UNIVERSITY OF TURKU

The association between pre-operative pain experience and post-operative pain in patients undergoing elective gastrointestinal surgery: a descriptive-comparative study

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Tavoitteet: Katsauksen tarkoituksena oli tiivistää ja koota yhteen tutkijoille ja kliinikoille tietoa laparoskooppisten potilaiden postoperatiiviselle kivulle altistavista tekijöistä ja vallitsevista postoperatiivisista hoitokeinoista. Kuvailevan-vertailevan tutkimuksen tarkoituksena oli tutkia aiempien kipukokemusten ja lääkityksen välisiä yhteyksiä postoperatiivisen kivun voimakkuuteen potilailla, joille tehdään elektiivinen ruoansulatuskanavan leikkaus, käyttäen tietoja, jotka on kerätty esineiden internetiin perustuvalla älykkäällä kivunarviointityökalulla.

Menetelmät: Katsausta varten tehtiin hakuja PubMed-, Web of Science- ja Embase-tietokannoista. ROBINS-I-työkalua käytettiin satunnaistamattomien tutkimusten laadun arviointiin, kun taas satunnaistettujen kontrolloitujen tutkimusten osalta käytettiin ROB 2-työkalua. Kuvailevaan-vertailevaan tutkimukseen otettiin mukaan 50 potilasta Turun yliopistollisessa sairaalassa tehtyjen ruoansulatuskanavan leikkausten jälkeen. Tutkimuksen aineistonkeruun suoritti Turun yliopiston henkilökuntaan kuuluva tutkija Turun yliopistollisessa sairaalassa. Aineiston analysoinnissa käytettiin kuvailevia ja vertailevia analyysimenetelmiä. Kuvailevia tilastoja käytettiin osallistujien tulosten, diagnoosien, toimenpiteiden ja kivun kokemiseen liittyvien muuttujien perusteella tehtyjen ryhmittelyjen esittämiseen ja analysointiin (esim. maksimaalisen kiputason graafinen mittaaminen numeerisella arviointiasteikolla). Vertailevia tilastoja käytettiin yhdistelmiin ja korrelaatioihin, jotka koskivat aiempia kiputiloja, lääkkeitä, pelkoa ja kivun odotusta maksimaalisen kiputason suhteen ruoansulatuskanavan leikkausten jälkeen Turun yliopistollisessa sairaalassa.

Tulokset: Katsauksen tulokset viittaavat siihen, että potilaan psykologinen profiili vaikuttaa moniin leikkauksen jälkeiselle kivulle altistaviin tekijöihin. Näihin tekijöihin kuuluvat ahdistus, pelko, masennus, kivun odotus ja muut ruoansulatuskanavan leikkaukseen liittyvät tekijät. Tämän katsauksen tuloksissa kuvataan kuitenkin myös akuutti preoperatiivinen kipu, kirurgiset tekijät, genetiikka, ikä, sukupuoli, lihavuus ja aiemmat kokemukset kivusta merkityksellisinä altistavina tekijöinä ruoansulatuskanavan leikkauksen jälkeiselle kivulle. Ruoansulatuskanavan leikkauksen jälkeisiin kivunhoitostrategioihin kuuluu farmakologisten ja ei-farmakologisten toimenpiteiden käyttö. Kirjallisuuden mukaan ei-farmakologisia toimenpiteitä käytetään liian vähän, ja niitä olisi edistettävä farmakologisten kivunhoitostrategioiden lisänä elektiivisen ruoansulatuskanavan leikkauksen jälkeen.

Kuvailevan ja vertailevan tutkimuksen tulokset ovat jossain määrin ristiriidassa nopean katsauksen tulosten kanssa. Aiemmat kipukokemukset tai aiempien kivuliaiden tapahtumien muistaminen eivät olleet yhteydessä ylimääräisen kipulääkityksen antamiseen leikkauksen jälkeen ($p = 0,741$). Leikkauksen jälkeiseen tulevaan kipuun liittyvä pelko ei ollut yhteydessä leikkauksen invasiivisuuteen ($p = 0,662$). Lisäksi kivun odotuksen ($p = 0,698$), tulevaan kirurgiseen toimenpiteeseen liittyvän kivun pelon ($p = 0,637$) ja leikkauksen jälkeisen lääkityksen ($p = 0,481$) välinen yhteys maksimaalisen leikkauksen jälkeisen kivun voimakkuuteen todettiin merkityksettömäksi. Tämän tutkimuksen tulokset viittaavat siihen, että potilaan odotukset ovat mahdollinen interventioalue, jolla voidaan parantaa leikkauksen jälkeistä kiputilannetta. Kipulääkityksen antaminen heräämössä ja kipulääkityksen määrä heräämössä olivat merkittäviä postoperatiivisen maksimaalisen kivun ennustajia ($p = .001$).

Pohdinta: Katsauksen tulokset viittaavat siihen, että mukana olleissa tutkimuksissa on suuri tai kriittinen harhan riski. Postoperatiiviselle kivulle altistavat tekijät vaihtelivat suuresti eri tutkimuksissa, mutta niihin sisältyi pääasiassa psykologisia tekijöitä postoperatiivisen kivun tekijöinä. Kivunhoitostrategioihin olisi sisällyttävä yksilöllinen lähestymistapa, ja niitä olisi sovellettava ennen leikkausta, sen aikana ja sen jälkeen. Kuvailevassa ja vertailevassa tutkimuksessa on huomattavia vaikeuksia havaita kipuhistorian tai -kokemuksen vaikutusta leikkauksen jälkeiseen kipuun fysiologisen tai subjektiivisen raportoinnin avulla tietoisten yksilöiden osalta, koska on olemassa harhan riski ja koska käytetään yksiulotteista lähestymistapaa.

Johtopäätökset: Kivunhoitostrategioihin olisi kuuluttava osallistujien biopsykososiaalisen profiilin huolellinen seulonta valintaleikkausta varten. Kuvaileva-vertaileva tutkimus viittaa siihen, että potilaiden tulevaan ruoansulatuskanavan leikkaukseen liittyvien kipuodotusten hallinnasta on mahdollista, joskin vähäistä hyötyä. Kipulääkkeiden määrä heräämössä on merkittävä leikkauksen jälkeisen maksimaalisen kivun ennustaja. Tulevaan tutkimukseen olisi sisällytettävä suurempi otos, enemmän kipuun liittyviä muuttujia ja jatkettava seurantaa.

Asiasanat: gastrointestinaalinen, postoperatiivinen, kipu, analgesia, anestesia

Master's thesis

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Abstract

Aims: The purpose of the rapid review was to summarize and aggregate information for researchers and clinicians about predisposing factors for post-operative pain in laparoscopic patients and the prevalent management approaches post-operatively. The purpose of the descriptive-comparative study was to explore the associations between previous pain experiences and medication on the intensity of pain post-operatively in patients undergoing elective gastrointestinal surgery, using data collected by the Smart Pain Assessment Tool Based on Internet of Things.

Methods: For the rapid review, the databases of PubMed, Web of Science and Embase were searched. ROBINS-I tool was used to evaluate the quality of non-randomized studies while ROB 2 tool was used for randomized controlled trials. For the descriptive-comparative study, 50 patients after gastrointestinal operations at Turku University hospital were included. The data collection of the study was done by a researcher belonging to Turku University staff at Turku University hospital. The data analysis was done by using descriptive and comparative methods of analysis. Descriptive statistics were used for the presentation and analysis of participants outcomes, diagnoses, procedures, and groupings based on variables related to the experience of pain (e.g., graphical measurement maximal pain levels using the numeric rating scale). Comparative statistics were used for associations and correlations regarding previous pain levels, medications, fear, and expectation of pain on maximal pain levels after gastrointestinal operations at Turku University Hospital.

Results: The result of the rapid review suggest many predisposing factors for post-operative pain are influenced by the psychological profile of the patient. Among these factors are anxiety, fear, depression, expectation of pain, and other factors related to gastrointestinal surgery. Nevertheless, the results of this review also describe acute pre-operative pain, surgical factors, genetics, age, gender, obesity, and previous experiences of pain as relevant predisposing factors to pain following gastrointestinal surgery. Pain care strategies following gastrointestinal surgery include the use of pharmacological and non-pharmacological interventions. The literature suggests, non-pharmacological interventions are under-utilized and should be encouraged as an adjunct to pharmacological pain control strategies following elective gastrointestinal surgery.

The results of the descriptive-comparative study somewhat contradict the results of the rapid review. Previous pain experiences or the recollection of preceding painful events were not associated with the administration of supplemental pain medication post-operatively ($p = 0.741$). Fear related to the upcoming pain following surgery was not associated with the level of invasiveness of the surgery ($p = 0.662$). In addition, the relationship between expectation of pain ($p = 0.698$), fear of pain related to the upcoming surgical procedure ($p = 0.637$) and medication post-operatively ($p = .481$) on the intensity of maximal post-operative pain was found to be negligible. The results of this study suggest patient expectation as a possible domain of intervention for better pain outcomes post-operatively. The administration of pain medication in the recovery room and the amount of pain medication in the recovery room were significant predictors of maximal post-operative pain ($p = .001$).

Discussion: The results of the rapid review suggest a high to critical risk of bias in the studies included. The predisposing factors for post-operative pain differed widely across studies, but mainly included psychological factors as factors for post-operative pain. Pain management strategies should include an individualized approach and be implemented before, during and after the operation. For the descriptive-comparative study, there are substantial difficulties in discerning the effect of pain history or experience on post-operative pain using physiological or subjective reporting for conscious individuals due to risk of bias and using a unidimensional approach.

Conclusion: Predisposing factors for post-operative pain should be screened in the pre-operative phase if possible, focusing on addressable factors whereas management of pain care strategies should include careful screening of participants biopsychosocial profile for elective surgery. The descriptive-comparative study suggests a possible, yet minimal benefit for managing patients' expectation of pain related to the upcoming gastrointestinal surgery. The amount of pain medication in the recovery room is a significant predictor of maximal post-operative pain. Future research should include a larger sample, more variables related to pain and continue with a follow-up.

Keywords: gastrointestinal, post-operative, pain, analgesia, anesthesia

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ABBREVIATIONS

VAS	**Visual analogue scale**
NRS	**Numeric rating scale**
IoT	**Internet of Things**
API	**Application programming interface**
SPA	**Smart assessment of pain project**
GI	**Gastrointestinal**
TAP	**Transversus abdominal plane block**
NSAIDS	**Nonsteroidal anti-inflammatory drug**
APS	**Acute pain services team**
PCA	**Patient-controlled analgesia**

1. Introduction

In the world of gastrointestinal surgery, laparoscopic surgery has become the golden standard for minimally invasive procedures and has far outgrown in popularity compared to open abdominal surgery, resulting in less painful patients and faster recovery [1]. Ostensibly, researchers are constantly looking for innovations in the field of gastrointestinal surgery and post-operative management. Robotic surgery and Internet-of-Things based pain monitoring are at the forefront of research, enabling the preservation of function in patients undergoing surgery with the goal of improving quality of life [2].

As much as 75% of surgical patients suffer from moderate to severe post-operative pain in the acute phase, making it a highly prevalent and treatable symptom [3]. Pain assessment and monitoring are significant procedures for the management of pain in gastrointestinal patients for the prevention of pain chronicity, delayed discharge, psychological distress, opioid addiction, and morbidity [4].

