant impact on the risk of postoperative pain intensity rated NRS ≥ 3 (OR age ≤ 40 years = 2.50, $p = 0.025$; OR female sex = 1.80, $p = 0.051$; and OR PVCP > 2 = 1.66, $p = 0.089$). However, when analyzing postoperative pain rated NRS ≥ 4, PVCP was a factor with a significant impact of its own in the multivariable regression (OR age ≤ 40 years = 2.2, $p = 0.042$; OR female sex = 2.15, $p = 0.010$; and OR PVCP > 2 = 2.06, $p = 0.012$).

In the AUC-analysis, using all three variables (age, sex and PVCP) as a model resulted in a stronger prediction than using each of them alone. AUC for PVCP 0.5758. for sex 0.5837, for age 0.6335 and for the model 0.6576 when relating to maximum postoperative pain intensity NRS ≥ 3. The model relating to maximum postoperative pain NRS ≥ 4 resulted in AUC 0.6812 (for PVCP 0.6176, for sex 0.5986 and for age 0.6356).

The results also corroborated previous findings that many patients experience severe pain in the PACU, despite multimodal pain management plans being in place. Approximately 30 % of the 255 patients reporting postoperative pain assessed their maximum postoperative pain intensity as NRS ≥ 6.

7:2 RESULTS IN STUDY II

Only three articles fulfilled the PICO terms. These were all from the same research center and were all designed as crossover studies, i.e., the patients randomized to HFHI TENS could cross over to the IV opioids arm if pain relief was not sufficient, and vice versa. There was no difference in the number of crossovers from both arms. No difference was found in pain intensity at discharge from the PACU between the TENS group and the opioids group using the VAS (MD −0.15, 95% CI −0.38 to 0.09, p = 0.21). Time in the PACU (minutes) was significantly shorter in the TENS group (MD −15.2, 95% CI −22.75 to −7.67). TSA demonstrated that the required sample size for amounting to firm evidence was reached. Opioid consumption in the PACU was significantly lower in the group primarily randomized to HFHI TENS (MD −3.42, 95 % CI −4.67 to −2.17, p<0.00001) (figure 3), and this result was also confirmed in a TSA.

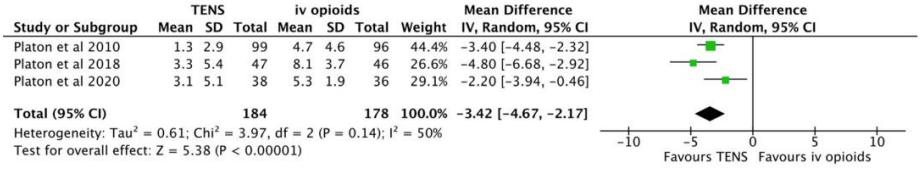


Figure 3. *Forest plot showing mean total consumption of opioids in the PACU (92).*

7:3 RESULTS IN STUDY III

Time in the PACU did not differ between the randomized groups (137.8 min [SD 69] for TENS versus 142.2 min [SD = 95] for opioids; p = 0.74). There was no difference regarding pain at baseline between the two groups (NRS 5.61 [SD = 1.51] for TENS versus NRS 5.66 [SD = 1.65] for opioids; p = 0.88). Change in pain from baseline to discharge was not significantly different between the groups (−3.9 NRS [SD =1.8] for TENS versus −4.1

NRS [SD = 1.7] for opioids; p = 0.54). However, opioid consumption was significantly lower in the group randomized to TENS versus the group randomized to opioids (4.5 MME [SD = 6.8] for TENS versus 11.0 MME [SD = 6.7] for opioids; p < 0.001). The HFHI TENS group and the opioid group both reported a mean decrease of 3 units on the NRS, representing a 70 % decrease in pain intensity. Responders to HFHI TENS, i.e. patients who did not need to supplement their pain treatment with opioids, were 54% in this cohort.

Both randomized groups reported acceptable mean pain intensity on the NRS at discharge from the PACU (NRS 1.7 [SD = 1.4] for TENS versus NRS 1.6 [SD = 1.3] for opioids; p = 0.58). Nausea and sedation were registered at arrival and at 15 and 30 minutes after intervention but did not significantly differ between randomized groups (e.g. at 30 minutes nausea in TENS group was NRS 0.478 [SD 1.023], opioid group was NRS 0.629 [SD 1.822] p = 0.61; at 30 minutes sedation was in TENS group Ramsey Sedation Scale, RSS, 2.20 [SD 0.50] and in opioid group was RSS 2.20 [SD 0.51] p = 1.00)

There was also no difference in satisfaction with pain treatment (NRS 8.8 [SD 1.7] for TENS versus NRS 9.2 [SD =1.5] for opioids; p = 0.08) or satisfaction with care (NRS 9.9 [SD 0.4] for TENS versus NRS 9.9 [SD 0.3] for opioids; p = 0,54). However, acceptability of pain treatment did differ, favoring the opioid treatment; (NRS 8.9 [SD = 1.8] for TENS versus NRS 9.4 [SD = 1.3] for opioids; p = 0.039).

We found no differences in median time to pain relief, and both the HFHI TENS group and the opioid group reported NRS < 3 after 10 minutes. However, differences were found after performing a post-hoc exploratory analysis of responders to TENS (those who received pain relief with HFHI TENS exclusively), non-responders to TENS (those who needed to supplement their pain relief with opioids), and those in the opioid group. Responders to TENS got pain relief reaching NRS < 4 within 2 minutes, and pain relief to NRS < 3 within 5 minutes. In contrast, those in the opioids group reached NRS < 3 within 10 minutes and non-responders to TENS within 15 minutes.

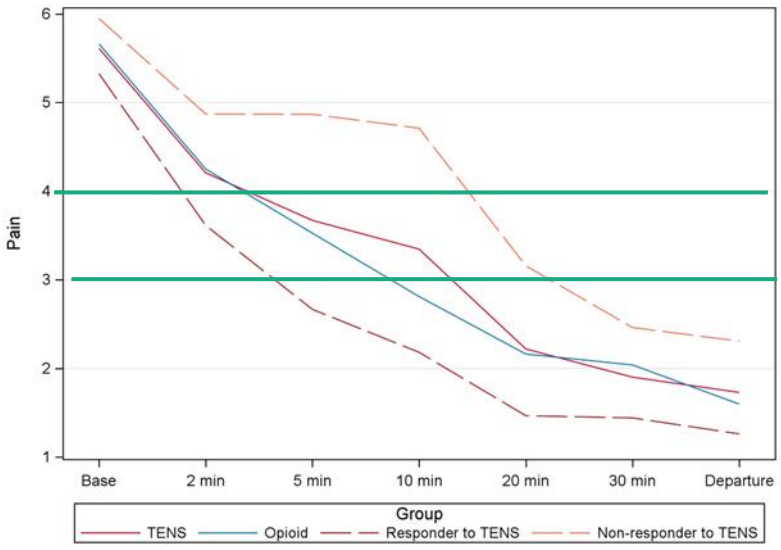


Figure 4. *Median time to pain relief for the TENS group, responders and non-responders to TENS, and the opioid group. The y-axis shows postoperative pain intensity rated using the NRS. The two green horizontal lines indicate NRS scores of 4 and 3 respectively (Study III).*

7:4 RESULTS IN STUDIES IV AND V

***Table 5**. Summary of main results (Study IV and V).*

Study number	Participants	Explored phenomenon	Identified benefits	Identified disadvantages	Points noted
IV	Patients 	Experience of TENS as a pain-relieving method in the PACU	Increases autonomy Feels safe Rapid onset and offset No feeling of being "chemically affected"	Does not work when pain is too intense Effect only while using TENS. Rapid offset can make the pain return	Desire to keep using TENS for pain relief at home
V	Healthcare professionals 	Experience of TENS as a pain-relieving method in the PACU	No serious adverse effects Feels safe	Requires more time and effort than administrating opioids	Difficulty separating TENS intervention from RCT-protocol
V	Healthcare professionals 	Practical management of HFHI TENS intervention	Prompt pain relief in responders	HFHI TENS can be uncomfortable	Creation of personalized support methods

7:4:1 RESULTS IN STUDY IV

Applying thematic analysis, we developed two themes: 1) TENS offers control, and 2) preference for TENS for pain relief. The results indicate that patients value the opportunity to choose non-pharmacological options, such as TENS, for postoperative pain management, as they desire alternatives to drugs for pain control in the postoperative setting. Patients emphasized the importance of being able to manage their pain independently, without relying solely on healthcare professionals. This sense of autonomy, to exert some control over the pain rather than total elimination of pain, was considered decidedly important.

While participants acknowledged both the benefits and limitations of TENS, they generally preferred it to pharmacological treatments. Not all patients

experienced adequate pain relief, and the findings suggest that TENS may be less effective when pain is intense.

Among those who reported sufficient pain relief, several advantages of TENS were highlighted, including a sense of increased control over pain management, rapid onset and offset of analgesia, absence of side effects, and a perception of TENS as a safer alternative to medications, especially opioids. Many participants expressed a strong desire to continue using TENS therapy after discharge.

7:4:2 RESULTS IN STUDY V

The findings in this study were expressed in two themes: 1) hesitation and 2) commitment to the patients. There were mixed experiences among the participants regarding the efficacy of TENS, but the prompt pain-relieving effect when a patient was a responder was acknowledged.

The theme of hesitation mostly concerned effectiveness, and the amount of time needed for the intervention. Of note, the participants had trouble demarcating the time needed to follow the RCT protocol and fill in the case report form, from administering the TENS intervention per se.

Participants often elicited comparisons with opioids, where opioids were perceived as the most effective, time-saving, and simplest solution. However, participants appreciated TENS' lack of serious adverse effects, and TENS was seen as a better option than opioids in this regard.

The participants shared their views on prerequisites for introducing TENS in postoperative care, highlighting the need for education and clinical guidelines.

The theme of commitment to the patients describes how the healthcare professionals created strategies beyond those provided in the RCT protocol to coach and support their patients. The actions taken by participants were all intuitively personalized, and identical actions were used regardless of the participants' stance toward TENS.

Overall, the findings demonstrate that more practical and theoretical knowledge about TENS is needed and desired, and that clinical guidelines for

using TENS would be necessary for it to be used as a routine intervention in the postoperative context. Further, the findings show that healthcare professionals in the PACU are ready to engage in personalized care, despite a hectic work environment.

"The only thing I thought was a shame was that you couldn't borrow it to take home. I would've loved that" (Participant in study IV).

8 DISCUSSION

This thesis confirms the high incidence of postoperative pain and demonstrates that using a "bedside test", i.e., assessing PVCP, can help healthcare professionals predict the risk of intense postoperative pain and time needed in the PACU. It also contributes new knowledge to the field regarding the use of HFHI TENS in the PACU, through a meta-analysis, an RCT, and interviews with patients and healthcare professionals. In summary, postoperative pain can be predicted using a simple clinical preoperative test, and HFHI TENS is an effective, opioid sparing alternative or complement for pain relief, desired by the patients.

This chapter discusses several aspects of the thesis: postoperative pain as a phenomenon; assessment of postoperative pain; prediction of postoperative pain; HFHI TENS vs opioids for postoperative pain relief; and person-centered care (PCC) in a postoperative context. The results from the different studies concerning HFHI TENS support each other, which will be discussed and visually demonstrated in table 6. Finally, methodological reflections about the methods used in the studies will be discussed.