In the field of pain research for gastrointestinal patients, the subjective assessment of pain has been conducted using either visual analogue scale (VAS) or a numeric scale ranging from 0 to 10, or alternatively 0 to 100. The VAS is considered the international standard for pain assessment [5]. This instrument offers a continuum of values from none to extreme and is considered a reliable and valid instrument whose use is widespread. Patient groups who are unable to communicate, such as those undergoing surgery, infants, persons with cognitive disabilities or otherwise unconsciously rendered individuals pose a challenge to the pain assessment process in gastrointestinal surgery [6].

Several pain assessment scales have been developed, and are continuing to be developed, for different types of noncommunicative patients (e.g., Nociception Coma Scale), yet continued innovative efforts are still required [7-8]. The challenges of using the VAS and contemporary pain scales occur due to the individual subjectivity of pain, the need for efficient communication between the healthcare provider and the patient, and the lack of proper assessment methods for individual cases [9].

The use of IoT in the healthcare field is widespread, and includes technologies such as wireless sensor networks, radio frequency identification chips relying on machine learning and the use of statistical methods [10].

Internet of Things-based pain assessments are most commonly conducted using an electronic pain diary via smartphones and mobile devices, but also include knowledge base support systems, facial expressions analysis such as crying or moaning, body position analysis, motor restlessness levels and multiple physiological parameters, all of which have been described in the literature (e.g. heart rate variability, respiratory rate, heart rate, skin temperature, galvanic skin response, electrical muscle activity and blood pressure) [6-8].

Numerous studies propose Internet of Things (IoT) based solutions using physiological parameters in the assessment of pain, and a smaller number of studies have included patient populations that are unable to properly communicate about their pain experience [6,11].There is clearly a need for innovative, advanced solutions in the field.

IoT-based solutions are designed by engineers and unfortunately, often do not integrate evidence-based information [11]. All things considered, the IoT

sensing device is a low-cost tool; the amount of time spent by healthcare providers on asking patients about pain can be reduced dramatically, treatment efficiency can be increased, and the technology enables the patient's family to be remotely and continuously kept up to date regarding the patient's condition [10]. Prospective IoT-based solutions should take into consideration all the above to create a device that is able to assess pain using physiological parameters.

The smart pain assessment (SPA) project or a smart pain assessment tool is based on Internet of Things, developed by the University of Turku. The SPA relies on multiple physiological parameters for the analysis of pain, using primarily galvanic skin responses combined with machine learning techniques and neural networks to reach this goal. Its advantage is that it combines the work of healthcare professionals with engineers from the University of Turku, collaborating with engineers from the University of California. Furthermore, it's the first pain model built using post-operative adult patients instead of healthy subjects. Its final goal is the assessment of pain in unresponsive patients and, to reach this goal, an algorithm must be constantly refined.

For this purpose, the phase II study of the SPA project took place in Turku University Hospital. The phase II study included 50 conscious patients undergoing gastrointestinal surgeries and was conducted at Turku University hospital, where the patients' pain levels were recorded before and following surgery in the recovery room using state-of-the-art devices to detect physiological parameters relevant to pain assessment. Predisposing factors to post-operative pain are constantly discovered and no ideal post-operative management strategy exists [3,12].

In this thesis, the first part consists of a rapid review aiming on the summarize, what are the up-to-date, measurable predisposing factors influencing pain levels post-operatively after a gastrointestinal operation? And what are the current strategies for pain management post-operatively following gastrointestinal surgery? The second part of this thesis relies on the data from Phase II study of the SPA project. This study design is descriptive-comparative research, focusing on the subjective pain experiences, described along with physiological parameters which were chosen considering the results of the rapid review, and were statistically analyzed.

The strength and significance of the second part of this study is made clear by its investigation of data collected from 50 elective gastrointestinal patients, exploring the relationship between previous pain experiences, pain history and medication on the intensity of pain post-operatively in patients undergoing elective gastrointestinal surgery.

This study adds value to the field of pain research to better understand the individual response to post-operative pain following elective gastrointestinal surgeries and provide information for researchers. This study offers the SPA project valuable information for further analysis in the development of the previously mentioned IoT device. The exploration conducted in this study of the relationship between pain history, medications and related post-operative pain is essential for the understanding of the nature of pain in the context of both elective gastrointestinal patients and the psychological factors prevalent in the studied population as well as overall pain research.

The results offer a perspective into possible opportunities for further research as well as for limitations the SPA project may encounter before progressing with the development of the device. This study also offers a cultural perspective into the experience of pain in a selected Finnish population, thus enabling more accurate pattern recognition for the SPA project while providing useful data for prospective research in the field of pain of elective gastrointestinal patients in Finland. The technological roadmap for this study can be seen in the following page, described with Figure 1.

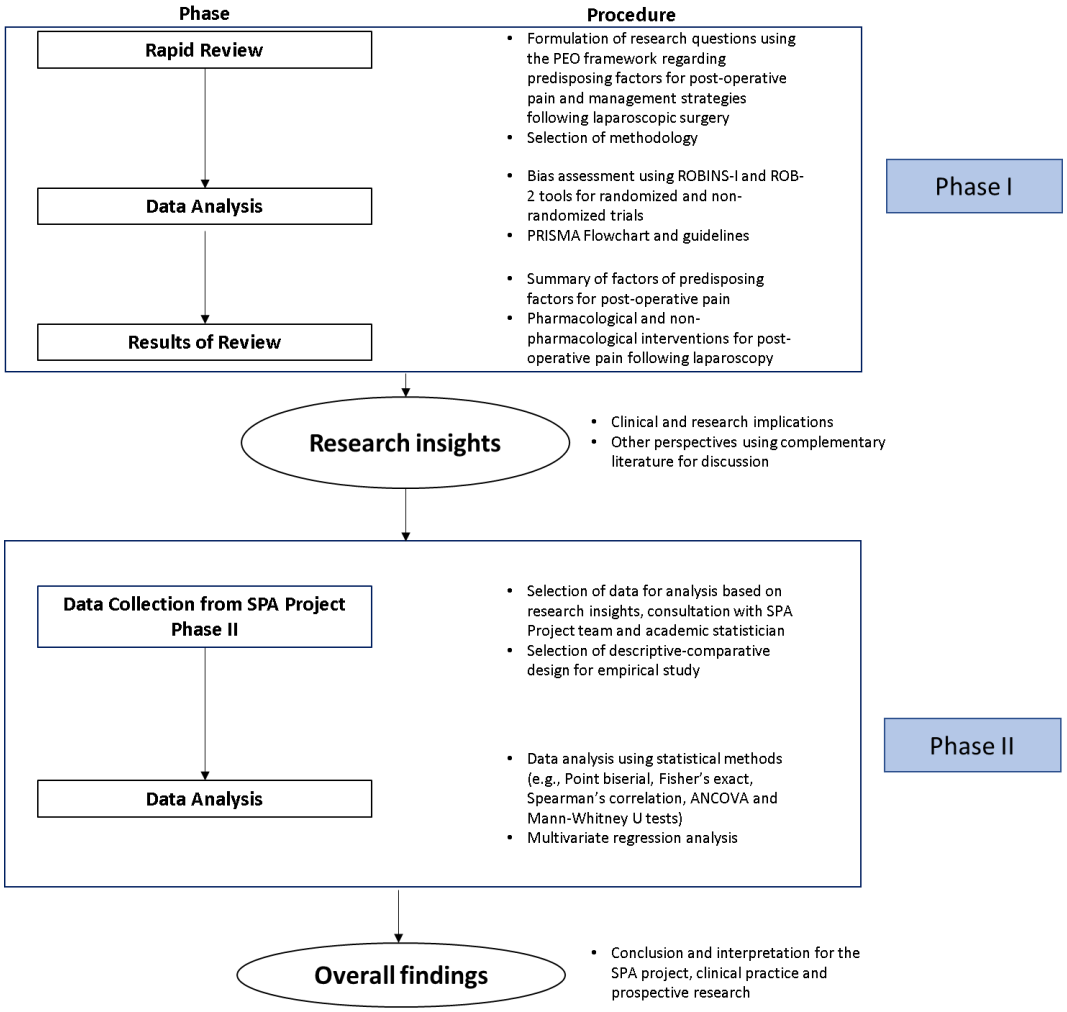


Figure 1. Technological roadmap

2. Review of the literature

2.1 Review purpose

The purpose of this rapid review was to summarize the predisposing factors associated with post-operative pain patients following laparoscopy,

and the relevant post-operative pain care management strategies following laparoscopic surgery.

2.2 Method

This review was not registered. The method of rapid review was chosen as the evidence base is large and its goal is to map the research in the area to identify existing gaps in knowledge, the review can later be used as a source of information for a guideline update for the target population [13]. Rapid reviews rely on the Cochrane Handbook for Systematic Reviews of Interventions and can be used for policy development or updating previously completed reviews. To maintain methodological quality, enhance critical appraisal and reproducibility of this work, the PRISMA 2020 statement (preferred reporting items for systematic reviews and meta-analyses) was used to guide the review [14]. See Appendix C. for the complete checklist.

2.3 Search strategy

The databases of PubMed, Web of Science and Embase were searched based on the inclusion criteria. The search strategy included the following keywords: (laparoscop* OR endoscop* OR "keyhole surger*" OR "key-hole surger*" OR sigmoidoscop*) AND (preoperative* OR "pre-operative*" OR "before surger*" OR "before operation*" OR “before procedure*” OR presurger* OR "pre-surger*" OR preprocedure* OR "pre-procedure*") AND (fear* OR anxi* OR "pain histor*" OR "recovery room*").

The searching process was based on the use of a PEO table, seen in Table 1. The reason for using the modified version was that the method

used in this thesis was a rapid review, therefore PICO was not relevant as this study does not intend to study a distinct intervention.

Table 1

PEO Elements

PEO ELEMENTS	KEYWORDS
P (Patient OR Population)	**Patients** undergoing abdominal surgery
E (Exposure)	**Laparoscopic surgery**
O (Outcome)	**Post-operative pain relief**

On another note, the databases were also searched to find articles, supplementary articles or guidelines informing about the topic which were included only in other sections of this thesis (e.g., discussion part) but not in the rapid review chapter.

2.4 Selection criteria

Articles selected included studies whose age of participants were 18 or higher, were conducted between 2011 and 2021, in the English language and focused on laparoscopic surgery in humans. Excluded articles were articles pertaining to pediatric surgery or articles where laparoscopic surgery was not conducted.

The review included literature from randomized controlled trials as well as non-randomized controlled trials as to provide a wide perspective on the topic. See Table 2 below for inclusion and exclusion criteria.

Table 2

Inclusion and Exclusion Criteria

INCLUSION	EXCLUSION
English language	Pediatric related
Adults (18+)	Non-GI related
Human subjects	
Published in the last 10 years	

2.5 Outcome

Data regarding predisposing factors for post-operative pain of patients undergoing laparoscopic surgery and pain care management strategies was reviewed. This study was conducted in two parts. This first part is a rapid review, aiming to answer the following questions:

a. What are the predisposing factors for post-operative pain following laparoscopic surgery?
b. What are the up-to-date management strategies for post-operative pain following laparoscopic surgery?

2.6 Search results

This literature review included 1920 citations from 3 different databases and excluded the articles based on the previously described inclusion and exclusion criteria. The result of the literature search was 14 relevant articles

which were extracted using the help of the university of Turku library consultation services. See Figure 2.

Figure 2. Search results

2.7 Risk of bias assessment

The findings included in this rapid literature review were assessed using the risk of bias assessment in non-randomized studies of interventions tool, ROBINS-I (Table 3.) [15]. This was followed by the assessment of the studies included in the literature review that are considered randomized controlled trials using the ROB-2 tool (Table 4.) [16]. The result of the bias analysis of the studies included in this rapid literature review, indicate that the literature regarding predisposing factors to post-operative pain and pain care strategies following laparoscopic surgery consists of studies at critical risk (3/14) to serious risk (2/14) of bias for non-randomized controlled trials, whereas the randomized controlled trials range from trials raising some concerns of bias (2/14) to those with high risk of bias (7/14). See Table 3 and Table 4 respectively.

Table 3

Risk of Bias Assessment Using the ROBINS-I Tool for Non-Randomized Studies of Interventions

Study	Confounding	Selection of participants	Classification of interventions	Deviations from intended interventions	Missing data	Measurement of outcomes	Selection of reported results	Overall
Wright et al. 2016	Critical risk	Moderate risk	Critical risk	Moderate risk	Serious risk	Serious risk	Critical risk	**Critical risk of bias**
Choi et al. 2020	Serious risk	Serious risk	Moderate risk	Moderate risk	Serious risk	Serious risk	Serious risk	**Serious risk**
Panda et al. 2020	Critical risk	Serious risk	Serious risk	Serious risk	Serious risk	Critical risk	Critical risk	**Critical risk**
Aceto et al. 2016	Moderate risk	Critical risk	Serious risk	Moderate risk	Low risk	Serious risk	Serious risk	**Critical risk**
Daoudia et al. 2015	Moderate risk	Moderate risk	Moderate risk	Low risk	Low risk	Serious risk	Serious risk	**Serious risk**

Table 4

Risk of bias assessment using the ROB-2 tool for randomized studies of interventions

Study	Risk of bias from the randomization process	Risk of bias due to deviations from the intended intervention	Risk of bias due to missing data	Risk of bias in measurement of the outcome	Risk of bias in selection of the reported result	Overall risk of bias
Ali et al. 2014	?	+	+	?	?	High risk
Sadati et al. 2013	?	-	-	-	?	High risk
Miao et al. 2020	+	?	?	?	?	High risk
Von Plato et al. 2019	+	?	+	?	+	Some concerns
Trujillo et al. 2019	+	?	-	?	+	High risk
Ying Xu et al. 2020	+	-	-	?	-	High risk
Anand et al. 2017	?	+	?	?	?	High risk
Peng et al. 2020	+	?	+	?	+	Some concerns
Khan et al. 2019	+	+	?	?	?	High risk

+ Indicates low risk
? Some concerns
- High risk
*Studies with more than 2 dimensions graded by "some concerns" are considered at high risk of bias

2.8 Findings of the rapid review

The findings of this rapid review should be interpreted with caution as post-operative pain evaluation following laparoscopic surgery should be assessed beyond 24 hours following surgery with the goal of making better, informed decisions, while various reasons (e.g., funding, lacks of follow-up,

etc) may have implicated the results of selected studies [4,17]. Nevertheless, anxiety seems to be a dominant predisposing factor to post-operative pain across studies and populations, which is not being adequately addressed using non-pharmacological interventions, proper pre-operative psychological profile screening and is often evaluated using different tools resulting in lack of standardization for the evaluation of patients undergoing gastrointestinal surgery [17-21].

In particular, the clinician should be aware of a special risk group for post-operative pain following laparoscopic surgery, consisting of young, obese females with high anxiety levels which may suffer worsened outcomes from surgery and offer up-to-date pain care strategies [12,18,19,22].

2.8.1 Predisposing factors to post-operative pain

Post-operative pain following gastrointestinal surgery is a significant burden which may lead to pain chronicity, it is associated with longer hospital stays and complications ranging from increased treatment costs to worsened quality of life for patients [1,4]. As such, post-operative pain is a known risk factor for chronic pain, prevalent in around 15%-60% of patients post-operatively depending on individual risk factors [1,4]. An information gap exists in the literature, lacking clear information on how predisposing factors for post-operative pain could be evaluated to improve the

management of post-operative pain. Some of these already explored factors are summarized below in Figure 3. [4,19]. Post-operative pain is often measured using the visual analogue scale both at rest and during movement and can be administered before a surgery and after for as long as necessary or deemed relevant [2,23]. During the evaluation of post-operative pain, factors such as heart rate, blood pressure, sedation, nausea, vomiting and other adverse events are often recorded [17]. Predisposing factors to post-operative pain may include: anxiety, fear of pain related to the surgery, expectation of pain, age, gender, previous experiences of pain, surgical factors and genetics [18,23].

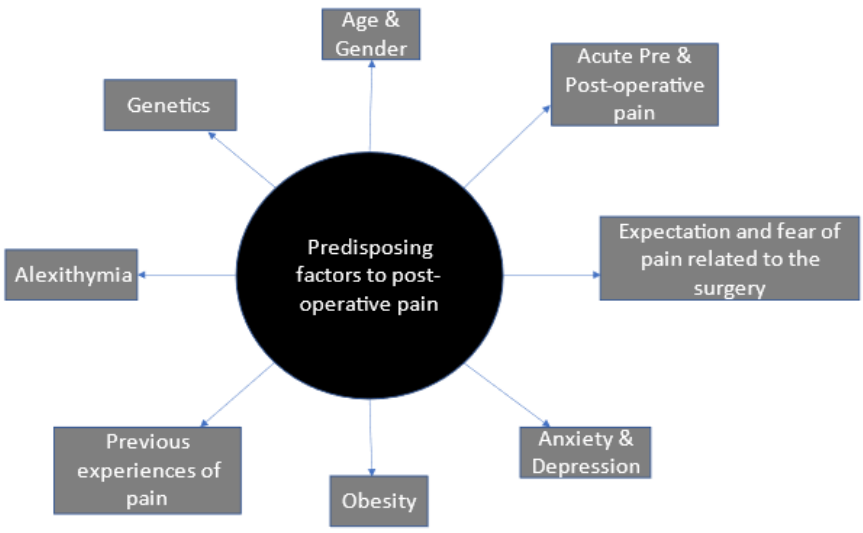


Figure 3. Predisposing factors to post-operative pain

2.8.1.1 Anxiety, fear, and depression

Anxiety is unequivocally a major risk factor contributing to post-operative pain, complications as well as overall morbidity post-operatively [19,21]. It is defined as a temporary emotional state of tension, nervousness, fear and high autonomic nervous system activity that affects the patients pain perception and is often provoked by events such as those that precede the process of surgery [20].

Pre-operative anxiety is measured using a variety of scales. Among these are the visual analogue scale where anxiety is assessed with a scale ranging from 0 (no pain) to 10 (severe pain) and the Beck's anxiety inventory questionnaire regarding 21 symptoms of somatic and cognitive anxiety with responses rating from 0 to 3 [19]. Lastly, the Hamilton-Hunt anxiety scale is another method of investigating 15 areas related to anxiety with each area having 3 to 8 items scored from 0 (absent) to 16 (very serious), and the full list of anxiety scales is beyond the scope of this study [4,12,18,22].

Anxiety is caused by a myriad of factors and is largely detrimental. It is argued that while a certain level of anxiety prepares the patient for surgery and its outcomes, it can have a negative influence on recovery from anesthesia [19,21]. Pre-operative anxiety is specific to candidates to surgery as it relates to the process from the start date of a specific operation to the intensifying process at the beginning of the operation; its prevalence is between 20%-80%, it is not dependent on demographic data and depends on the surgery in question, though prolonged hospital stay has been associated with increased preoperative anxiety scores [19,21]. Firstly, fear and expectation of pain from the surgery exist already in the pre-operative

phase due to the fear of a poor outcome of an operation and the administration of anesthesia is yet another significant fear of patients [22]. The incidence of nausea and vomiting as well as high cortisol levels have been associated with higher anxiety levels [19]. The group which is most predisposed to higher anxiety level and lower satisfaction levels from surgery are young individuals, specifically young females, displaying more fatigue, reduced quality of life, higher morbidity and high post-operative pain compared to male patients [12]. Another group displaying a high incidence of anxiety are obese patients, with low pain thresholds predisposing them to severe post-operative pain [18,24].

Depression, along with anxiety are both significant factors associated with acute post-operative pain intensity but are rarely evaluated pre-operatively [1,23]. Increased levels of anxiety pre-operatively are not only positively associated with increased pain levels post-operatively but also higher morbidity [17,19]. Anxiety can alter and reduce the pain threshold by activating the hippocampus thereby becoming more attentive to pain [18]. The perception of pain in patients undergoing surgery is negatively affected by anxiety as study groups with higher anxiety levels retain higher overall pain levels up to 12 hours post-operatively too; This is often due to a pre-existing fear related to the pain of the surgery causing patients to become more attentive to pain post-operatively, and more anxious which in response amplifies and continues the cycle of pain and anxiety [19]. Research suggests that both preoperative anxiety and preoperative sensitivity to cold pressor induced pain are important independent predictors of early post-operative pain, with new methods of assessment such as quantitative sensory testing being developed, with the latter being more closely correlated with post-operative pain [12]. More rescue analgesic

doses are administered to patients who display higher levels of anxiety and depression both pre- as well as post-operatively, thereby suggesting a relationship between the psychosocial profile of patients and behavioral factors with acute post-operative pain [18]. Anxiety is therefore a significant predictor of analgesic requirements and post-operative pain perception, nevertheless, the use of anxiolytic agents pre-operatively is not sufficient to prevent post-operative anxiety [12,18]

2.8.1.2 Expectation of pain

On another note, the expectation of pain regarding an upcoming surgery, influences the pain experience post-operatively. In one study, patients who scored highest on the post-operative pain scores were observed to have a lower neutrophil-to-lymphocyte ratio (NLR) which assesses the inflammatory status of patients and worse mood levels pre-operatively than other patients who were expecting a lower level of pain [12]. Overall, patients are afraid of changes both before and after surgery, and neither previous experiences of pain nor pre-existing chronic pain has suggested a linear relationship between the variables [2,4]. Surprisingly, chronic pain, former experiences of severe pain (defined as above NRS equal or greater to 6) and expectation of pain do not always correlate with acute post-operative pain levels but should be explored [4].

2.8.1.3 Other factors

Other surgical factors associated with the development of post-operative pain include the duration of surgery, the type of surgery and the size of the incision (with larger incision size more predictive of post-operative pain) [1,12]. Traditional open surgery which is extensive in nature has become less

prevalent than laparoscopic surgery in gastrointestinal surgery patients as a choice of intervention, as surgery results in reduced manipulation of the digestive system, less scarring and considerably less acute post-operative pain [20].

Genetics too may contribute to the development of acute post-operative pain and later to the development of chronic pain, with early works regarding the promoter region containing the gene 5-HTTLPR polymorphism, specifically the S allele which has been suggested to predispose individuals for anxiety and depression in the presence of major stressful life events [23]. However, studies are not unequivocal and more importance is attributed to the psychological profile of the patient [23,25].

In practice, risk assessment of post-operative pain often includes the use of questionnaires with domains focusing on previous pain experiences, duration of existing pain, expectation of pain post-soperatively (which does not necessarily predict post-operatively pain intensity), fear of pain post-operatively, psychological factors and levels of anxiety assessed pre-operatively [4].