8:1 POSTOPERATIVE PAIN

Despite the advances made in pain theory and the development of new medicines and methods, postoperative pain continues to be undertreated. Globally, many patients report moderate-to-severe pain after surgery (7, 8, 32). Bringing a spotlight on this, Corell et al. (2014) stated that there is "no evidence of real progress in treatment of acute pain" (137). Furthermore, Zaslansky et al. (2022) published results from Pain Out, an international quality improvement and registry project for post-operative pain, in an article titled: "Status quo of pain-related patient-reported outcomes and perioperative pain management in 10,415 patients from 10 countries" (138). In Study I, we found that the incidence of moderate postoperative pain (NRS 3 - 5) in our cohort was 37 % and that of severe pain (NRS ≥ 6) about 32 %, despite the use of multimodal analgesia, confirming the existence of this problem. Moreover, the three studies included in Study II, the meta-analysis, uniformly reported postoperative pain as NRS > 5 before treatment after surgical abortion, hysteroscopy, and gynecological laparoscopy.

Efforts were made to improve pain treatment through campaigns in the 1990s, naming pain the fifth vital sign (the other four being respiratory rate, blood pressure, pulse frequency, and body temperature). However, the sole option to treat intense pain was increasing the amount of opioids administered and prescribed, which had the unintended result of contributing to the opioid crisis in the Western world (54, 139). This crisis has led to a retreat from relying on high doses of opioids to treat postoperative pain and introduced opioid-sparing pain management plans during perioperative care (140). Nevertheless, surgery and postoperative care are contexts where many patients are exposed to opioids for the first time, setting the stage for the risk of persistent use of opioids.

Several clinical guidelines have been created to improve postoperative pain management (141-143). Still, their effectiveness remains uncertain. Evidence does not yet indicate that postoperative pain relief has significantly improved in clinical practice. TENS is mentioned in some guidelines as a potential adjunct in multimodal pain treatment, but the recommendations are expressed rather hesitantly, which likely contributes to the limited adoption of this recommendation by healthcare professionals.

Poorly managed postoperative pain encompasses the risk of serious physical, psychological, and social consequences in the short- and long-term (22). As healthcare professionals, we need to be aware that what we do or do not do regarding pain relief in the PACU contributes to shape the future of pain experience for each individual patient.

8:2 PREDICTION OF POSTOPERATIVE PAIN

Predicting postoperative pain intensity for an individual patient is precarious, and it is essential to find simple, clinical methods to guide us in creating personalized pain management plans. Postoperative pain is ubiquitous and often of severe intensity, with short- and long-term consequences for the patient. This has repeatedly been demonstrated in the literature, despite the use of novel methods and guidelines.

If we could predict an individual's risk of postoperative pain preoperatively, truly personalized pain management plans could be created. Then, healthcare professionals could work preventively instead of reactively and could avoid overtreating or undertreating pain. The ability to predict postoperative pain

has been the object of many studies. However, most efforts to predict risk of postoperative pain, or pain sensitivity, depend on procedures that are not feasible during the assessment for surgery due to limited resources in the clinical context (36-38).

Compared to existing procedures, performing a simple, bedside test of PVCP seems to be the least cumbersome, most feasible way of testing a patient's pain sensitivity, and it is possible to perform it in an ordinary routine surgery context. It has the added benefit of preoperatively teaching a patient to use the NRS or VAS, one of the basic principles in many guidelines to improve postoperative pain management (77). In Study I, we explored the effect of using PVCP, age, and sex for the prediction of the risk of postoperative pain rated NRS ≥ 3. Using all three variables in an ROC model resulted in an AUC of 0.6576 (CI 0.5841 – 0.7311), not a great result since an AUC ≥ 0.7 is considered acceptable and anything less is considered poor (144). However, although these factors alone do not constitute a comprehensive understanding of the experience of postoperative pain, they can still aid in personalizing treatment.

Perhaps adding a few simple questions about smoking status, sleep quality and mood, and asking patients to assess their stress and concerns about the surgery using the NRS (as done when asking about satisfaction in study III), could lead to improved prediction of risk for postoperative pain and improved treatment for each individual patient.

8:3 ASSESSMENT OF POSTOPERATIVE PAIN

In postoperative pain assessments, what is usually measured is the intensity of pain. For this, we use self-reporting scales combining them with assessing the patient's appearance and behavior. This routine was followed in Studies I and III. Ideally, the initial assessment and reassessments should be documented, but this is seldom done adequately or sufficiently; this practice can be improved by education (79, 145). The unidimensional scales for pain assessment are useful when deciding if a pain-relieving intervention has influenced the intensity of pain. However, Vila et al. (2005) have questioned if unidimensional pain scales contribute to the incidence of opioid-induced ventilatory impairment (OIVI) by leading to overdoses of opioids (146), and

Bowen et al. (2020) have proposed using sedation scales to identify OIVI in the PACU and on wards (67).

We assume that a decrease in pain intensity implies something about the ability to function. It could be argued that pain assessments could be improved if we included overt questioning about function. To this regard, Gordon proposed an assessment tool comprising items such as "change in pain", "comfort", and "functioning" (54), more recently mirrored in the IMI-PainCare PROMPT core outcome set of patient reported outcome measures (PROMs) for assessing perioperative pain management (147). This core outcome set divides pain assessment into four important domains: pain intensity, physical function, self-efficacy and adverse events.

Assessing pain intensity and managing pain in healthcare settings requires a degree of trust between healthcare professionals and an individual as the patient. Both the patient having pain and the healthcare professional are involved in this dialogue and this reporting. Several phenomena impact the reporting and the assessment of pain. The literature mostly focuses on the patient: what makes the patient state a particular number on the scale? The answer encompasses biological issues and psychosocial ones. One can easily imagine the pain as being more severe, related to the magnitude of the surgical process, and related to the amount of pain-relieving treatment administered. But all patients do not report the same intensity of pain after the same procedure and after receiving the same multimodal pain treatment (148). There exist biological reasons for this, e.g., sex, genetics, and age, but psychological and sociological factors also play an important part (149). For example, it has been demonstrated that anxiety and catastrophizing contribute to postoperative pain by alerting the stress system and thereby the pain-facilitating pathways (150, 151). But where should we sort the fact that different (sub)cultures have diverse opinions about what is the appropriate way to show and speak about your pain, if not among the sociological factors (57)?

The assessment (of pain) is an ongoing interaction between the reporter of the pain, i.e., the patient, and the assessor, i.e., the provider of pain relief. This interaction has been described as a "social transaction" (54) and a patient's choosing of a number or word on a scale as "a statement in need of interpretation" (152). In the interaction, the patient can understate their pain for different reasons, e.g., wanting to show an image of a "strong" person

who can tolerate pain, or a feeling that the nurses are busy and not wanting to increase their workload by asking for pain relief, or being scared that the pain is a sign of a worsening condition. Conversely, a patient can overstate their pain for different reasons, e.g., being afraid of not receiving adequate pain relief or having a stress system that is so alerted that they cannot separate anxiety from pain (153). These distinctions are not facilitated by our unidimensional scales, where all we ask about is pain intensity. Listening to the pain report presupposes healthcare professionals trusting the report. This issue is more complex than it might appear. A patient reports their pain intensity verbally, with or without behavioral cues, for the healthcare professionals to acknowledge it, in the hope of receiving help. If there is a mismatch between the verbal report and behavior, this can raise doubts about the reality of the pain for the healthcare professional. If healthcare professionals, for example, believe that the patient is opioid seeking, they can feel affronted. If the patient senses that reaction, they can, in turn, feel invalidated and stigmatized. This can cause conflicts about the correct measure to deal with the pain report (154). However, this also speaks for a partnership as described within person-centered care, to achieve the best possible pain relief in collaboration with the individual patient.

Focusing on the other person in this interaction, i.e., the healthcare professional, we must acknowledge that they, too, have a biopsychosocial background. Yet, the consequences thereof on patient-healthcare professional interactions are not widely documented in the literature. Healthcare professionals can feel stressed by their workload, they have biases (155, 156) that work for or against the patient, and they are a part of the culture in the ward (157).

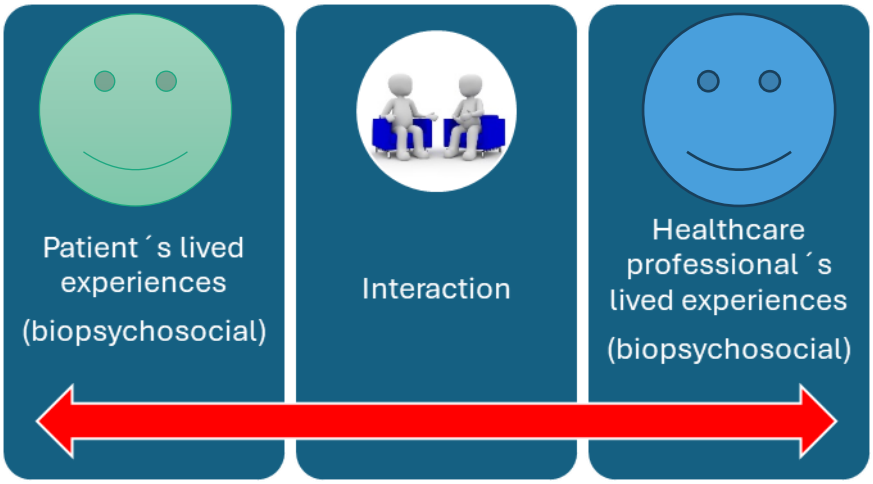


Figure 5. *Patients and healthcare professionals background and experiences affect each other when interacting.*

Healthcare professionals are influenced by what they have already done to alleviate the patient's pain (158). How they express themselves can affect the patient, as through our language, we can make a patient feel either trusted or distrusted (159). The way that we express ourselves also affects our own emotions and in what frame of mind we perform our actions (160).

8:4 HFHI TENS VERSUS OPIOIDS IN THE PACU

There is a need of including something new in the multimodal analgesia pain management plans, preferably something simple but effective, which does not interact with other methods.

Opioids are effective for nociceptive pain but have adverse effects. In the limited postoperative view, patients may experience various adverse effects. A survey in 2014 found that 79% of those receiving pain medication experienced a minimum of one adverse effect (8). The adverse effects of opioids may disturb or hinder the mobilization goals needed for recovery, as expressed by the concept of DrEaMing (drinking, eating, mobilizing) (161).

The adverse effects associated with opioids also have a potential consequence in that fear of adverse effects may cause healthcare professionals to limit doses without replacing opioids with another intervention and thus circumscribe optimal analgesia. From a more recent perspective concerning opioids, there exists the risk of developing persistent use, physical dependence, and even opioid use disorder to varying degrees, and tapering of opioids after surgery can be difficult to achieve (10, 162). Long-term use of opioids may result in drug-related harm, such as endocrinopathy, metabolic changes, and sleeping disorders (9, 163). NSAIDs have also been used persistently after surgery (164), which may lead to harm as well, such as gastro-intestinal, renal and cardiovascular adverse events (165).

Having to use opioids for pain relief gives rise to many negative thoughts and emotions, as demonstrated by Aljohani et al. (2024). Addiction, side effects and opioid stigma were common concerns among patients using opioids for postoperative pain relief (166). Being able to taper opioids after surgery results in improved quality of life (167).