2.8.2 Pain care of post-operative pain

2.8.2.1 Post-operative pain care following laparoscopy

Pain is the most prevalent post-operative symptom; as such, the symptom of pain following laparoscopy is usually localized but can project to the back or shoulders and patients have reported diffuse pain too depending on the surgery [1]. Patient satisfaction often goes hand in hand with post-operative pain levels, for example, common practice dictates that when pain exceeds

the score of 3-4 on the VAS post-operatively, rescue analgesia should be administered to avoid severe pain (VAS≥6) that can result in pain chronicity [1,17]. The ideal pain relief method post-operatively should be simple to perform, not costly and result in minimal morbidity with minimal side effects [4,17]. Pain assessment should occur pre-operatively, immediately following surgery and for as long as it is deemed necessary. Nevertheless, most patients are not strictly followed up after laparoscopy and the recovery time is often longer than expected, resulting in more work days missed and increased costs [1,23].

Vital parameters such as heart rate, respiratory rate, oxygen saturation but also the use of rescue analgesia are recorded in studies regarding interventions for better post-operative pain management [18,24].

Considerably more predictive of pain perception, psychosocial and behavioral factors are often underutilized in post-operative pain management strategies despite the importance they have on pain intensity [23]. For example, inappropriate management of anxiety preoperatively results in prolonged recovery, pain and increases the risk of complications [21].

2.8.2.2 Non-pharmacological pain care for post-operative patients

One dimension which has been suggested for the management of anxiety through which we can affect post-operative pain levels are nursing visitations; The physical visitation of nurses already in the pre-operative phase can inform the patients side-by-side throughout the process of surgery, anesthesia, rehabilitation and even offer music therapy interventions as a possible adjunct which has shown to reduce pain and anxiety in women who underwent laparoscopic surgery [21]. Earlier studies

point out that pre-operative nursing visits are also safe and have investigated the positive effect of mere preoperative phone visits on decreasing cortisol levels of laparoscopic patients and significantly less pain reported both 4 hours as well as 24 hours post-operatively allowing those same patients to cooperate more during coughing exercises, become rapidly mobile, thereby avoiding complications related to higher pain levels [20].

Another possibility of intervention for the alleviation of worries before laparoscopic surgery has been the implementation of an anesthesia service platform (ASP), allowing for the direct communication with the anesthesiology doctor beforehand, as fear of anesthesia is a very significant factor contributing to anxiety [19]. Another study suggested that there is a legitimate role for preoperative education; for example, the ASP which is implemented using a mobile phone, enables patients to communicate with the attending anesthetist thereby increasing the availability of information, decreasing anxiety levels, reducing complications, increasing confidence following surgery, decreasing length of stay in the hospital, improving prognosis and decreasing on the short-term post-operative pain levels (though pain and medication consumption may increase within 12 hours due to sensitization to pain) [22].

Psychological intervention in the form of relaxation pre-operatively initially manifests physiologically as increased cortisol and epinephrine in the immediate post-operative period. However, it is associated with a focused, adaptive immune response following surgery, resulting in decreased consumption of rescue analgesia [12]. Clearly, the importance of implementing pre-operative relaxation techniques as part of a pain management strategy have a role in post-operative pain management [1,12].

Not less important, there is a need for the development of coping skills and addressing the personal needs of the patients with regards to the level as well as kind of support that is needed (e.g., reassurance), with referral to a trained psychologist if necessary [23] . This is not surprising considering the guidelines of the American Pain Society regarding the management of post-operative pain which state that preventative pain management should be based on individual risk assessment of elective surgery patients [4]. All in all, the literature recognizes that more studies should be conducted on non-pharmacological interventions for the management of psychopathologies associated with the post-operative pain experience, however, common practice still relies on anxiolytic medication (e.g., alprazolam) [17-18].

2.8.2.3 Pharmacological care of post-operative patients and risks

The literature is abundant with investigations of pharmacological interventions pre, intra and post-operatively for laparoscopic surgeries with conflicting evidence as to their efficacy regarding the management of post-operative pain, though lack of consensus regarding correct timing, dosage or a unison international guideline for all patients prevails (e.g. special populations such as the morbidly obese) [4,25]. It is agreed that analgesic requirements depend on the type, pharmacokinetics and pharmacodynamics of the medication in conjunction with addressing the physiology and psychological needs of the patient and his or her individual response following surgery [12,24].

Preventative analgesia regards the administration of drugs pre-operatively as means to decrease peripheral and central responses to pain by interrupting the inflammation-pain-hyperalgesia circle and minimize the painful stimuli [25]. For this purpose, opioids are commonly prescribed and

expressed by morphine equivalence or by calculating the number of times a patient has requested an analgesic medication [12]. Opioid pose a vivid risk for respiratory depression in general, and for obese patients undergoing gastrointestinal surgery [24]. It is important to note, that regardless of medication, there are a group of patients who will experience severe pain post-operatively following laparoscopy even when opioid is prescribed or other medication strategies are used [4].

Oral gabapentinoids are a group of non-opioid medications (e.g. Pregabalin, Gabapentin) often used in the treatment of post-operative pain in order to decrease opioid addiction, minimize adverse events and increase analgesic medications efficacy [4,24].

Pregabalin is considered a potent preventative analgesic medication as it is a quick acting (30 minutes to 2 hours) and effective (half-life around 6 hours) adjunct medication that is commonly used preoperatively as well as following laparoscopic surgery for the reduction of anxiety, nausea, vomiting, rescue analgesia consumption (in the form of opioid medication) and most importantly post-operative pain [17].

In addition, a recent study regarding the medication has reported better patient satisfaction from pain management post-operatively for the group which received a single dose Pregabalin pre-operatively, albeit in that same study adverse events (e.g., headache, dizziness, and visual disturbances) were observed in at least 20% of the patients, with other studies suggesting no more adverse events between the placebo group and the group which received Pregabalin [4,17]. Moreover, the combination of Pregabalin with opioid medication can lead to undesired side effects (e.g., respiratory depression and negative cognitive effects) [17]. Alternatively, the medication

Gabapentin, is also used for pain care and anxiety reduction post-operatively, showing somewhat promise in obese patients undergoing gastrointestinal surgery [24].

To further make things complicated, literature fails to reach a consensus regarding the duration of treatment, dosage of administration and goes even further to warn that though results regarding preventative analgesia use are promising, common practice is in its infancy [4,17,25].

Tramadol is an opioid that can be prescribed alongside Pregabalin intravenously following laparoscopy as a first-line rescue analgesia [17]. Compared to other opioid-based medication for the treatment of mild to moderate post-operative pain, Tramadol is considered safe, yet is inefficient as an anxiolytic agent [18-19]. The administration of opioid based medication in the recovery room such as Tramadol is also possible using patient-controlled analgesia, consisting of a pump connected intravenously to the patient, allowing the administration of low doses of the drug (e.g., 4mg) up to 36 hours or more following surgery and is a viable strategy when patients are unable to communicate pain levels [18].

More pharmacological strategies following laparoscopy include the combination of Opioid medication (e.g., Tramadol 50mg) with non-steroidal anti-inflammatory medications (e.g. Ketorlac 30mg or Diclofenac 75mg) such as Paracetamol (given 1g orally or intravenously) or alternatively, using potent opioid medication such as Oxycodone (e.g. 3mg intravenously) when pain exceeds 4 on the VAS [4]. In a recent study regarding pain intensity following laparoscopy, the consumption of opioid medication stood at around 20% out of a population of 148 patients,

however, this can differ from general practice where individual risk assessment for post-operative pain is not yet common practice [1].

Describing every initiative or medication for pain care in detail goes beyond the scope of this study, but one emerging strategy is the enhanced recovery after surgery (ERAS), or ERAS, which promotes multimodal analgesic strategies for the care of post-operative pain, resulting in patients with fewer complications, higher satisfaction rates, lower anxiety levels, faster intestinal recovery, faster bed turnover and incorporates a psychological element that is missing in many unidimensional pharmacological interventions, thereby affecting prognosis [24,26].

Regardless of choice of medication, more than a third of patients will experience severe pain post-operatively during the first hours in the recovery room, and though under constant debate in the literature, the amount of analgesics needed often does not correlate with post-operative pain [4].

2.8.3 Conclusion and evaluation of the rapid review

Previous experiences of pain do not seem to predict the intensity of post-operative pain, though controversy prevails, and most studies included in this review range are warranted [4,12].

There is also a lack of cohesion across studies as to when should rescue analgesia be administered, with some studies proposing self-administration by the patient under supervision (e.g. Patient-controlled analgesia), some relying on pain intensity that is above 3 on the VAS and others on the occurrence of severe pain, indicated as 6 or above on the VAS [1,4,17]. Clearly more research is to be done with regards to the timing of rescue

analgesia post-operatively to create standardization, but even more so with regards to the dosage of pain medication already pre-operatively (e.g., the growing use of preventative analgesia for pain care that is still in its infancy) [4,25].

The monitoring of physiological parameters seems to be prevalent in studies regarding post-operative pain and is often studied in pain research, however, no significance is given to one parameter over the other [18,24].

With regards to the SPA project, future studies should include pain assessment of patients beyond 24 hours following gastrointestinal surgery. A prospective study should include both non-pharmacological and pharmacological pain care strategies summarized in this study (see Table 5.), with psychological screening pre-operatively and explore the weight of each physiological parameter measured for the refinement of the pain assessment algorithm.

Table 5 ***Pain care strategies post-operatively***

NON-PHARMACOLOGICAL	PHARMACOLOGICAL
Nursing visits	**Anxiolytic medication (e.g. Alprazolam)**
Music Therapy	**Standard Opioid medication (e.g. Tramadol)**
Anesthesia service platform	**NSAIDS (e.g. Diclofenac)**
Development of coping skills	**Potent opioid medications (e.g. Oxycodone)**
Referral to a psychologist	**Combining opioid medication with NSAIDS**
ERAS	**ERAS**

3. Purpose of the descriptive-comparative research

The purpose of this study was to explore the relationship between previous pain experiences and medication on the intensity of pain post-operatively in patients undergoing elective gastrointestinal surgery. For this purpose, we aimed to answer the following questions: Is there an association between previous pain levels, medication, fear, and expectation of pain on maximal pain levels post-operatively?

➢ The following part is the descriptive-comparative study based on phase II of the SPA project's data and includes the statistical analysis of the relationships between previous pain experiences and medication on the intensity of pain post-operatively in patients

undergoing elective gastrointestinal surgery. In essence, the second part of this study aims to answer, what are the effects of predisposing factors for post-operative pain based on the data acquired by the researcher for the final phase of the SPA project.

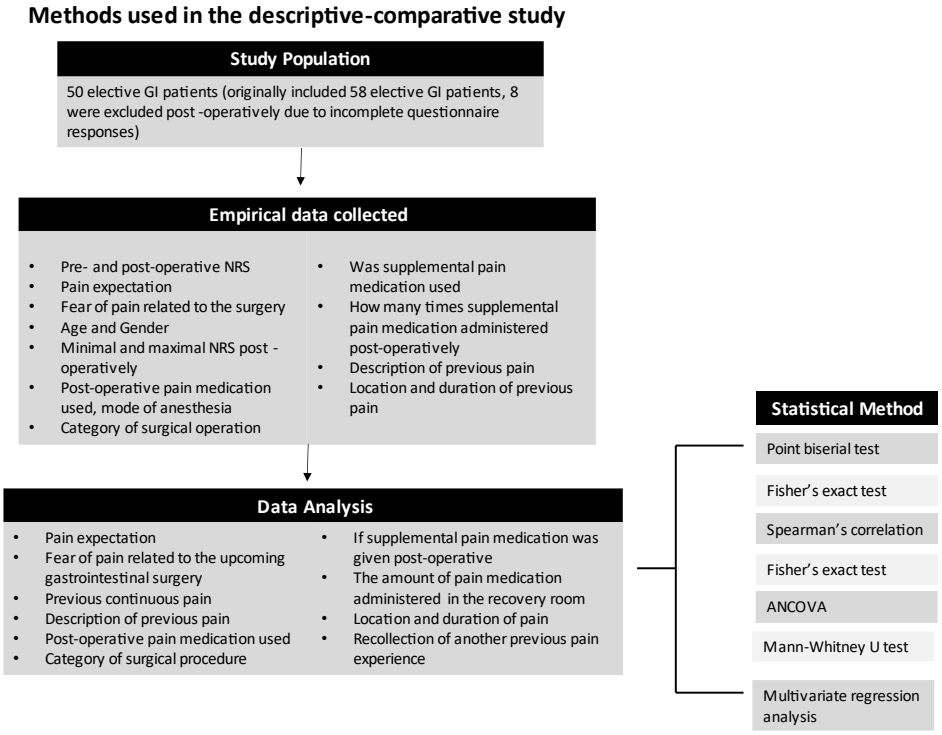
4. Methodology of the descriptive-comparative study

4.1 Study design

The design of this study incorporates the use of a rapid review focusing on predisposing factors to post-operative pain of laparoscopic surgery patients and the most up-to-date management strategies offered for those same patients, as described in the previous part. The second part of this thesis uses responses from Phase II of the SPA project reported by 50 elective GI

patients operated at Turku university hospital for statistical analysis of outcomes (See Figure 4.).

Figure 4. Methods used in the descriptive-comparative study



This study is part of a larger study named "Smart Pain Assessment Tool Based on Internet of Things". The larger study aims to produce a medical device for the measurement of pain in individuals with consciousness disorders using state-of-the-art sensors measuring physiological parameters using bioelectrical electromyography signals as well as heart rate, respiratory rate, oxygen saturation and galvanic skin response. The results measured by the sensors will be further developed and integrated with the use of modern wearable sensors, device, and algorithm.

Phase I of the SPA project but not this study included the testing, evaluation, utility, and accuracy of an IoT-based innovation for the measurement of pain in healthy, working age volunteers in a laboratory environment. In phase II study of the project, 50 patients with the ability to communicate underwent different types of elective gastrointestinal (GI) surgeries for their respective conditions. The final phase of the SPA project has not yet taken place. It is aimed at testing the smart pain assessment tool in uncommunicative patients in a multicenter, multinational setting.

The aim of this current descriptive-comparative study was to explore the relationship between previous pain experiences and medication on the intensity of pain post-operatively in 50 patients undergoing elective gastrointestinal surgery at the University of Turku hospital, using a descriptive-comparative study, see Methods used in the descriptive-comparative study in Figure 4. In the grand scheme of things, this study focuses on the data analysis phase leading to an adjunct outcome before Phase III in the SPA project, seen in Figure 5.

This study as descriptive studies are, does not test any hypothesis of study efficacy. However, it explores relationships using statistical methods and displays gathered information from patients using descriptive methods such as means, percentages and counts. This method was chosen due to pre-existing data analyzed in phase II of the SPA project.

A correlation study does not control the allocation of subjects to specific groups of intervention and the researcher decides on the outcomes of interest which are clearly defined [27].

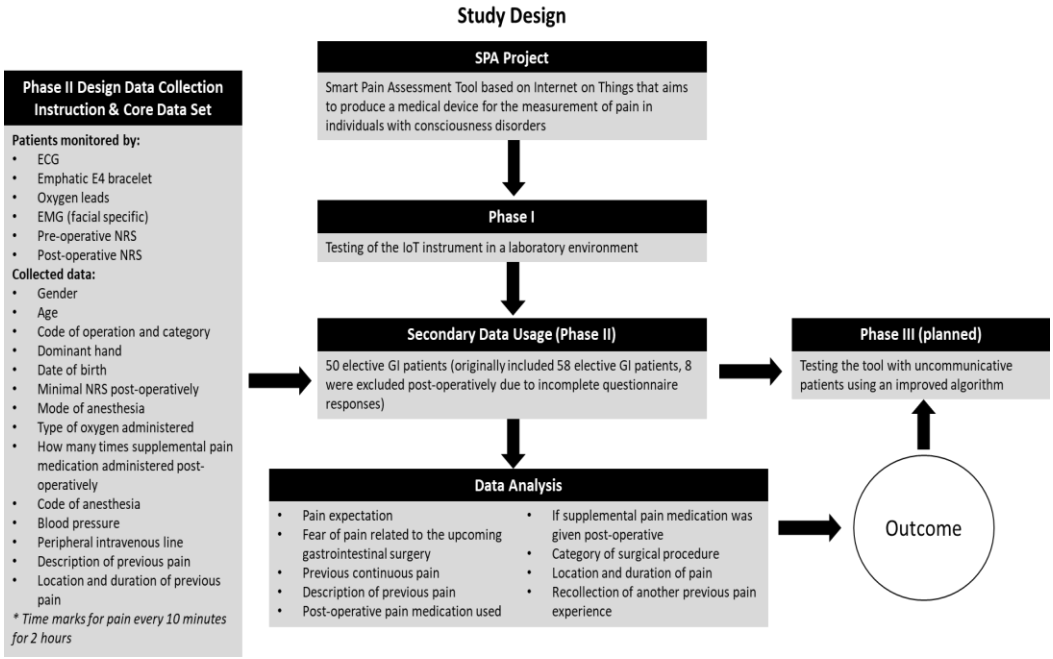


Figure 5. SPA study design

4.2 Setting and sampling

This study included 50 participants who were appointed for elective gastrointestinal surgery at the Turku University Hospital and went through anaesthesia, were above the age of 18, and whose expected pain levels post-surgery were expected to be moderate to severe pain. The sample size was based on receiver operator analysis (ROC) from phase I of the

SPA study [6]. The participants were interviewed by a research nurse at the Turku University hospital with regards to the location, duration, fear, expectation, and previous experiences of pain.

In addition, the inclusion criteria demanded patients that were able to verbally communicate, were asked to give written informed consent and had to have healthy facial hair. Exclusion criteria include subjects with a condition affecting cognitive functions such as those classified by the International classification of disease (ICD) with codes F00-F99 and G00-G99 (see Appendix B. for ICD codes). Candidates with tattoos in bodily areas where the sensors were attached or candidates whose surgery involved hands where pulse oximetry and galvanic skin reactions were recorded as well as candidates that had surgeries where facial muscle activity was measured were excluded from the study of Phase II.

4.3 Data collection procedures and instruments

Initially, a designated nurse in the preoperative ward performed the interviews for 50 candidates for surgery a week prior to their elective surgery and informed the study group of the possible participants. In the following week, patients gave their written consent. During the study, they were under general anaesthesia during the operation and under different types of medications post-operatively (epidural, local, transversus abdominal plane block or epidural and the latter). Patients were monitored using a 5-lead electrocardiogram (ECG), Empatica E4 bracelet, Oxygen leads, as well as facial surface electromyography (EMG) attached to the left frontalis muscle. In addition, the patients were asked to rate the level of pain preceding the operation, as well as in the recovery room (multiple

times) using the numeric rating scale (NRS) and for up to 2 hours post-operatively. Rating of the intensity of pain was done using numeric values between 0 to 10 (i.e., no pain to worst pain you can imagine). The study nurse attached a note to the patient file to inform the operating room staff about the study participation and asked for the use of 5-lead ECG, recovery room bed and if possible, to leave one hand and arm without intravenous line during the operation for the study. The study nurse informed the technician about the estimated operation schedule.

The study nurse entered the subject ID to a Philips monitor, followed by the arrival of the participant. The nurse checked for the ECG and oxygen leads. Empatic E4 bracelet was used to measure galvanic skin response and was placed on the wrist without an IV-line, facial specific EMG and ECG were sanitized using alcohol wipes and sensors were attached to the left side of the face as mentioned. Recording of electronic measurement began for the pre- and post-operative period, if the study participant was awake, the study nurse informed the participant regarding the ongoing measurement. Approximately every 10 minutes or when the participant reported pain, the study nurse asked about the intensity of pain using the NRS. The study nurse also requested a print of the anesthetic record including the name and codes for operation, anesthesia use and administered pain medication.

Pain expectation, fear of pain, previous continuous pain and previous pain experiences were recorded using a yes or no response. The location of pain was depicted using a pain map to localize the pain and its duration was to be described using numbers. The previous pain experience was also depicted using a pain map and an option to verbally elaborate on the pain experience was made available (See Appendix A. for detailed information).

The collected data in the pre-operative interview included: gender, age, date of birth, subject ID, visitation date, dominant hand side, pain expectation, fear of pain, previous continuous pain experiences, location of pain, duration of pain, previous pain experiences, description of previous pain, and NRS value before the operation. After the operation the collected data included: mean NRS post-operatively, maximal NRS post-operatively, minimal NRS post-operatively, mode of anesthesia, number of times supplemental pain medication was administered, type of supplemental oxygen administered, number of times supplementation pain medication was administered, category of surgical procedure, intravenous hand side, saturation hand side with location, form of blood pressure monitoring, pain monitoring start and end times, E4 Empatica hand side with location, code of anaesthesia used in the operation, anesthesiology log ID and code for operation procedure. The post-operative assessment also included information such as the anaesthetic record number, peripheral intravenous line, electrocardiogram, blood pressure as well as time marks for pain measured using the NRS and its location described in words.

The numeric rating scale was recorded and resembles the VAS scale as previously described. Facial expressions were reported as well as vital signs (i.e., heart rate and respiratory rate) with the addition of galvanic skin response (GSR).

The data chosen for analysis included variables regarding pain history, subjective assessments, and pain experience pre- and post-operatively as seen in Table 6.

Table 6 ***Data chosen for statistical analysis***

Pain expectation
Fear of Pain related to the surgery
Previous continuous pain experience
Location of pain (using a pain map)
Duration of pain
Previous pain experience
Description of previous pain
NRS value pre-operatively
Minimal and maximal NRS values post-operatively
Was supplemental pain medication administered
Post-operative pain medication used
Number of supplemental pain medication administered
Categories of surgical procedures

The reason that pain expectation was chosen for the analysis relied on the thorough rapid review conducted, showing a possible correlation between pain expectation, and expected pain outcomes [28-29].

Fear of pain related to the upcoming gastrointestinal surgery was selected for the analysis as literature suggests a correlation between psychological factors such as anxiety and depression with higher pain outcomes for those with high catastrophizing scores [3]. The recollection of previous pain experiences often indicates a previously experienced pain perception and is hypothesized to be associated with a higher consumption of supplemental pain medication post-operatively. Pre-existing chronic pain

too, is hypothesized to be associated with an increased consumption of supplemental pain medication post-operatively.

The use of a pain map for this study was based on the literature where examples of such a strategy for the better comprehension of the pain experience is indicated (e.g., McGill Pain map). The recording of pain according to location is considered a reliable and valid approach in the study of the distribution of pain in populations [30].

The patient's electronic health records were used as well as the physiological parameters gathered from the technologies previously mentioned were collected. For this study, the pre- and post-operative maximal pain levels as well as responses from questions number 1,2,3.1 and 4 were statistically analysed (see Appendix A for pain questionnaire). Other variables were collected but not analysed and were described using descriptive statistics (e.g., demographic information).

4.4 Data analysis and statistical methods

This analysis is a post-hoc analysis as the phase II study has already taken place. The author of this thesis was not present at Turku University Hospital during phase II of the study or dealt with the initial processing of the collected data to SPSS, nevertheless, the researcher was contacted for further clarification of the data collected when necessary.