Patients treated with opioids require intensive supervision. In clinical reality, this often means balancing limited resources, i.e., availability of healthcare professionals and floorspace in the PACU, with the patient's anticipation of pain relief. This leads to discharging the patients from the PACU at a set NRS assessment, usually NRS ≤ 3. However, patients are seldom asked to decide what is an acceptable intensity of pain for them. Pain management with TENS can be used postoperatively without supervision, though the patients need to be provided with instructions and ideally followed up with troubleshooting over the first postoperative week. The results from Study IV suggest that offering patients non-pharmacological options such as TENS can enhance their sense of autonomy and satisfaction with postoperative pain management. Still, TENS cannot be used by everyone as there are contraindications, and it is not effective when the pain is intense, as seen in Studies III, IV and V.

Healthcare professionals may experience the administration of TENS as bothersome, including more work than administering a pill or an injection of opioids. This might have to do with habit and routine. Healthcare professionals working in the PACU have considerable experience in administering opioids, and they may be quite comfortable dealing with the adverse effects of opioids. In contrast, most healthcare professionals working

in the PACU have never received education about using TENS, neither in undergraduate education nor at work. Furthermore, most patients expect to receive opioids in the PACU, though they appear to embrace the opportunity of a non-pharmacological option when offered (168, 169).

Another point that needs to be discussed in this context is the time after hospital discharge, which occurs on the day of surgery in outpatient surgery. This is a vulnerable period for patients. After discharge, patients are left to process the emotional impact of the surgery alone (170), and they must manage their postoperative pain themselves without access to healthcare professionals guiding them or an acute pain service team to help them if problems arise (171-173). In Study III, we interviewed patients during follow-ups on days 1 and 7 after surgery. On day 1, 88 patients (59%) claimed that they would have desired to borrow a TENS unit (the opioids group was also asked), and by day 7, 18 patients (13%) had required help from healthcare providers, most regarding pain or adverse effects of analgesics. The pain-relieving effects of peripheral nerve blocks, often performed in outpatient surgery, typically cease after 18-24 hours (174). After discharge, TENS could be a viable option for pain relief, as it is easy to manage and poses no risk of overdose. However, its use at home depends on the availability of a loan system – either through the healthcare facility upon discharge or via general practitioners prior to surgery.

Since TENS is safe, effective, and has no adverse effects or interactions with pharmaceuticals (114), I suggest that it should be included as a component of every postoperative multimodal pain management plan where no contraindications exist, just as paracetamol/acetaminophen is currently so included. The question is simply when to offer it in the postoperative process. Study III demonstrated that one of the predictors of response to TENS was less intense pain, and the patients also told us so in Study IV. Intense pain as a predictor of non-response to TENS was also identified in a study by Olausson et al. (2024) in the context of pain management after obesity surgery with opioid-free anesthesia (175). Therefore, the use of TENS in multimodal analgesia could be time-dependent; if postoperative pain is reported as ≥ 6 on the NRS, the results of Studies III, IV, and V lead us to suggest starting treatment first with opioids and introducing TENS at a later stage, when pain intensity is lower (NRS ≤ 5).

In Study V, we found that healthcare professionals would like to enhance their knowledge about TENS. Diwan et al. (2024) reported that healthcare professionals' knowledge about TENS is poor, encompassing a lack of theoretical and practical knowledge on the part of clinicians and a lack of clinical guidelines (176). Contributing to this is the dearth of TENS education in the professional curriculum of nurses, assistant nurses, and physicians.

8:5 PERSON-CENTERED CARE IN THE PACU

Santana et al. (2018) described PCC as "doing things *with* people rather than *to* or *for* them", which neatly captures the essence of the ethics implicated in PCC, namely regarding the patient as a person just like yourself, with innate rights to be treated courteously, and to be seen as capable of taking important decisions concerning your care (177). The starting point is really the ethics, which leads us to co-create care with an individual patient (178). The existentialist philosopher Martin Buber (1878-1965) stated that humans have two ways of relating to others: as I – It and I – Thou ("I and Thou" 1923). He went on to state that a good meeting only happens between those who regard each other as equal human beings, as in I – Thou. This is an appealing ethical stance to have when you meet persons in a vulnerable, exposed situation, such as being a patient in pain after surgery. Evidence supports that shared decision-making, coupled with adequate, timely information, is a crucial approach to make the patient feel safe and in control (179), to help prepare for the peri-operative experience (125), and to improve patient outcomes (180). Shared decision-making has itself been described as essential to holistic care and a necessary component of the art of medicine (181). Patients themselves efficiently recognize when PCC is offered (182), and among the most important factors recounted are how healthcare professionals listen and communicate verbally and non-verbally (183).

In peri-operative care, time constraints frequently limit the duration of interactions between patients and healthcare providers, necessitating the ability to establish a trusting relationship within just minutes. This is a challenge for healthcare professionals and patients alike (124, 184).

To arrive at person-centered care, healthcare professionals should ask themselves: "*What matters to my patient?"* rather than *"What is the matter with my patient?*", as the Swedish public service innovation network Esther expresses the issue (185). This could be accomplished with a question in the words of Ulrica Nilsson (2019): "What is most important to you now?" (186). Note that this could be *not* wanting to participate in decision-making about care, as some patients have the desire to leave such decisions to the healthcare professionals, feeling incompetent because of a lack of knowledge and/or effects of surgery and anesthesia (180).

To successfully implement PCC, changes need to be made at all levels of healthcare, by including PCC in basic training for professionals, continuing education, and training during work (177) – much as the changes required to implement TENS in multimodal pain management plans. While the quantitative studies (Studies I – III) included in this thesis do not clearly outline the importance of PCC, they are undertaken with the ethics of PCC and personalization of postoperative pain management plans in mind. To use variables like PVCP, age, and sex to predict risk for postoperative pain (Study I) and to offer TENS as an option in the PACU (Studies II and III) are attempts to tailor pain treatment for the individual, which could represent personalized care with shared decision-making and a partnership between the patient and the healthcare professional. If this cannot be called true PCC, at least it could be regarded as a step towards it. The qualitative studies (Studies IV and V), however, examine the findings through a PCC lens, revealing patients' appreciation for personalized care and healthcare professionals' readiness to engage in such care, albeit without explicitly labelling these notions as PCC.

8:6 SYNTHESIS OF RESULTS FROM STUDIES CONCERNING HFHI TENS

Summarizing the studies concerning HFHI TENS in this thesis reveals a consistent pattern of findings that reinforce one another. For example, the results from Studies II and III provide statistical evidence for the opioid-sparing effects of HFHI TENS. This quantitative evidence is further substantiated by the qualitative findings from the interview studies, in which

patients reported not feeling “chemically affected,” and healthcare professionals observed faster recovery and reduced impairment when using HFHI TENS compared to opioid-based treatment. The convergence of these results strengthens the argument for incorporating HFHI TENS into multimodal pain management plans.

Other issues with supporting data from the quantitative and the qualitative research can be found in table 6.

Table 5. *Collation of data from quantitative and qualitative research.*

Issue	In meta-analysis	In RCT	In patient interviews	In healthcare professional interviews
Pain relief	Crossover numbers from HFHI TENS to opioid and vice versa were the same No difference in pain at the time of discharge from the PACU between the patient groups	No difference in pain at the time of discharge from the PACU between the patient groups 54% of patients randomized to HFHI TENS were responders Difference in time to pain relief (pain intensity NRS ≤ 3) Responders 5 min, non-responders 15 min, opioid 10 minutes Satisfaction with pain relief NRS 8.8 in TENS group, 9.2 in opioid group (p = 0.08)	"The TENS really took away the pain — morphine just cuts the edge off the worst pain." "Yeah, I thought it worked really well"	"It's fantastic when it works. When you see how it just sort of releases —you connect it and within a minute … all of a sudden, the pain is just gone." "It does not help that many, but the one whom it helps obtains help rapidly." "It was amazing to see how she went from being in quite a lot of pain to almost none at all, like down to zero or one."
TENS does not help when pain is too intense		Predictors for TENS response: older age, less intense pain when presenting in the PACU 46 % of those randomized to TENS were non-responders Acceptability of pain treatment NRS 8.9 in TENS group, 9.4 in opioid group (p = 0.039)	"I had a strong preference for TENS since morphine significantly affects me. Sadly, it didn't provide the relief I was looking for at the time."	"If I had to choose between giving the patient TENS […] or opioids, I would probably spontaneously choose opioids, I know that it works. And then you might feel nauseous and so on. But yes, I know that it [opioids] helps."
HFHI TENS hurts		The mean intensity was 40.7mA, ranging between 14 and 60mA.	"I could feel it where the pads were, but on the other hand… it was a welcome pain, it kind of took away the other pain."	"If the patient is not actively participating, it would be like an assault [to administer TENS]. Putting something on that hurts more for a minute" "They [the patients] are the ones who decide if we should discontinue [the HFHI TENS] or not. How high we should go, if we should decrease [the intensity of the stimulation]."
Decreased need of opioids	MD HFHI TENS group – opioid group: - 3.42 (p<0.00001)	MD HFHI TENS group – opioid group: -6.4 (p<0.001)	"You don't feel chemically affected even though you've had anesthesia and all that. It's not the same feeling at all. I've had surgery once before, and this time it was so nice to just be able to get up and then quietly return to bed, lie down, and switch on this TENS"	"Most importantly, the patient is less fatigued and less impaired. Opioids, on the other hand, cause much stronger impairment."
Using TENS at home		59 % of the patients would have desired to borrow a TENS unit	"The only thing I thought was a shame was that you couldn't borrow it to take home."	"The patient got more pain when we took away the TENS, and she would have wanted to take it with her home"

8:7 METHODOLOGICAL CONSIDERATIONS

8:7:1 PARADIGMS

A paradigm represents the ontology, epistemology, and methodology of the researcher's stance in designing and performing research (187).

Studies I – III are within the positivistic paradigm, as is usual with quantitative research. Here, we find the ontology of viewing the world as one absolute reality, with the consequent epistemological view that knowledge is produced by weighing and measuring quantifiable objectives. This ontology and epistemology are never outright stated in quantitative work but accepted as given, and neutrality towards the data is assumed. The methodology here includes surveys, RCTs, and observations. Analysis methods involve statistics.

In contrast, Studies IV and V are within the interpretivist paradigm, where the ontology views reality as including non-measurable entities such as feelings and meaning. This ontology recognizes multiple subjective realities, formed by the participants' social and historical experiences of the world. We can only understand and know this reality through their experience, and consequently, the epistemology requires listening to narratives and observing behavior. In this research, researchers deliberately discloses their preunderstanding, and the assumption here is that neutrality is neither possible nor desirable. The researcher always regards data through their own personal lens, which must be acknowledged for readers to evaluate the reported results. The methodology in this paradigm includes interviews, focus groups, and ethnographic research. Analysis methods require immersion of the researcher in the data, organizing it, and drawing conclusions, all in an iterative manner.

Both qualitative and quantitative research must demonstrate transparency regarding the study's procedures and analysis to be considered credible/trustworthy and replicable/transferable. However, it remains uncertain whether any study, qualitative or quantitative, can truly be exactly replicated. In quantitative research, it is always acknowledged as a limitation that the findings apply only to the studied population within the specified context. Similarly, in qualitative research, it seems reasonable to assume that

if the participants or the researchers were different individuals, the results might differ, even if the same researchers posed the same questions. Nevertheless, in both cases, assumptions can be made about the potential applicability of the findings to other populations and contexts.