The standard Statistical software for social sciences (SPSS) 25 was used to analyze the data. The statistical methods used in the analysis of the collected data include the use of descriptive statistics. P-values less than 0.05 (two-tailed) were considered as statistically significant. Q-Q plots of all variables were examined for normalcy. Results to descriptive questions are

reported in frequency counts and standard deviations whereas results to questions of relationships are described using correlation coefficients or p values. Measures of central tendency, specifically the use of median values were used for questions of comparison.

The relation between fear of related pain and expectation of pain resulting from the upcoming GI surgery with maximal post-operative pain levels were explored using the point biserial test as data proved normally distributed. Spearman's correlation testing was used for investigating the relationship between pre and maximal post-operative pain levels.

Moreover, Fisher's exact test was used to explore the possible relationship between previous continuous pain and previous pain experience with the administration of pain medications post-operatively as well as the levels measured on the NRS controlling for pre-operative pain levels. If the ANCOVA result was significant, pairwise comparisons and relationship between the magnitude of invasiveness of the surgical procedure and fear of pain related to the upcoming elective gastrointestinal surgery. Using Fisher's exact test as indicated as the study sample included only 50 participants and the results were based on a dichotomous variable of yes or no.

A one-way ANCOVA was conducted to determine a statistically significant differences between the different types of medications on post-operative pain post-hoc analysis. The use of ANCOVA was indicated due to the confounding factor of pre-operative pain levels which may alter the results indicating a difference between the medications used post-operatively and the maximal post-operative pain levels.

An exact Mann-Whitney U test was performed to test maximal pain level differences between the group that was expecting pain post operatively and the group that was both expecting pain post operatively and fearful of pain related to the upcoming procedure. The choice of a non-parametric test was made after consultation with a statistician. The Q-Q plots indicated normalcy, but the use of the Shapiro-Wilk test was not indicated, and the statistical tests previously performed might have missed important association and correlations.

The multiple regression analysis was used to determine what factors may result in maximum post-operative pain levels measured on the NRS using the data collected. The analysis focused on the prediction of maximal post-operative pain levels using the following variables: was pain medication administered post-operatively (Yes/No) and the number of times pain medication was given post-operatively (0-6). The previously described variables were selected after multicollinearity was checked between independent variables as well as relevancy. The variables not included due to irrelevance or multicollinearity were pain expectation, fear of pain related to the upcoming surgery, previous continuous pain, previous pain experiences, NRS value pre-operatively, post-operative pain medication used and category of surgical procedures.

A statistician working at the University of Turku, Miko Pasanen was continuously consulted during the making of this thesis. An operating room manager at Turku University hospital, Henry Suhonen was also consulted regarding the classification of gastrointestinal operation based on level of invasiveness, furthermore, Mr. Suhonen was present at the time of the study and provided the author of this study more information regarding the conduction of the phase II study at Turku University hospital.

4.5 Ethical considerations

When applying an IoT based solution, the potential issue of privacy should be addressed at each level of the analysis as only authorized people may always have access to the measured information. The use of multiple security techniques should be implemented such as multimedia compression, stenography and encryption [11]. Commonly, IoT based solutions for healthcare lack the visibility of data between various devices and create dependencies and interdependencies which are difficult to follow and further complicate research. Information collected by wearable smart things may have detrimental properties such as leading to surveillance monitoring of interconnected things, leading to negative influences of autonomy, aggregation of personally identifiable information in databases, personal emotional monitoring, leakage of private data to undesirable third parties and denial of service (DOS). Denial of service is a cyber-attack in which the attacker makes the network unavailable to its intended users temporarily and thus impairs the use of the data in emergency situations, such attacks are on the rise as well as information theft, and disruption of the flow of information which can all lead to wrong medical decisions and risk the overall safety of sensitive patient information [31].

The general data protection regulation act of the European Union must be adhered. According to the act, any virtual or physical location where personal data regarding an individual (i.e., collected data regarding the physical or mental wellbeing of a patient) is store. Information should be made accessible to the individual whose data is being stored, regardless of the state of that same individual (problematic when a patient is in a

noncommunicative state). Moreover, stored data should be made available to the individual in question whether it be by Universal serial bus (USB) sticks, compact discs (CD) or other means of personal distribution. Each IoT based device should be individually secured and it is the responsibility of the researcher to do so [31].

The 2002 European Charter of patients' rights clearly states that there is a right to avoid unnecessary suffering and pain [32]. The unnecessary suffering and pain act also includes the simplification of patients access to treatment. Furthermore, the European charter of patient's right clearly states that patients have a right of access to information regarding pain medication therapy as part of general information regarding scientific research they take part in. The information can come from public or private sources if it is accurate, reliable, and transparent [32].

Finnish law No. 785, section 5 regarding the patients right to be informed states that patients have a right to be informed about alternative forms of treatment and the effects of choosing a treatment, except in situations where giving that information causes a hazard to the health of the patient. In detail, patients have a right to the pain chart data regarding themselves. In addition, examinations, treatment, and rehabilitation should be informed using a plan for the patient ensuring his or her understanding. In the case where the patient is unable to communicate, significant others or a legal representative should be informed regarding the plan that was drawn up for the patient in question [33]. In Finland all research should comply with the guidelines on responsible conduct of research. The research participant is always allowed to give consent in writing, orally and electronically, discontinuation of participation should also be made possible without any

negative consequences. This study is part of a larger study that has ethical approval, and therefore did not need a separate statement [34].

During phase 1 and 2 of the previous study, the privacy and anonymity of the subjects were respected. The collected data were stored in such a manner that the identity of the subjects will not be revealed and the subjects in the preoperative ward were informed by means of written consent whereas information about the study was given orally. This was followed by assigning the subject number to the patient which is thereafter entered on the case report forms. The study uses sensitive information such as anesthetic record and log sheets, nevertheless, the identification details are removed after the subject's assignment to a subject ID. Discontinuation of the study is made possible at any given point of the study. Access to the data could only be given to those named as researchers following approval. Moreover, the study permission was applied from Turku's central hospital and the ethical approval from the ethics committee, Hospital district of Southwest Finland. The trial is also registered in the clinical trials registry [35].

The research is funded by the Academy of Finland (287075). No provision is paid for the principal investigators. The data collection is done by the healthcare personnel during their regular working hours and no additional provision is paid. The study subjects are not paid for the participation. The study subjects are insured based on the patient insurance. Since the study is conducted at Turku University Hospital normal patient insurance covers research. No extra insurance is therefore needed.

5. Findings of the descriptive-comparative study

5.1 General characteristics of participants

The mean age of the 50 participants included in the analysis was 63±13.306 years of age with a gender ratio of 1:1, with an equal number of men and women. No patient was under the age of 18, and the ages ranged between 18 to 83 years of age. The median intensity of pain pre-operatively was very low (Mdn = 0, SD = 1.163) based on the NRS. Previous continuous pain was prevalent among 24/50 participant and only 22/50 participants recalled a previous pain experience. Most participants required supplemental pain medication except for 17/50 participants. The location of continuous pain was assessed using a pain map (See Appendix A). See secondary data analysis results in Table 7.

Table 7 ***Secondary data analysis results based on demographic, outcome, diagnosis, and procedures***

Demographic, outcome, diagnosis, and procedures		N	%
Gender distribution (female/male)		**1/1**	
	Mean age(male)	63±10.734	50%
	Mean age(female)	64±14.90	50%
Outcome			
	Prevalence of continuous pain	24	48%
	Participants who required supplemental pain medication post-operatively	17	34%
	Participants who recalled another previous pain experience	22	44%
Diagnosis			
	Malignant neoplasms	30	60%
	Benign neoplasms	4	8%
	Neoplasms of unknown nature	2	4%
	Other GI pathologies	14	28%
Procedures,			
	Minimally invasive operations	45	90%
	Extensive operations	5	10%

The duration of participants' continuous pain ranged from 5 days to 20 years. Participants were also asked to describe the location of continuous pain preceding the operation (see Figure 6.). As many as 26 participants did not provide an answer to the question due to reasons such as falling asleep, nausea, confusion, an inability to understand Finnish (Swedish speaking participants), deterioration of general condition and other conditions which may have affected the ability to respond in detail.

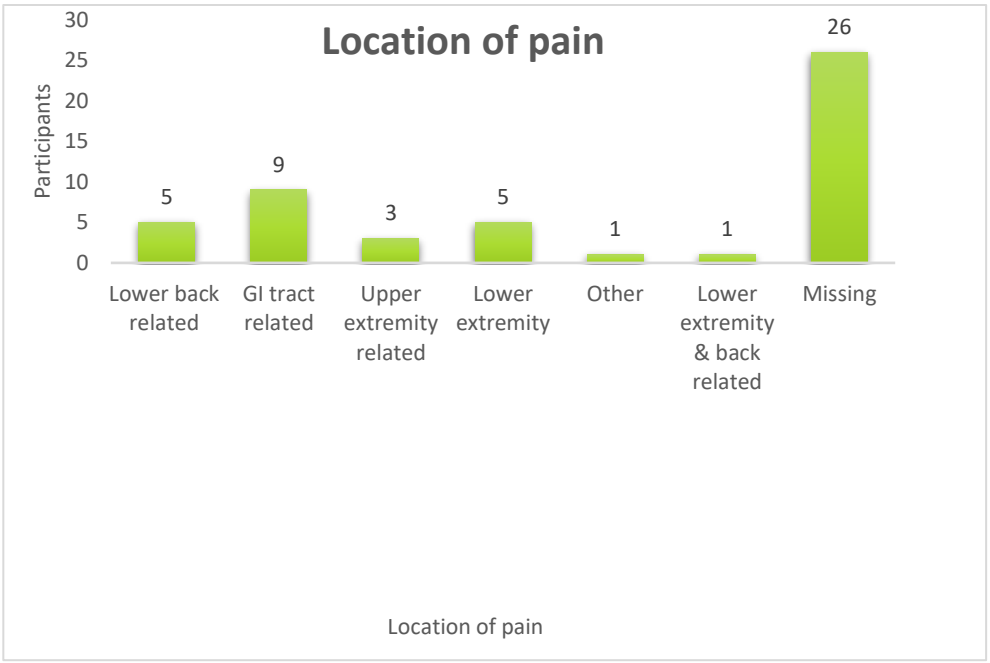


Figure 6. The location of continuous pain described by participants.

15/50 Participants reported chronic pain that lasted 3 months or more, 13/50 participants experienced pain less than 3 months and 22/50 participants did not provide an answer with regards to the duration of their pain for reasons unknown to the author of this study. The chronic pain

conditions varied; however, continuous back pain was most prevalent chronic condition in the population under investigation (See Figure 7.).

Participants with chronic pain were often diagnosed with continuous back pain related disorders such as previous back surgery, disc bulge, disc prolapse and nonspecific low back pain. Other chronic pain conditions included in the study consisted of diagnoses such as Crohn's disease, lower extremity pain, plantar fasciitis, hip pain, neuropathic pain, rheumatoid arthritis, previous shoulder surgery and persistent rectal pain.

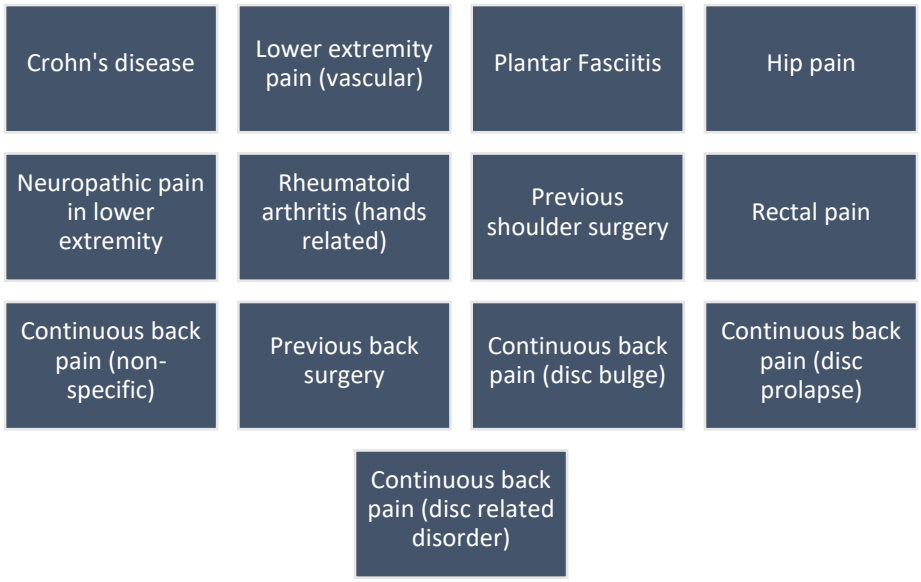


Figure 7. Chronic pain conditions included in the analysis

Pathologies of the 50 elective surgery participants included in the analysis were further classified based on diagnosis. Diagnosis-based classification is helpful when trying to understand correlations between pre- and post-operative pain, as previously discussed, the existence of a malignancy may influence the expected pain outcomes negatively [36]. The pathologies included in this study were benign neoplasms (4/50), malignant neoplasms

(30/50), neoplasms of unknown nature (2/50) and other GI pathologies (14/50). The surgical procedures the patients were scheduled for showed great variability.

Operations were divided into two groups. Participants undergoing minimally invasive operations, which included most participants (i.e., 45/50) of the study and participants undergoing open, extensive surgery (5/50). See Table 8. for minimally invasive and open operations.

For example, several surgeries incorporated the use of the minimally invasive technique “laparoscopy”, whereas more open surgeries may have included minimally invasive procedures but have had in addition a component of excision or an operation requiring a larger intervention (e.g., laparoscopy and perineal excision of rectum).

Minimally invasive surgery is considered a cutting-edge technique relying on endoscopic images, providing detailed information, and is done using small incision and a few stitches. It is often laparoscopic, meaning a tube-like structure with light and lens are inserted for viewing to guide the surgery. The instruments of surgery are small and resultant outcomes are often less pain, scarring and insult to the soft tissues compared to open surgery [37]. Other surgeries that are considered minimally invasive may include endoscopy, arthroscopy, bronchoscopy, thoracoscopy, cystoscopy, gastroscopy, hysteroscopy, laryngoscopy, sigmoidoscopy and colonoscopy. Alternatively, open surgery is more traditional and relates to the cutting of skin and soft tissue to allow a full view of the compromised organ to the surgeon (e.g. Roux-en-y surgery) [38].

Table 8 *Minimally invasive and open (extensive) operations*

Type of Procedure	N(%)
Minimally invasive, n(%)	**45(95%)**
Partial proctectomy and end colostomy	1(2%)
Closure of loop colostomy without resection	3(6%)
Left & right hemicolectomy	3(6%)
Pancreatoduodenectomy	2(4%)
Resection of sigmoid colon with partial proctectomy	4(8%)
Partial proctectomy with partial excision of colon	3(6%)
Stricturoplasty in small intestine	1(2%)
Biopsy of liver	1(2%)
Pancreatectomy, distal	2(4%)
Laparoscopic right hemicolectomy	6(12%)
Laparoscopic ileocecal resection	1(2%)
Laparoscopic gastric bypass	1(2%)
Closure of loop enterostomy without resection	3(6%)
Antireflux reoperation	1(2%)
Closure of terminal colostomy with anastomosis	1(2%)
Anastomosis of bile duct to jejunum	1(2%)
Closure of enterostomy with resection of exteriorized loop	1(2%)
Closure of fistula of small intestines	3(6%)
Closure of loop colostomy without resection	1(2%)
Abdominoperineal excision of rectum	1(2%)
Local excision of lesion of stomach	1(2%)
Laparotomy	1(2%)
Repair of incisional hernia	1(2%)
Partial proctectomy with partial excision of mesor	1(2%)

Open operation, n(%)	5(10%)
Excision of lesion of colon	1(2%)
Total gastrectomy roux-en-y and oseophagojejunostomy	1(2%)
Laproscopic total colectomy and ileostomy	1(2%)
Transabdominal total splenectomy	1(2%)
Laparoscopic and perineal excision of rectum	1(2%)

5.2 Pain expectation and fear

Participants undergoing gastrointestinal surgeries were asked if they expect to feel pain with respect to their upcoming procedure. Responses were recorded using a dichotomous response consisting of a Yes or No answer. The results of the analysis indicated that most participants had expected pain post operatively (32/50), with only 18/50 participants rejecting the expectation of pain (Table 9.). Preoperative expectation of pain with maximal pain levels post-operatively showed very weak positive correlation and was statistically insignificant (r^{pb} = .056, p < .698).

Table 9 ***Pain expectation preceding elective GI surgery***

PRE-OPERATIVE PAIN EXPECTATION DISTRIBUTION, (N)%	
Yes	(32)64%
No	(18)36%

In addition, participants were also questioned about their fear of possible pain related to the upcoming gastrointestinal procedure. Responses were recorded using a dichotomous response consisting of Yes or No answer.

The results of the analysis (Table 10.) suggest most respondents were not afraid of the resulting pain post-operatively (i.e., 37/50 participants).

Fear of the pain related to the surgical procedure showed very weak negative correlation with maximal pain levels post operatively and results were statistically insignificant (r^{pb} = -.068, p < .637).

Table 10 ***Fear of pain related to the upcoming elective gastrointestinal surgery***

FEAR OF PAIN DISTRIBUTION	(N)%
Yes	(13)26%
No	(37)74%

The relationship between the level of invasiveness of the surgical procedure and fear of pain related to the upcoming elective gastrointestinal surgery was explored. The results of the Fisher's exact test suggest no association between the fear related to the upcoming surgery and the level of invasiveness (two-tailed significance test, p = 0.662).

When analyzing the groups together, three distinctions were made pre-operatively for this analysis. The first group consisted of those only experiencing fear related to the pain post-operatively (1/50), followed by a group of those who were expecting pain of the upcoming procedure but were not afraid of the procedure (30/50). Lastly, the third group included those that were both fearful of the upcoming procedure and expected pain post-operatively (Table 11). These results conclude, that in this study, more than a third (19/50 participants) of elective GI surgery participants were

both fearful of the pain related to the upcoming procedure and expecting pain post-operatively.

Table 11 ***Distribution of fear, expectation of pain related to the procedure and both***

FEAR-BASED GROUP DISTRIBUTION	(N)%
Fear	(1)2%
Expectation of pain	(30)60%
Fear and expectation of pain	(18)38%

5.3 Pain pre- and post-operatively

The median of minimal post-operatively pain level was zero (Mdn = 0, SD = 1.604), whereas the median of maximal levels of post-operative pain observed was moderate (Mdn = 4.0, SD = 2.663). Overall, the median levels of pain observed post-operatively was mostly low across participants (Mdn = 2.0, SD = 2.207) and only two participants reported very severe pain post-operatively (i.e., 9 out of 10 on the NRS).

Spearman's correlation coefficient was used to assess the relationship between pre-operative pain levels and maximum post-operative pain levels. There was no significant correlation between the two, and the results were statistically insignificant, r_s=-0.027, p = .853, N = 50.

5.4 Pain history and medication

The participants were asked whether they remember other previous pain experiences before the operation that is not related to the current pain they

are experiencing, and supplemental pain medication given in the recovery room was recorded as well as their response to the pain question by a study nurse. Most participants required supplemental pain medications (i.e., 33/50). The highest amount of supplemental pain medication given was 6 times, observed in one participant. Most participants (i.e., 30/50) consumed between one to four supplemental pain medications post-operatively within the 2 hours period assessed.

The relationship between remembering another previous pain experience preceding the operation and pain medication administered in the recovery room was explored. The results of the Fisher's exact test suggest no such association between the variables (two-tailed significance test, $p = 0.741$).

Furthermore, when examining the relation between previous continuous pain and pain medication administered in the recovery room, the results of the Fisher's exact test further suggest no association between the variables (two-tailed significance test, $p = 0.559$).

All patients were under general anesthesia. The different types of pain medications administered to the patients post-operatively included: epidural injection, local injection, transversus abdominal plane block (TAP) and the combination of TAP with epidural injection (Table 12). Oxycodone was the choice of supplemental pain medication in addition to the standard post-operative analgesia described.

Table 12 ***Post-operative pain medication***

TYPES OF MEDICATION RECEIVED	(N)%
Epidural injection	(19)38%
Local injection	(9)18%
TAP	(18)36%
TAP with epidural	(4)8%

Based on the analysis of covariance (ANCOVA), there was no significant effect of post-operative medication type on post-operative pain levels in elective gastrointestinal surgery participants after controlling for pre-operative pain levels measured on the NRS, F(3, 45) = 837, p< .481. See Table 13.

Table 13 ***ANCOVA Results for pain medication post-operatively and maximal pain levels***

Type of pain medication	**Mean**	**Standard deviation**	**F**	**P**
Epidural (19)	3.31	2.80	.837	.481
Tap (18)	4.61	2.22		
Local (9)	3.55	2.78		
Tap & Epidural(4)	4.50	3.69		

Maximum pain levels post-operatively were slightly higher for those expecting pain post-operatively (Mdn = 5) than the mixed group who were both fearful of pain related to the upcoming procedure and expecting pain post-operatively (Mdn = 4.5). A Mann-Whitney test indicates that this difference was not statistically significant, U = 110, p < .694. See Table 14.

Table 14 ***Summary of differences between participants expecting pain and participants both expecting pain and fearful of the upcoming operation (Mann-Whitney U Test)***

Groups	N	Mean Rank
Expecting pain	20	17.00
Fearful of the upcoming operation and expecting pain	12	15.67

A multiple linear regression was calculated to predict maximal post-operative pain measured by the NRS based on whether pain medications were administered post-operatively and the number of times pain medications were given post-operatively. A significant regression equation was found ($F(2,47) = 43.812$, $p<.001$), with an R^2 of .651. Participants maximum pain levels is equal to 1.059 + .523 (number of times pain medication was administered in recovery room) +2.910 (was pain medication administered post-operatively), where pain medication administered in the recovery room is coded or measured as 0 = No, 1= Yes, and number of times pain medication were administered in the recovery room are coded or measured by counting (0-6). Maximum pain levels post-operatively increased 2.910 (NRS) for each response as to whether participants received pain medication post-operatively (yes/no) and .523 depending on the amount of pain medication administered post-operatively (0 to 6). Both the administration of pain medication and the number of pain medication administered post-operatively were significant

predictors of maximal post-operative pain levels. See Table 15. for detailed information.

Table 15 ***Effect of the administration of pain medication post-operatively and the number of given pain medication post-operatively on maximal post-operative pain levels***

Independent Variable	Coefficient
Was pain medication administered in the recovery room	2.910 (.755)*
The amount of pain medication administered post-operatively	.523 (.214)*
Constant	1.059
R^2	.651
F-ratio	43.812
n	50

* $p < .001$

Note: Coefficients are unstandardized OLS partial regression slopes with standard errors in parenthesis.