The research question is what decides the approach. It is vital to consider the research question and critically evaluate whether the collected data and analytical methods are relevant to and appropriate for addressing it. By applying both quantitative and qualitative approaches to investigate different domains of knowledge about HFHI TENS, this thesis arrives at a deeper understanding of how we should use the intervention in the context of outpatient surgery. The data we have collected concerning HFHI TENS are complementary and support each other. For example, the RCT (Study III) concludes that a predictor for TENS response is pain rated as NRS ≤ 5 when presenting in the PACU, and the interview with patients (Study IV) tells us that "TENS does not work when the pain is too intense".

8:7:2 METHODOLOGICAL CONSIDERATIONS IN STUDIES I AND III

Studies I and III recruited patients due for elective surgery to participate in an observational study and an RCT, randomizing participants either to HFHI TENS as a first instance of pain-relief, or to standard treatment with opioids postoperatively, respectively. The strengths of these studies lie in their being conducted at two different PACUs and in their examination of previously unreported outcomes, namely the time to pain relief with different pain-relieving methods, patient satisfaction and the impact of PVCP on length of stay in the PACU.

However, we readily admit to certain limitations. One patient withdrew consent when randomized to opioids, which highlights a possible self-selection bias in the study, i.e., that patients with a favorable attitude toward TENS were more likely to choose to participate than patients with a negative or no opinion of TENS. This could affect the generalizability of the results. There could also exist a risk of patients overrating the level of pain relief when randomized to TENS, due to their desire for the treatment to work. However, the study protocol specified that if two interventions with HFHI

TENS did not achieve pain relief, the treatment strategy should be changed to IV opioids. This change was made for a total of 39 (46%) patients randomized to HFHI TENS, showing that patients did not, in fact, underreport their level of pain.

We could have carried out a power calculation for our first outcome in Study I (PVCP > 2 related to postoperative pain NRS ≥ 3). We did not do so, as we relied on power calculations done in another study (for postoperative pain NRS ≥ 4) (46). We had recruited more than 100 patients in excess of the requirement in that study, and we thought that this would be sufficient, though in fact it was not sufficient to be able to show statistical significance in the multivariable regression, demonstrating that age and sex may be confounders for PVCP when related to postoperative pain NRS ≥ 3. However, we also analyzed PVCP > 2 related to postoperative pain NRS ≥ 4. The predictive value of PVCP differed depending on the cut-off used for postoperative pain. At NRS ≥3, PVCP was associated with postoperative pain in univariable analysis, but lost statistical significance after adjustment for age and sex. In contrast, when a cut-off of NRS ≥4 was applied, PVCP remained significantly associated with higher pain ratings both before and after adjustment, indicating that PVCP NRS > 2 is an independent predictor of more severe postoperative pain. Still, assessing pain is not an exact science. The relationship between PVCP and postoperative pain is evident in the correlation analysis, which demonstrates that higher PVCP values are associated with an increased risk of postoperative pain. Rather than attempting to predict whether an individual patient will report their pain as, for instance, NRS 3 or 4, it is more meaningful to recognize that a PVCP > 2 on NRS is likely to correspond to more intense postoperative pain and to take appropriate measures to mitigate this pain.

There is also the concern over non-blinded studies and those performed without a sham TENS arm. However, in Study III, we wanted to compare HFHI TENS to standard opioid treatment in the simplest possible way. The Helsinki Declaration (2024) also tells us to compare to the gold standard: “The benefits, risks, burdens, and effectiveness of a new intervention must be tested against those of the best proven intervention” (188). Moreover, it is difficult to blind patients to the sensation of receiving HFHI TENS. During the minute that it takes to relieve the pain, a patient receives high-intensity stimulation at their own choosing, again making it impractical to apply a

sham contraption that could not provide this sensation. This issue is a concern even with conventional TENS. In a recent RCT by Parseliunas et al. (2021), more than half of the patients were able to accurately distinguish which treatment they received, i.e., sham or active TENS (93).

The primary outcome in Study III was "time in the PACU". This was chosen because we had seen that the results from three prior studies performed at our center showed that HFHI TENS decreased time in the PACU compared to opioids after gynecological outpatients surgery (99, 132, 133). The variable chosen could be criticized because it depends on accurate registration of arrival time and departure time from the PACU. However, it is reasonable to expect that potential discrepancies would affect both the HFHI TENS group and the opioid group to a similar extent, both in Study II and Study III.

One exclusion criterion in Studies I and III was "habitual use of opioids". This was because it is known that long-term use of opioids can create a cross-tolerance for TENS (102, 189).

8:7:3 METHODOLOGICAL CONSIDERATIONS IN STUDY IV - V

Qualitative research needs to have rigor and trustworthiness, just as quantitative research needs to have internal and external validity. Rigor relates to the quality of the process, while trustworthiness pertains to the quality of the results. What is specific to qualitative research is reflexivity, which in this context also is a feature of transparency, i.e., it involves critically reflecting on how the researcher influences the research and acknowledges that a researcher is not a neutral observer.

The method chosen in Studies IV and V was interviews. This is an accurate method for examining others' experiences. In Study V, a possible alternative could have been an ethnographic study where we "shadowed" the healthcare professionals in the PACU. This would have been informative, as studies have shown that there can exist a discrepancy between what healthcare professionals say and what they do (190). However, that would have required more resources than were available.

"It was amazing to see how she went from being in quite a lot of pain to almost none at all, like down to zero or one." (Participant in study V)

9 CONCLUSIONS

In summary, this thesis supports that TENS could be offered in multimodal postoperative pain management plans because of its efficiency and because patients desire alternative options for pain relief postoperatively. PVCP should be considered when prescribing peri-operative pain relief, because it helps healthcare professionals to predict postoperative pain intensity and time in the PACU.

- PVCP assessment can predict the intensity of postoperative pain and time needed in the PACU for individual patients. Each one-point increase in PVCP measured with the NRS is associated with a higher risk of intense postoperative pain.
- Time in the PACU and opioid consumption can be reduced in the gynecological outpatient surgery cohort by using HFHI TENS.
- Opioid consumption can be reduced after outpatient laparoscopic cholecystectomy by using HFHI TENS.
- HFHI TENS is a potent intervention with a prompt pain-relieving effect in the PACU in responders to TENS.
- Patients desire alternatives to pharmacological analgesics after surgery. HFHI TENS offers autonomy in the postoperative context.
- Nurses and assistant nurses can efficiently use HFHI TENS in the PACU. However, there is a need for educational support and clinical guidelines regarding TENS.

The bedside test of PVCP and the use of HFHI TENS are two simple, easily available methods by which postoperative pain relief might be improved after outpatient surgery.

"The advantage is that you can control it more than if you just take some other medicine that you swallow. Because if you get side effects from medication, you just must wait until they wear off — but with TENS, you can just switch it off if you don't like it. You can control it yourself, adjust the intensity up and down, and that's something I think is good." (Participant in study IV)

10 FUTURE DIRECTIONS

This thesis contributes knowledge that can be used to improve multimodal postoperative pain plans in outpatient surgery by providing methods to predict and treat postoperative pain. However, several questions remain.

10:1 TENS RESPONSE

In Study V, healthcare professionals commented that patients who had prior experience of using TENS had an advantage in tolerating higher intensity stimulation. This could be a possible predictor for response to HFHI TENS treatment and suggests that it would be advantageous if stimulation could be tested at the preoperative assessment. This ought to be evaluated in research.

A negative predictor for response is presenting in the PACU after surgery with intense pain, as seen in Study III. With this knowledge, the healthcare provider can rethink when to offer which treatment in the postoperative process (see appendix). A regime, starting with a dose of opioids in case of intense pain, warrants evaluation, particularly as to whether HFHI TENS will still be opioid sparing and whether patients approve of this postoperative pain management approach.

To support the evidence about HFHI TENS' effects, the RCT in Study III needs to be repeated in the context of other surgical populations.

To implement TENS in routine clinical practice, we need to change the healthcare professionals' and the public's knowledge and attitudes concerning the method. We need to spread the word that there exists a non-invasive neuromodulation method that works without adverse effects to ameliorate pain, and we need to enlighten all healthcare professionals about TENS, both theoretically and in a practical, "hands-on" way, starting in basic education. Applying TENS is a craft, like inserting a peripheral venous cannula, and healthcare professionals need the opportunity to practice regularly to become proficient in this craft (191). We need to create guidelines for the use of TENS in hospitals, in the PACU, and in the wards, and these guidelines need to be implemented.

10:2 USING TENS AT HOME

Outpatient surgery includes the challenge of being left without professional help after discharge to manage postoperative pain, which can be severe (171). Reluctance of patients to adhere to recommended pain treatment, fearing adverse effects of opioid and/or non-opioid analgesics, is one factor with an impact on pain management after discharge. Gramke et al. (2007) proposed patient education to improve compliance (172). As the adverse effects patients fear include obstipation, nausea, and/or dependence, it would seem reasonable to provide them with a complementary approach by loaning out a TENS unit.

For how long after surgery should TENS treatment continue? Patients expect recovery after outpatient surgery to be prompt, but pain, nausea, and restricted mobility can impair recovery for weeks (192).

There is a risk of analgesic tolerance when TENS is used continuously for several days, applying a daily dose at the same intensity, frequency, and duration. This can be mitigated by increasing the intensity and/or using a mixed-frequency stimulation regime (103). This concern demonstrates the need for troubleshooting advice from healthcare professionals, which can be achieved digitally, by phone or by visits in the form of "hospital at home" or homecare, projects that are currently reconstructing healthcare approaches in Sweden (193). Follow-up studies examining the effects of at-home TENS use are vital.

10:3 PREDICTING POSTOPERATIVE PAIN

It would seem logical to explore if an enhanced pain management protocol, including HFHI TENS postoperatively, would, in fact, improve pain relief in the PACU in patients reporting PVCP as NRS > 2. It would be interesting to find out exactly how we should formulate questions to capture further issues that have the potential of impacting postoperative pain, and what this might add to the accuracy of prediction.

10:4 PERSONCENTERED CARE IN THE PACU

PCC is a working model and presupposes a change of culture in the ward (194). There exists much research performed in medical wards, and this research needs to be extended to the postoperative context, involving all levels of healthcare (120). Some questions to explore would be asking patients what postoperative level of pain is acceptable to them, and what resources they habitually use to deal with pain in their lives. In the context of postoperative care, much of the work of listening to and documenting the patient's narrative will need to take place preoperatively. This necessitates a mapping of the potential resources within healthcare settings to facilitate such practices.

"You're still clear in your head, you don't feel chemically affected even though you've had anesthesia and all that. It's a completely different feeling. I've had surgery once before, and this time it was such a relief to just be able to get up, walk back to bed, lie down, and hook it up." (Participant in study IV)

USE OF GENERATIVE AI

The author has used Google to search for subjects of interest and to find articles, and Chat GPT to translate certain paragraphs and sentences, and to structure one table where the analysis already was done.

The author takes full responsibility for the content of the thesis and its scientific accuracy.

"The TENS really took away the pain — morphine just cuts the edge off the worst pain." (Participant in study IV)

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REFERENCES

1. Abbey J, Piller N, De Bellis A, Esterman A, Parker D, Giles L, et al. The Abbey pain scale: a 1-minute numerical indicator for people with end-stage dementia. Int J Palliat Nurs. 2004;10(1):6-13.
2. https://www.iasp-pain.org/resources/terminology/. IASP terminology.
3. Narayan MC. Culture's effects on pain assessment and management. Am J Nurs. 2010;110(4):38-47; quiz 8-9.
4. Yang MMH, Hartley RL, Leung AA, Ronksley PE, Jetté N, Casha S, et al. Preoperative predictors of poor acute postoperative pain control: a systematic review and meta-analysis. BMJ open. 2019;9(4):e025091.
5. Schnabel A, Yahiaoui-Doktor M, Meissner W, Zahn PK, Pogatzki-Zahn EM. Predicting poor postoperative acute pain outcome in adults: an international, multicentre database analysis of risk factors in 50,005 patients. Pain Rep. 2020;5(4):e831.
6. Papadomanolakis-Pakis N, Haroutounian S, Sørensen JK, Runge C, Brix LD, Christiansen CF, et al. Predicting acute postsurgical pain in the postanesthesia care unit: risk tool development and internal validation. PAIN Reports. 2025;10(5):e1329.
7. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. Anesth Analg. 2003;97(2):534-40.
8. Gan TJ, Habib AS, Miller TE, White W, Apfelbaum JL. Incidence, patient satisfaction, and perceptions of post-surgical pain: results from a US national survey. Current medical research and opinion. 2014;30(1):149-60.
9. Benyamin R, Trescot AM, Datta S, Buenaventura R, Adlaka R, Sehgal N, et al. Opioid complications and side effects. Pain physician. 2008;11(2 Suppl):S105-20.
10. Brummett CM, Waljee JF, Goesling J, Moser S, Lin P, Englesbe MJ, et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults. JAMA Surgery. 2017;152(6):e170504-e.
11. Lindeberg FCB, Bell M, Larsson E, Hallqvist L. New prolonged opioid consumption after major surgery in Sweden: a population-based retrospective cohort study. BMJ open. 2023;13(4):e071135.
12. Hoofwijk DM, Fiddelers AA, Peters ML, Stessel B, Kessels AG, Joosten EA, et al. Prevalence and Predictive Factors of Chronic Postsurgical Pain and Poor Global Recovery 1 Year After Outpatient Surgery. Clin J Pain. 2015;31(12):1017-25.

13. Bisgaard T, Rosenberg J, Kehlet H. From acute to chronic pain after laparoscopic cholecystectomy: A prospective follow-up analysis. Scandinavian Journal of Gastroenterology. 2005;40(11):1358-64.
14. Boko MF, Khanna AK, D'Aragon F, Spence J, Conen D, Patel A, et al. Incidence and Risk Factors of Chronic Postoperative Pain in Same-day Surgery: A Prospective Cohort Study. Anesthesiology. 2024;141(2):286-99.
15. Moka E, Aguirre JA, Sauter AR, Lavand'homme P. Chronic postsurgical pain and transitional pain services: a narrative review highlighting European perspectives. Regional Anesthesia & Pain Medicine. 2025;50(2):205-12.
16. Johnson MI. Transcutaneous electrical nerve stimulation (TENS) as an adjunct for pain management in perioperative settings: a critical review. Expert Rev Neurother. 2017;17(10):1013-27.
17. Lee A, Chan SKC, Fan LTY. Stimulation of the wrist acupuncture point PC6 for preventing postoperative nausea and vomiting. Cochrane Database of Systematic Reviews. 2015(11).
18. Bäckryd E. Pain assessment 3 × 3: a clinical reasoning framework for healthcare professionals. Scandinavian journal of pain. 2023;23(2):268-72.
19. Dong HJ, Bäckryd E. Teaching the biopsychosocial model of chronic pain: Whom are we talking to? Patient education and counseling. 2023;110:107645.
20. Karos K, Williams ACC, Meulders A, Vlaeyen JWS. Pain as a threat to the social self: a motivational account. Pain. 2018;159(9):1690-5.
21. Chapman CR, Tuckett RP, Song CW. Pain and stress in a systems perspective: reciprocal neural, endocrine, and immune interactions. The journal of pain : official journal of the American Pain Society. 2008;9(2):122-45.
22. Delande S, Lavand'homme P. Acute pain management and long term outcomes. Current Opinion in Anesthesiology. 2023;36(2):222-7.
23. Latremoliere A, Woolf CJ. Central sensitization: a generator of pain hypersensitivity by central neural plasticity. The journal of pain : official journal of the American Pain Society. 2009;10(9):895-926.
24. Melzac RW, PD. Pain mechanisms: A New Theory. Science. 1965;150(699):971-9.
25. Braz J, Solorzano C, Wang X, Basbaum AI. Transmitting pain and itch messages: a contemporary view of the spinal cord circuits that generate gate control. Neuron. 2014;82(3):522-36.
26. Ossipov MH, Morimura K, Porreca F. Descending pain modulation and chronification of pain. Current opinion in supportive and palliative care. 2014;8(2):143-51.

27. Bannister K, Dickenson AH. What do monoamines do in pain modulation? Current opinion in supportive and palliative care. 2016;10(2):143-8.
28. Fregoso G, Wang A, Tseng K, Wang J. Transition from Acute to Chronic Pain: Evaluating Risk for Chronic Postsurgical Pain. Pain physician. 2019;22(5):479-88.
29. Lee GI, Neumeister MW. Pain: Pathways and Physiology. Clinics in plastic surgery. 2020;47(2):173-80.
30. Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and prevention. J Pain Res. 2017;10:2287-98.
31. Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, et al. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. The journal of pain : official journal of the American Pain Society. 2016;17(2):131-57.
32. Gerbershagen HJ, Aduckathil S, van Wijck AJ, Peelen LM, Kalkman CJ, Meissner W. Pain intensity on the first day after surgery: a prospective cohort study comparing 179 surgical procedures. Anesthesiology. 2013;118(4):934-44.
33. Chapman CR, Vierck CJ. The Transition of Acute Postoperative Pain to Chronic Pain: An Integrative Overview of Research on Mechanisms. The Journal of Pain. 2017;18(4):359.e1-.e38.
34. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. The Lancet. 2006;367(9522):1618-25.
35. Persson AK, Dyrehag LE, Åkeson J. Prediction of Postoperative Pain From Electrical Pain Thresholds After Laparoscopic Cholecystectomy. Clin J Pain. 2017;33(2):126-31.
36. Werner MU, M.D., D.M.Sc., Mjöbo HN, M.D., Nielsen PR, M.D., Rudin Å, M.D., Ph.D. Prediction of Postoperative Pain: A Systematic Review of Predictive Experimental Pain Studies. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2010;112(6):1494-502.
37. Abrishami A, Chan J, Chung F, Wong J, Warner DS. Preoperative Pain Sensitivity and Its Correlation with Postoperative Pain and Analgesic Consumption: A Qualitative Systematic Review. Anesthesiology. 2011;114(2):445-57.
38. Mogianos K, Åkeson J, Persson AKM. Systematic Review of Methods for Individual Prediction of Postoperative Pain. Pain research & management. 2025;2025:1331412.
39. Chowdhury NS, Bi C, Furman AJ, Chiang AKI, Skippen P, Si E, et al. Predicting Individual Pain Sensitivity Using a Novel Cortical Biomarker Signature. JAMA Neurology. 2025.

40. Kotikalapudi R, Kincses B, Zunhammer M, Schlitt F, Asan L, Schmidt-Wilcke T, et al. Brain morphology predicts individual sensitivity to pain: a multicenter machine learning approach. PAIN. 2023;164(11):2516-27.
41. Ho CN, Fu PH, Hung KC, Wang LK, Lin YT, Yang AC, et al. Prediction of early postoperative pain using sleep quality and heart rate variability. Pain practice : the official journal of World Institute of Pain. 2024;24(1):82-90.
42. Kalkman J, Visser K, Moen J, Bonsel J, Grobbee E, Moons M. Preoperative prediction of severe postoperative pain. Pain. 2003;105(3):415-23.
43. Sipilä RM, Haasio L, Meretoja TJ, Ripatti S, Estlander A-M, Kalso EA. Does expecting more pain make it more intense? Factors associated with the first week pain trajectories after breast cancer surgery. PAIN. 2017;158(5):922-30.
44. Bayman EO, Parekh KR, Keech J, Larson N, Vander Weg M, Brennan TJ. Preoperative Patient Expectations of Postoperative Pain Are Associated with Moderate to Severe Acute Pain After VATS. Pain medicine (Malden, Mass). 2019;20(3):543-54.
45. Ledowski T. Objective monitoring of nociception: a review of current commercial solutions. Br J Anaesth. 2019;123(2):e312-e21.
46. Persson AK, Pettersson FD, Dyrehag L-E, Åkeson J. Prediction of postoperative pain from assessment of pain induced by venous cannulation and propofol infusion. Acta Anaesthesiologica Scandinavica. 2016;60(2):166-76.
47. Persson AKM, Åkeson J. Prediction of Acute Postoperative Pain from Assessment of Pain Associated With Venous Cannulation. Pain Practice. 2019;19(2):158-67.
48. Orbach-Zinger S, Aviram A, Fireman S, Kadechenko T, Klein Z, Mazarib N, et al. Severe pain during local infiltration for spinal anaesthesia predicts post-caesarean pain. Eur J Pain. 2015;19(9):1382-8.
49. Peng F, Li Y, Ai Y, Yang J, Wang Y. Application of preoperative assessment of pain induced by venous cannulation in predicting postoperative pain in patients under laparoscopic nephrectomy: a prospective observational study. BMC anesthesiology. 2020;20(1):86.
50. Carvalho B, Zheng M, Aiono-Le Tagaloa L. Evaluation of experimental pain tests to predict labour pain and epidural analgesic consumption. Br J Anaesth. 2013;110(4):600-6.
51. Mears L, Mears J. The pathophysiology, assessment, and management of acute pain. British journal of nursing (Mark Allen Publishing). 2023;32(2):58-65.

52. McCaffery M, University of California LACftHS. Nursing Practice Theories Related to Cognition, Bodily Pain, and Man-environment Interactions: UCLA Students' Store; 1968.
53. Dunwoody CJ, Krenzischek DA, Pasero C, Rathmell JP, Polomano RC. Assessment, physiological monitoring, and consequences of inadequately treated acute pain. Pain management nursing : official journal of the American Society of Pain Management Nurses. 2008;9(1 Suppl):S11-21.
54. Gordon DB. Acute pain assessment tools: let us move beyond simple pain ratings. Current Opinion in Anesthesiology. 2015;28(5):565-9.
55. Höök A, Hylén M, Björk M, Nilsson S, Bai J, Berlin H, et al. The Electronic Faces Thermometer Scale (eFTS)-Construct Validity for Pain Assessment in Pediatric Postoperative Care in Sweden. Paediatric anaesthesia. 2025.
56. Charlton JE, editor. Core curriculum for professional education in pain. third edition ed. Seattle: IASP press; 2008.
57. Rogger R, Bello C, Romero CS, Urman RD, Luedi MM, Filipovic MG. Cultural Framing and the Impact On Acute Pain and Pain Services. Curr Pain Headache Rep. 2023;27(9):429-36.
58. Cepeda MS, Africano JM, Polo R, Alcala R, Carr DB. What decline in pain intensity is meaningful to patients with acute pain? Pain. 2003;105(1-2):151-7.
59. Olsen MF, Bjerre E, Hansen MD, Hilden J, Landler NE, Tendal B, et al. Pain relief that matters to patients: systematic review of empirical studies assessing the minimum clinically important difference in acute pain. BMC medicine. 2017;15(1):35.
60. Myles PS, Myles DB, Galagher W, Boyd D, Chew C, MacDonald N, et al. Measuring acute postoperative pain using the visual analog scale: the minimal clinically important difference and patient acceptable symptom state. Br J Anaesth. 2017;118(3):424-9.
61. Miller CJ, Bilker WB, DeLorey I, Argoff CE, Bell RL, Conroy A, et al. Minimum clinically important differences in acute pain: a patient-level re-analysis of randomized controlled analgesic trials submitted to the US Food and Drug Administration. PAIN. 2025:10.1097/j.pain.0000000000003645.
62. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. PAIN. 2005;113(1).
63. Declaration of Montreal [Internet]. 2010. Available from: https://www.iasp-pain.org/advocacy/iasp-statements/access-to-pain-management-declaration-of-montreal/.
64. Nimmo SM, Foo ITH, Paterson HM. Enhanced recovery after surgery: Pain management. Journal of surgical oncology. 2017;116(5):583-91.

65. Joshi GP. Rational Multimodal Analgesia for Perioperative Pain Management. Curr Pain Headache Rep. 2023;27(8):227-37.
66. Laporta ML, Sprung J, Weingarten TN. Respiratory depression in the post-anesthesia care unit: Mayo Clinic experience. Bosn J Basic Med Sci. 2021;21(2):221-8.
67. Bowen J, Levy N, Macintyre P. Opioid-induced ventilatory impairment: current 'track and trigger' tools need to be updated. Anaesthesia. 2020;75(12):1574-8.
68. Fletcher D, Martinez V. Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis. Br J Anaesth. 2014;112(6):991-1004.
69. Paul AK, Smith CM, Rahmatullah M, Nissapatorn V, Wilairatana P, Spetea M, et al. Opioid Analgesia and Opioid-Induced Adverse Effects: A Review. Pharmaceuticals (Basel, Switzerland). 2021;14(11).
70. Simpson JC, Bao X, Agarwala A. Pain Management in Enhanced Recovery after Surgery (ERAS) Protocols. Clin Colon Rectal Surg. 2019;32(2):121-8.
71. Srivastava D, Hill S, Carty S, Rockett M, Bastable R, Knaggs R, et al. Surgery and opioids: evidence-based expert consensus guidelines on the perioperative use of opioids in the United Kingdom. British Journal of Anaesthesia. 2021;126(6):1208-16.
72. Bell RF, Kalso EA. Ketamine for pain management. Pain Rep. 2018;3(5):e674.
73. Neil MJ. Clonidine: clinical pharmacology and therapeutic use in pain management. Curr Clin Pharmacol. 2011;6(4):280-7.
74. Darvall J, Handscombe M, Maat B, So K, Suganthirakumar A, Leslie K. Interpretation of the four risk factors for postoperative nausea and vomiting in the Apfel simplified risk score: an analysis of published studies. Canadian Journal of Anesthesia/Journal canadien d'anesthésie. 2021;68(7):1057-63.
75. Twycross R, Ross J, Kotlinska-Lemieszek A, Charlesworth S, Mihalyo M, Wilcock A. Variability in response to drugs. Journal of pain and symptom management. 2015;49(2):293-306.
76. Cepeda MS, Carr DB. Women Experience More Pain and Require More Morphine Than Men to Achieve a Similar Degree of Analgesia. Anesthesia & Analgesia. 2003;97(5):1464-8.
77. Levy N, Quinlan J, El-Boghdadly K, Fawcett WJ, Agarwal V, Bastable RB, et al. An international multidisciplinary consensus statement on the prevention of opioid-related harm in adult surgical patients. Anaesthesia. 2021;76(4):520-36.

78. Niyonkuru E, Iqbal MA, Zhang X, Ma P. Complementary Approaches to Postoperative Pain Management: A Review of Non-pharmacological Interventions. Pain and therapy. 2025;14(1):121-44.
79. Heikkilä K, Peltonen LM, Salanterä S. Postoperative pain documentation in a hospital setting: A topical review. Scandinavian journal of pain. 2016;11:77-89.
80. Sakko Y, Aimagambetova G, Terzic M, Ukybassova T, Bapayeva G, Gusmanov A, et al. The Prevalence, Indications, Outcomes of the Most Common Major Gynecological Surgeries in Kazakhstan and Recommendations for Potential Improvements into Public Health and Clinical Practice: Analysis of the National Electronic Healthcare System (2014-2019). Int J Environ Res Public Health. 2022;19(22).
81. Munro A, Sjaus A, George RB. Anesthesia and analgesia for gynecological surgery. Current Opinion in Anesthesiology. 2018;31(3):274-9.
82. Wang X, Yu W, Jiang G, Li H, Li S, Xie L, et al. Global Epidemiology of Gallstones in the 21st Century: A Systematic Review and Meta-Analysis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2024;22(8):1586-95.
83. Pak M, Lindseth G. Risk Factors for Cholelithiasis. Gastroenterology nursing : the official journal of the Society of Gastroenterology Nurses and Associates. 2016;39(4):297-309.
84. Shaffer EA. Epidemiology of gallbladder stone disease. Best Practice & Research Clinical Gastroenterology. 2006;20(6):981-96.
85. Jiang B, Ye S. Pharmacotherapeutic pain management in patients undergoing laparoscopic cholecystectomy: A review. Advances in clinical and experimental medicine : official organ Wroclaw Medical University. 2022;31(11):1275-88.
86. Melly C, McGeehan G, O'Connor N, Johnston A, Bass G, Mohseni S, et al. Patient-reported outcome measures (PROMs) after laparoscopic cholecystectomy: systematic review. BJS Open. 2022;6(3).
87. Bisgaard TMDDS. Analgesic Treatment after Laparoscopic Cholecystectomy: A Critical Assessment of the Evidence. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2006;104(4):835-46.
88. Johnson MI. Transcutaneous Electrical Nerve Stimulation (TENS): Research to support clinical practice: Oxford University Press; 2014 01 Apr 2014.
89. Lang T, Barker R, Steinlechner B, Gustorff B, Puskas T, Gore O, et al. TENS Relieves Acute Posttraumatic Hip Pain During Emergency Transport. Journal of Trauma and Acute Care Surgery. 2007;62(1):184-8.

90. Mora B, Giorni E, Dobrovits M, Barker R, Lang T, Gore C, et al. Transcutaneous electrical nerve stimulation: an effective treatment for pain caused by renal colic in emergency care. J Urol. 2006;175(5):1737-41; discussion 41.
91. Grover CA, McKernan MP, Close RJH. Transcutaneous Electrical Nerve Stimulation (TENS) in the Emergency Department for Pain Relief: A Preliminary Study of Feasibility and Efficacy. The western journal of emergency medicine. 2018;19(5):872-6.
92. Piasecki A, Ögren C, Thörn SE, Olausson A, Svensson CJ, Platon B, et al. High-frequency, high-intensity transcutaneous electrical nerve stimulation compared with opioids for pain relief after gynecological surgery: a systematic review and meta-analysis. Scandinavian journal of pain. 2023.
93. Parseliunas A, Paskauskas S, Kubiliute E, Vaitekunas J, Venskutonis D. Transcutaneous Electric Nerve Stimulation Reduces Acute Postoperative Pain and Analgesic Use After Open Inguinal Hernia Surgery: A Randomized, Double-Blind, Placebo-Controlled Trial. The journal of pain : official journal of the American Pain Society. 2021;22(5):533-44.
94. DeSantana JM, Sluka KA, Lauretti GR. High and low frequency TENS reduce postoperative pain intensity after laparoscopic tubal ligation: A randomized controlled trial. Clinical Journal of Pain. 2009;25(1):12-9.
95. Rakel B, Frantz R. Effectiveness of transcutaneous electrical nerve stimulation on postoperative pain with movement. The Journal of Pain. 2003;4(8):455-64.
96. Moran F, Leonard T, Hawthorne S, Hughes CM, McCrum-Gardner E, Johnson MI, et al. Hypoalgesia in Response to Transcutaneous Electrical Nerve Stimulation (TENS) Depends on Stimulation Intensity. The Journal of Pain. 2011;12(8):929-35.
97. Bjordal JM, Johnson MI, Ljunggreen AE. Transcutaneous electrical nerve stimulation (TENS) can reduce postoperative analgesic consumption. A meta-analysis with assessment of optimal treatment parameters for postoperative pain. European Journal of Pain. 2003;7(2):181-8.
98. Johnson MI. Resolving Long-Standing Uncertainty about the Clinical Efficacy of Transcutaneous Electrical Nerve Stimulation (TENS) to Relieve Pain: A Comprehensive Review of Factors Influencing Outcome. Medicina (Kaunas, Lithuania). 2021;57(4).
99. Platon B, Mannheimer C, Andréll P. Effects of high-frequency, high-intensity transcutaneous electrical nerve stimulation versus intravenous opioids for pain relief after gynecologic laparoscopic surgery: a randomized controlled study. Korean J Anesthesiol. 2018;71(2):149-56.

100. Andréll P. Neuromodulation for Refractory Angina and Heart Failure. In: Krames E PH, Rezai A., editor. Neuromodulation 2e, VOL3 p 1279-1292 ISBN: 97801280535392018.
101. Leonard G, Goffaux P, Marchand S. Deciphering the role of endogenous opioids in high-frequency TENS using low and high doses of naloxone. PAIN. 2010;151(1):215-9.
102. Léonard G, Cloutier C, Marchand S. Reduced Analgesic Effect of Acupuncture-like TENS but Not Conventional TENS in Opioid-Treated Patients. The Journal of Pain. 2011;12(2):213-21.
103. Vance CGT, Dailey DL, Chimenti RL, Van Gorp BJ, Crofford LJ, Sluka KA. Using TENS for Pain Control: Update on the State of the Evidence. Medicina (Kaunas, Lithuania). 2022;58(10).
104. Sirucek L, Ganley RP, Zeilhofer HU, Schweinhardt P. Diffuse noxious inhibitory controls and conditioned pain modulation: a shared neurobiology within the descending pain inhibitory system? Pain. 2023;164(3):463-8.
105. Bannister K, Dickenson AH. The plasticity of descending controls in pain: translational probing. J Physiol. 2017;595(13):4159-66.
106. Leone C, Truini A. The CPM Effect: Functional Assessment of the Diffuse Noxious Inhibitory Control in Humans. Journal of Clinical Neurophysiology. 2019;36(6):430-6.
107. Rakel BA, Zimmerman MB, Geasland K, Embree J, Clark CR, Noiseux NO, et al. Transcutaneous electrical nerve stimulation for the control of pain during rehabilitation after total knee arthroplasty: A randomized, blinded, placebo-controlled trial. Pain. 2014;155(12):2599-611.
108. Dailey DL, Rakel BA, Vance CGT, Liebano RE, Amrit AS, Bush HM, et al. Transcutaneous electrical nerve stimulation reduces pain, fatigue and hyperalgesia while restoring central inhibition in primary fibromyalgia. PAIN®. 2013;154(11):2554-62.
109. Vance CGT, Zimmerman MB, Dailey DL, Rakel BA, Geasland KM, Chimenti RL, et al. Reduction in movement-evoked pain and fatigue during initial 30-minute transcutaneous electrical nerve stimulation treatment predicts transcutaneous electrical nerve stimulation responders in women with fibromyalgia. Pain. 2021;162(5):1545-55.
110. Zhang Y, Zhang J, Wang L, Wang K, Svensson P. Effect of transcutaneous electrical nerve stimulation on jaw movement-evoked pain in patients with TMJ disc displacement without reduction and healthy controls. Acta Odontol Scand. 2020;78(4):309-20.
111. Gürgen SG, Sayın O, Çetin F, Tuç Yücel A. Transcutaneous Electrical Nerve Stimulation (TENS) Accelerates Cutaneous Wound Healing and Inhibits Pro-inflammatory Cytokines. Inflammation. 2014;37(3):775-84.
112. Penfold JA, Wells CI, Du P, Bissett IP, O'Grady G. Electrical Stimulation and Recovery of Gastrointestinal Function Following Surgery: A

Systematic Review. Neuromodulation : journal of the International Neuromodulation Society. 2019;22(6):669-79.
113. Karthik N, Lodha M, Baksi A, Dutt A, Banerjee N, Swathi M, et al. Effects of transcutaneous electrical nerve stimulation on recovery of gastrointestinal motility after laparotomy: A randomized controlled trial. World J Surg. 2024;48(7):1626-33.
114. Johnson MI, Paley CA, Jones G, Mulvey MR, Wittkopf PG. Efficacy and safety of transcutaneous electrical nerve stimulation (TENS) for acute and chronic pain in adults: a systematic review and meta-analysis of 381 studies (the meta-TENS study). BMJ open. 2022;12(2):e051073.
115. Ekman I, Swedberg K, Taft C, Lindseth A, Norberg A, Brink E, et al. Person-Centered Care — Ready for Prime Time. European Journal of Cardiovascular Nursing. 2011;10(4):248-51.
116. Coulter A, Oldham J. Person-centred care: what is it and how do we get there? Future hospital journal. 2016;3(2):114-6.
117. Standard for patient participation in person-centered care. https://www.gu.se/en/gpcc/standard-for-patient-participation-in-person-centred-care2020.
118. WHO. People-centred health care : a policy framework. https://www.who.int/pubtlications/i/item/97892906131762013.
119. Institute of Medicine Committee on Quality of Health Care in A. Crossing the Quality Chasm 2001. Available from: https://www.ncbi.nlm.nih.gov/books/NBK222274/.
120. Ekman I, Ebrahimi Z, Olaya Contreras P. Person-centred care: looking back, looking forward. European journal of cardiovascular nursing : journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology. 2021;20(2):93-5.
121. Towards state of the science in person-centred care. Gupea; University of Gothenburg2024. Available from: https://gupea.ub.gu.se/bitstream/handle/2077/84469/Towards%20state%20of%20thbe%20science%20in%20person-centred%20care%202024.pdf?sequence=2&isAllowed=y.
122. Gustavsson K, van Diepen C, Fors A, Axelsson M, Bertilsson M, Hensing G. Healthcare professionals' experiences of job satisfaction when providing person-centred care: a systematic review of qualitative studies. BMJ open. 2023;13(6):e071178.
123. McCance T, McCormack B. The Person-centred Nursing Framework: a mid-range theory for nursing practice. J Res Nurs. 2025:17449871241281428.
124. Arakelian E, Swenne CL, Lindberg S, Rudolfsson G, von Vogelsang A-C. The meaning of person-centred care in the perioperative nursing context from the patient's perspective – an integrative review. Journal of clinical nursing. 2017;26(17-18):2527-44.

125. Leonardsen AL, Wolf A, Nilsson U. Patient-Centeredness in the Perioperative Period-A Rapid Review of Current Research. J Perianesth Nurs. 2024;39(5):915-20.e3.
126. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Systematic reviews. 2016;5(h1):210.
127. Higgins JPT SJ, Page MJ, Elbers RG, Sterne JAC. Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane, 2022. Available from https://training.cochrane.org/handbook/current/chapter-08 2022. Available from: https://training.cochrane.org/handbook/current/chapter-08.
128. The Nordic Cochrane Centre TCC, 2014, Copenhagen, Denmark. Rev-Man software version 5.3. 2014.
129. GRADEpro GDT. GRADEpro Guideline Development Tool [Software]. [Internet]. Available from: https://gdt.gradepro.org/app/handbook/handbook.html.
130. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. Journal of clinical epidemiology. 2011;64(4):383-94.
131. Wetterslev J, Jakobsen JC, Gluud C. Trial Sequential Analysis in systematic reviews with meta-analysis. BMC Medical Research Methodology. 2017;17(1):39.
132. Platon B, Andréll P, Raner C, Rudolph M, Dvoretsky A, Mannheimer C. High-frequency, high-intensity transcutaneous electrical nerve stimulation as treatment of pain after surgical abortion. PAIN. 2010;148(1):114-9.
133. Platon B, Thörn S-E, Mannheimer C, Andréll P. Effects of high-frequency, high-intensity transcutaneous electrical nerve stimulation versus intravenous opioids for pain relief after hysteroscopy: a randomized controlled study. Obstetrics & gynecology science. 2020;63(5):660-9.
134. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3(2):77-101.
135. Braun V, Clarke V. Reflecting on reflexive thematic analysis. Qualitative Research in Sport, Exercise and Health. 2019;11(4):589-97.
136. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. Jama. 2013;310(20):2191-4.
137. Correll DJ, Vlassakov KV, Kissin I. No evidence of real progress in treatment of acute pain, 1993-2012: scientometric analysis. J Pain Res. 2014;7:199-210.

138. Zaslansky R. Status quo of pain-related patient-reported outcomes and perioperative pain management in 10,415 patients from 10 countries: Analysis of registry data. Eur J Pain. 2022;26(10):2120-40.
139. Levy N, Sturgess J, Mills P. Pain as the fifth vital sign and dependence on the numerical pain scale is being abandoned in the US: Why? British Journal of Anaesthesia. 2018;120(3):435-8.
140. McEvoy MD, Raymond BL, Krige A. Opioid-Sparing Perioperative Analgesia Within Enhanced Recovery Programs. Anesthesiology clinics. 2022;40(1):35-58.
141. Mariano ER, Dickerson DM, Szokol JW, Harned M, Mueller JT, Philip BK, et al. A multisociety organizational consensus process to define guiding principles for acute perioperative pain management. Reg Anesth Pain Med. 2022;47(2):118-27.
142. El-Boghdadly K, Levy NA, Fawcett WJ, Knaggs RD, Laycock H, Baird E, et al. Peri-operative pain management in adults: a multidisciplinary consensus statement from the Association of Anaesthetists and the British Pain Society. Anaesthesia. 2024;79(11):1220-36.
143. Schug SA, Palmer GM, Scott DA, Halliwell R, Trinca J. Acute pain management: scientific evidence, fourth edition, 2015. Med J Aust. 2016;204(8):315-7.
144. Mandrekar JN. Receiver operating characteristic curve in diagnostic test assessment. J Thorac Oncol. 2010;5(9):1315-6.
145. Dang H, Stafseth SK. Documentation for Assessing Pain in Postoperative Pain Management Pre- and Post-intervention. J Perianesth Nurs. 2023;38(1):88-95.
146. Vila HJ, Smith RA, Augustyniak MJ, Nagi PA, Soto RG, Ross TW, et al. The Efficacy and Safety of Pain Management Before and After Implementation of Hospital-Wide Pain Management Standards: Is Patient Safety Compromised by Treatment Based Solely on Numerical Pain Ratings? Anesthesia & Analgesia. 2005;101(2):474-80.
147. Pogatzki-Zahn EM, De Lucia S, Weinmann C, Heitkamp H, Hummelshoj L, Liedgens H, et al. A core outcome set of measurement instruments for assessing effectiveness and efficacy of perioperative pain management: results of the international IMI-PainCare PROMPT Delphi consensus process. Br J Anaesth. 2025;134(5):1460-73.
148. Fillingim RB. Individual differences in pain: understanding the mosaic that makes pain personal. Pain. 2017;158 Suppl 1(Suppl 1):S11-s8.
149. Small C, Laycock H. Acute postoperative pain management. The British journal of surgery. 2020;107(2):e70-e80.
150. Khan RS, Ahmed K, Blakeway E, Skapinakis P, Nihoyannopoulos L, Macleod K, et al. Catastrophizing: a predictive factor for postoperative pain. Am J Surg. 2011;201(1):122-31.

151. Baagil H, Baagil H, Gerbershagen MU. Preoperative Anxiety Impact on Anesthetic and Analgesic Use. Medicina (Kaunas, Lithuania). 2023;59(12).
152. Schiavenato M, Craig KD. Pain Assessment as a Social Transaction: Beyond the "Gold Standard". The Clinical Journal of Pain. 2010;26(8):667-76.
153. Felicione NJ, Blank MD, Wright CD, McNeil DW. Pain, Fear, Anxiety, and Stress: Relations to the Endogenous Opioid System. Adv Neurobiol. 2024;35:157-82.
154. Kappesser J, Williams ACC. Give and take: an evolutionary framework for social transactions in pain. Pain. 2025.
155. Zhang L, Losin EAR, Ashar YK, Koban L, Wager TD. Gender Biases in Estimation of Others' Pain. The journal of pain : official journal of the American Pain Society. 2021;22(9):1048-59.
156. Palermo TM, Davis KD, Bouhassira D, Hurley RW, Katz JD, Keefe FJ, et al. Promoting Inclusion, Diversity, and Equity in Pain Science. Pain medicine (Malden, Mass). 2023;24(2):105-9.
157. Lauzon Clabo LM. An ethnography of pain assessment and the role of social context on two postoperative units. Journal of advanced nursing. 2008;61(5):531-9.
158. Kim HS, Schwartz-Barcott D, Tracy SM, Fortin JD, Sjöström B. Strategies of pain assessment used by nurses on surgical units. Pain management nursing : official journal of the American Society of Pain Management Nurses. 2005;6(1):3-9.
159. Koban L, Jepma M, Geuter S, Wager TD. What's in a word? How instructions, suggestions, and social information change pain and emotion. Neuroscience and biobehavioral reviews. 2017;81(Pt A):29-42.
160. Törneke N. Learning RFT: An introduction to relational frame theory and its clinical application. Oakland, CA, US: New Harbinger Publications, Inc.; 2010. xviii, 267-xviii, p.
161. Kehlet H. Postoperative recovery: DrEaMing as a wake-up call? Br J Anaesth. 2022;129(1):1-3.
162. Uhrbrand P, Phillipsen A, Dreyer P, Nikolajsen L. Opioid tapering after surgery: a qualitative study of patients' experiences. Scandinavian journal of pain. 2020;20(3):555-63.
163. Karavitaki N, Bettinger JJ, Biermasz N, Christ-Crain M, Gadelha MR, Inder WJ, et al. Exogenous Opioids and the Human Endocrine System: An Endocrine Society Scientific Statement. Endocr Rev. 2024;45(6):773-94.
164. Alam A, Gomes T, Zheng H, Mamdani MM, Juurlink DN, Bell CM. Long-term Analgesic Use After Low-Risk Surgery: A Retrospective Cohort Study. JAMA Internal Medicine. 2012;172(5):425-30.

165. Marcum ZA, Hanlon JT. Recognizing the Risks of Chronic Nonsteroidal Anti-Inflammatory Drug Use in Older Adults. Ann Longterm Care. 2010;18(9):24-7.
166. Aljohani DM, Almalki N, Dixon D, Adam R, Forget P. Experiences and perspectives of adults on using opioids for pain management in the postoperative period: A scoping review. European journal of anaesthesiology. 2024;41(7):500-12.
167. Brooke BS, Bayless K, Anderson Z, Holeman TA, Zhang C, Hales J, et al. Opioid tapering after surgery and its association with patient-reported outcomes and behavioral changes: a mixed-methods analysis. Regional Anesthesia & Pain Medicine. 2024;49(10):699-707.
168. Angelini E, Josefsson C, Ögren C, Andréll P, Wolf A, Ringdal M. Patients´ experiences of TENS as a postoperative pain relief method in the post-anesthesia care unit after laparoscopic cholecystectomy: a qualitative study. BMC anesthesiology. 2025;25(1):18.
169. Xu W, Varghese C, Wells CI, Bissett IP, O'Grady G. Patient-Administered Transcutaneous Electrical Nerve Stimulation for Postoperative Pain Control After Laparoscopic Cholecystectomy: A Randomized, Sham-Controlled Feasibility Trial. Neuromodulation : journal of the International Neuromodulation Society. 2020;23(8):1144-50.
170. Gobbo M, Saldaña R, Rodríguez M, Jiménez J, García-Vega MI, de Pedro JM, et al. Patients' Experience and Needs During Perioperative Care: A Focus Group Study. Patient Prefer Adherence. 2020;14:891-902.
171. Park R, Mohiuddin M, Arellano R, Pogatzki-Zahn E, Klar G, Gilron I. Prevalence of postoperative pain after hospital discharge: systematic review and meta-analysis. Pain Rep. 2023;8(3):e1075.
172. Gramke HF, de Rijke JM, van Kleef M, Raps F, Kessels AG, Peters ML, et al. The prevalence of postoperative pain in a cross-sectional group of patients after day-case surgery in a university hospital. Clin J Pain. 2007;23(6):543-8.
173. Berg K, Årestedt K, Kjellgren K. Postoperative recovery from the perspective of day surgery patients: A phenomenographic study. International journal of nursing studies. 2013;50(12):1630-8.
174. Barry GS, Bailey JG, Sardinha J, Brousseau P, Uppal V. Factors associated with rebound pain after peripheral nerve block for ambulatory surgery. Br J Anaesth. 2021;126(4):862-71.
175. Olausson A, Angelini E, Heckemann B, Andréll P, Jildenstål P, Thörn SE, et al. Patients' perioperative experiences of an opioid-free versus opioid-based care pathway for laparoscopic bariatric surgery: A qualitative study. International journal of nursing studies advances. 2024;6:100201.
176. Diwan S, Olausson A, Andréll P, Wolf A, Jildenstål P. Knowledge, attitudes, and practices of transcutaneous electrical nerve

stimulation in perioperative care: A Swedish web-based survey. Scandinavian journal of pain. 2025;25(1).
177. Santana MJ, Manalili K, Jolley RJ, Zelinsky S, Quan H, Lu M. How to practice person-centred care: A conceptual framework. Health Expect. 2018;21(2):429-40.
178. Ekman I. Practising the ethics of person-centred care balancing ethical conviction and moral obligations. Nursing philosophy : an international journal for healthcare professionals. 2022;23(3):e12382.
179. Larsson F, Strömbäck U, Rysst Gustafsson S, Engström Å. Perception of feeling safe perioperatively: a concept analysis. Int J Qual Stud Health Well-being. 2023;18(1):2216018.
180. Forsberg A, Vikman I, Wälivaara BM, Engström Å. Patients' Perceptions of Quality of Care During the Perioperative Procedure. J Perianesth Nurs. 2015;30(4):280-9.
181. Montori VM, Ruissen MM, Hargraves IG, Brito JP, Kunneman M. Shared decision-making as a method of care. BMJ Evidence-Based Medicine. 2023;28(4):213-7.
182. Ekman N, Moons P, Taft C, Boström E, Fors A. Observable indicators of person-centred care: an interview study with patients, relatives and professionals. BMJ open. 2022;12(4):e059308.
183. Lancaster KE, Bourque J, Hyrkas K. Adult Patient Perceptions of Nurse Listening Behaviors in an Ambulatory Surgery Setting. J Perianesth Nurs. 2025.
184. Abelsson A, Falk P, Sundberg B, Nygårdh A. Empowerment in the perioperative dialog. Nurs Open. 2021;8(1):96-103.
185. Mulvale G, Green J, Robert G, Larkin M, Vackerberg N, Kjellström S, et al. Adopting, implementing and assimilating coproduced health and social care innovations involving structurally vulnerable populations: findings from a longitudinal, multiple case study design in Canada, Scotland and Sweden. Health Res Policy Syst. 2024;22(1):42.
186. Nilsson U. What is Most Important for You Now? Person-Centered Postoperative Care in the PACU. J Perianesth Nurs. 2019;34(4):877-8.
187. Weaver K, Olson JK. Understanding paradigms used for nursing research. Journal of advanced nursing. 2006;53(4):459-69.
188. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Participants. Jama. 2025;333(1):71-4.
189. Chandran P, Sluka KA. Development of opioid tolerance with repeated transcutaneous electrical nerve stimulation administration. PAIN. 2003;102(1):195-201.

190. Dihle A, Bjølseth G, Helseth S. The gap between saying and doing in postoperative pain management. Journal of clinical nursing. 2006;15(4):469-79.
191. Yılmaz E, Karakaya E, Baydur H, Tekin İ. Effect of Transcutaneous Electrical Nerve Stimulation on Postoperative Pain and Patient Satisfaction. Pain management nursing : official journal of the American Society of Pain Management Nurses. 2019;20(2):140-5.
192. Brattwall M, Warrén Stomberg M, Rawal N, Segerdahl M, Jakobsson J, Houltz E. Patients' assessment of 4-week recovery after ambulatory surgery. Acta Anaesthesiol Scand. 2011;55(1):92-8.
193. Benefits and risks of hospital at home compared with in-hospital care according to current Swedish healthcare routine 2025 [Available from: https://mellanarkiv-offentlig.vgregion.se/alfresco/s/archive/stream/public/v1/source/available/sofia/su4372-2081313122-157/native/2025_143%20HTA-rapport%20Benefits%20and%20risks%20of%20hospital%20at%20home%202025-06-30.pdf.
194. Britten N, Ekman I, Naldemirci Ö, Javinger M, Hedman H, Wolf A. Learning from Gothenburg model of person centred healthcare. Bmj. 2020;370:m2738.

APPENDIX

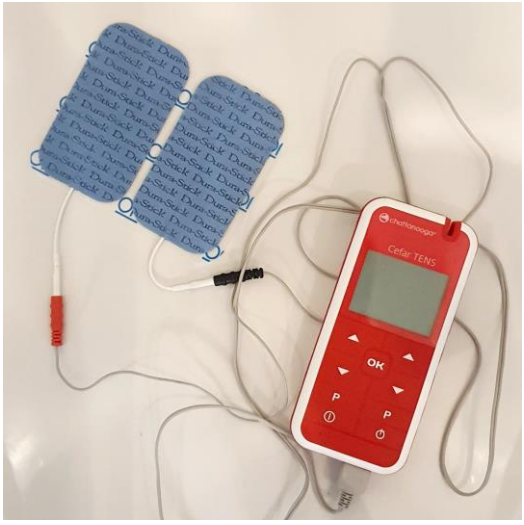


Figure 6. *TENS unit with pads Photo T. Ögren.*

Suggestions for how to use HFHI TENS in a postoperative context-recommendations based on results from study III - V

Establish contraindications: Do not use TENS if the patient is in the first trimester of pregnancy, the patient has any electronic implants, the patient is not willing to use TENS, or the patient has any neurologic deficiencies or somatosensorial impairment in the area where TENS will be applied.

Ask the patient to assess pain intensity according to the NRS, VAS, or any other scale you are using in the PACU.

If the pain intensity is reported to be 3 – 5 on NRS, or at a similar level on another scale, it is often useful to try TENS as the first option. If the pain intensity is reported to be NRS > 5, or at a similar level on another scale, it could be best to start with a small dose of opioids and introduce TENS at a later stage in the treatment management plan. However, if the patient reports a pain intensity > 5 on the NRS, or at a similar level on another scale, and still wants to start with TENS, this should obviously be respected.

Define the most painful area. Place electrode pads surrounding that area; think dermatome-wise. Be observant, so that you place the pads outside bandages to not risk infection and to ensure the pads adhere.

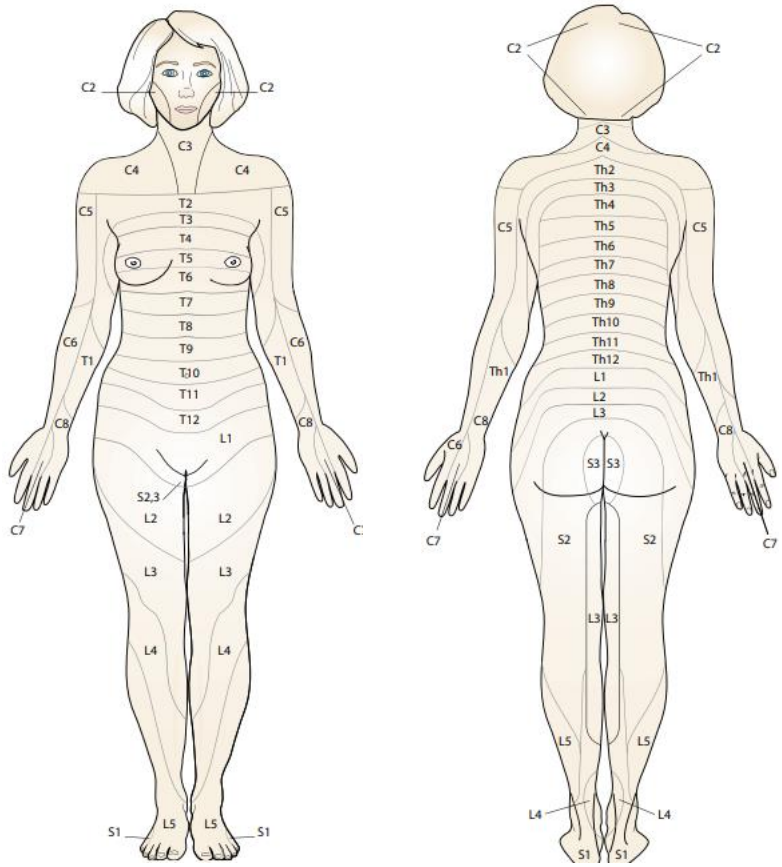


Figure 7. *Map of dermatomes. Permission to use by courtesy of MD Elisabeth Andersson, Enovis*

Start a high-frequency program and increase the intensity slowly over 30 to 60 seconds to the highest intensity the patient accepts, preferably between 40 – 60 mA. Increasing the intensity slowly allows the patient to get used to the sensation and the skin to adapt. The patient decides what intensity is acceptable. This requires you to work in close contact with the patient, continually checking verbally that the treatment is acceptable and being very

attentive to non-verbal cues that imply that the patient desires to decrease the intensity or to stop the treatment altogether.

When you and the patient, in collaboration, have decided on the highest intensity acceptable, you need to time the length of the intervention. It should be dosed at **60 seconds** exactly. Then the device is turned off, and you ask the patient to assess pain intensity once again.

If the pain relief is not sufficient, you can repeat the intervention once. Maybe the pads should be moved a bit, or maybe you can reach a higher intensity for the next administration of TENS, because the patient now knows what to expect, and the skin has adapted.

If the pain relief is adequate after one or two stimulations, the patient can be offered to take control of the device. Your task now is to teach the patient about the device so that they can move the pads, change the intensity, and the program according to their needs. This aims for autonomy.

If the pain relief is not adequate after two doses of this stimulation regime, you need to change the strategy for pain relief and administer opioids. The TENS intervention described above takes no more than 5 minutes at the most to deliver and evaluate, allowing inception of an alternate strategy without delay.