The outcome-based study design in Figure 8. summarizes the statistical exploration performed for the purpose of this study and exploring relationships between pain history, pain experiences and post-operative pain.

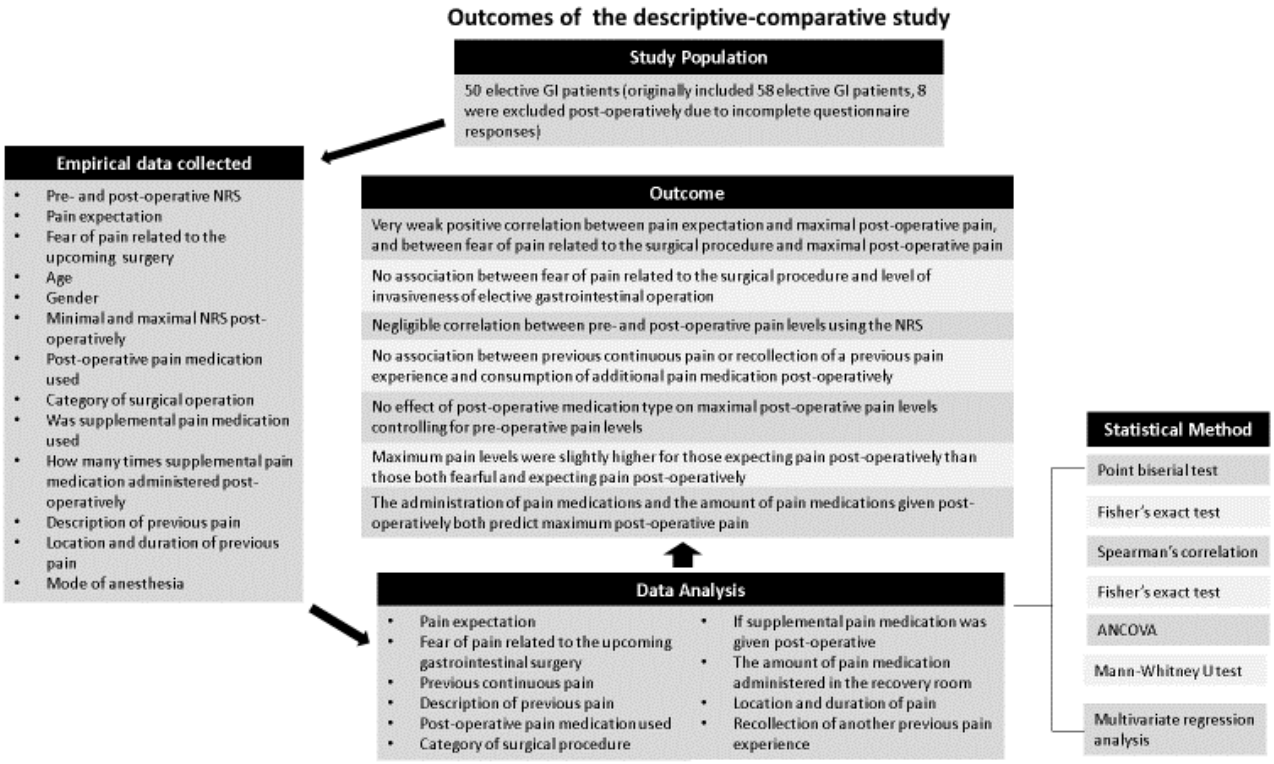


Figure 8. Outcomes of the descriptive-comparative study

6. Discussion of findings of the descriptive-comparative study

6.1 Preoperative pain and maximal post-operative pain

The results of this analysis of 50 elective gastrointestinal participants at Turku University hospital indicated a negligible correlation between pain pre-operatively and maximal pain levels post-operatively measured using the numeric rating scale. This contrasts with other literature not included in the review, suggesting a correlation between neuropathic pain or the existence of malignancies with severe post-operative pain which was rarely observed in the results of this study. There were 30 participants diagnosed with malignant neoplasms included in this analysis. Other literature suggests, severe pain should follow the removal of cancerous tumors of the gastrointestinal tract [3]. According to the rapid review, pre-operative pain levels could correlate with maximal post-operative pain levels if quantitative sensory testing would have been used or cold sensitivity checked, albeit this was not used in this descriptive-comparative study [19].

The SPA project aims to recognize potential patients with consciousness disorders and quantify the level of perceived pain in those same unresponsive patients. The results of this study suggest a substantial hurdle with regards to the difficulty of correlating between pre- and post-operative pain in conscious and responsive individuals using a pain questionnaire. The task of quantifying pain using technological means in unresponsive patients may prove impossible when relying solely on pre- and post-operative NRS correlations. Correct build-up of a pain

measurement algorithm by the integration of a variety of physiological parameters in addition to the unidimensional numeric rating scale results pre, peri and post-operatively, will allow the researcher to receive a more accurate analysis of the perceived pain experience.

Pain following gastrointestinal surgeries should range from moderate to severe pain, ranging numerically between 4-10 on the NRS [3], however, in this study, the median of maximal pain levels post-operatively was moderate (4.0 on the NRS scale). Since relatively few largely invasive surgeries were performed on the participants, it is not surprising that severe post-operative pain was not a prevalent outcome in surgeries with decreased incision sizes compared to full-scale operations [39].

More recent and similar studies have also displayed these results among post-operative participants where the distribution of pain levels among participants was too, imbalanced, and median pain scores were low [40].

The differentiation between minimally invasive operations and open, extensive surgeries was done initially using a web search using standard search engines as well as PubMed. This was followed by an expert consult who was the operating room nurse manager, where the study took place. Sufficient preparation for surgery could have been a contributing factor to observed low post-operative pain levels as the population in question included elective GI participants.

On the other hand, another possible explanation of the lack of correlation between pre- and post-operative pain levels could be that the participants were carefully screened for psychiatric conditions such as anxiety or depression. Anxious participants often catastrophize which is associated

with higher pain levels post-operatively, lower patient satisfaction, and are especially noticeable when high catastrophizing scores are observed [1,23].

The advancement of post-operative pain medication regimen could also have had a tremendous effect on the lack of correlation between pre- and post-operative pain levels, with some studies also showing an incongruency between pre-operative pain levels and severe post-operative pain [41]. As previously discussed, the use of opioid and opioid sparing strategies is already implemented worldwide, and Finland is no exception. An inference cannot be made about the Finnish healthcare regimen post-operatively based on one single study, yet favorable outcomes and lack of correlation between pre- and maximal post-operative pain levels indicate a high degree of pain management strategies and standard of care. In this study, it is plausible to assume that experienced nurses and anesthesiologists were involved in the study and were responsible for pain management strategies more than the average post-operative patient.

The reader should bear in mind that the results of this analysis included maximal pain ratings that were collected only 1 day post-operatively, whereas other studies suggest that the highest pain levels are experienced on the second day following major gastrointestinal operations and some studies assessing pain for up to 6 consecutive days post-operatively [36,41,42]. Pain experienced after discharge following major operations remains a major and relatively unexplored problem [43].

The choice of maximal post-operative pain levels is also questionable. The post-operative pain level mean should have been calculated and compared with pre-operative pain level mean of each individual participant to provide an even more accurate analysis of the perception of post-operative pain.

This study measured pain for 2 hours post-operatively, for every 10 minutes, albeit not all 50 participants were included. The analysis of specific time stamps where pain was recorded would have been advised but is beyond the scope of this study, as significant data is missing for the author of this study.

The assessment of pain is multifaceted and should include a variety of methods to improve validity and reliability. The perception of pain relies on activation of nociceptors, which are the sensing neurons in charge of sending signals to the spinal cord and brain in response to potential damaging stimuli [6].

Tools such as the NRS should include adjuncts such as the analgesic ladder recommended by the World Federation of Societies of Anesthesiologists, or the Pain Management Index (PMI) specialized for hospitalized pain patients. Its use in quantifying pain management with pharmacological interventions could provide further information for the recovery period post-operatively.

To offer a more holistic view of the patient post-operatively, more tools should be used such as the brief pain inventory (BPI) measurement of pain intensity and the impact of pain on daily activities which offers another view of the patient, focusing on the level of interference the surgery has consistently had or caused on his or her life. This tool includes interference with general activity, mood, walking ability, working life, relationships, sleep, and enjoyment of life. Modification of the brief pain inventory for the immediate short post-operative period is therefore called for.

Regardless of the tool chosen, the focus should be on quality of life and quality of recovery with the patient being in the center. Thus, the goal of

pain assessment pre- and post-operatively is to give as wide perspective as possible into the subjective experience of pain and its meaning for the individual, as well as its ramifications in all domains of life.

These multimodal measurements made possible by biopsychosocial tools should be combined to better understand mere pre- and post-operative correlations.

Pain has cognitive, affective, and social domains. It is of no surprise then that the quantification of the subjective perception of pain produces contradictory results, observed in this study. This study did not include a thorough investigation into each domain and cannot be used to predict maximal pain levels or the development of chronic pain where many variables interchange as this was beyond the scope of the study. No quality-of-life tools were implemented at the beginning of the study, therefore even if this study had followed the patients through time, vital information would still be missing from the analysis. Another possibility for the research could have been for example, a blood test measuring inflammatory markers both pre- and post-operatively could offer a glimpse into predisposing markers such as high cytokine levels.

6.2 Previous pain experiences and administration of medications post-operatively

Previous pain experiences pertain to the existence of pain preceding the operation as well as recalling a painful experience of the participants. Research indicates that recalling painful memories can negatively affect mood which could have predisposed the participants to increased negative emotions, one of which is anxiety [44]. In this study, participants were asked

to pinpoint using a pain map the location of their continuous pain experience pre-operatively. No association was observed between preceding continuous pain experiences and the administration of supplemental pain medication. The recollection of a previous pain experience was also not associated with the administration of supplemental pain medication.

Initiatives such as the previously described ERAS are integrated before, during and after surgery and are combined with non-pharmacological protocols which may explain the lack of association between previous pain experiences and administration of supplemental medications post-operatively [26,45,46].

Here too, the level of pain only one day post-operative is expected to be low, thereby requiring less supplemental pain medication as compared to post-operative day number two, which could have suggested a different association. Information regarding chronic pain patient is relevant yet ideally should be followed at a later point as chronic pain patients often report greater levels of pain 4 days post operatively compared to controls [41].

Other literature suggests the screening of participants with chronic diagnoses preceding surgery based on psychological conditions using instruments such as the pain catastrophizing scale or the hospital anxiety and depression scale [47]. Though not measured in this study, we know that the level of anxiety and depression are not necessarily correlated with post-operative opioid use in all literature but are often associated with worse patient satisfaction if left untreated [19].

This study included participants with chronic pain without the assistance of mental health professionals in the study procedure. Nevertheless, previous pain experiences were not associated with the consumption of supplemental pain medication. The results could be explained by a selection bias that has altogether reduced the pain levels post-operatively across the chosen population of elective gastrointestinal patients, thereby requiring less medications in the recovery room.

Selection bias occurred in this study when the follow-up time of these study participants' consumption of supplemental pain medication was chosen to be up to 2 hours post-operatively. Follow-up time out of the study in the results section is missing. The follow-up time out of study is considered important data that associations can be drawn from.

6.3 Choice of post-operative medication and post-operative pain

In this study, the choice of post-operative medication had no significant effect on post-operative pain levels when controlled for pre-operative pain levels in the analysis of covariance (ANCOVA).

The choice of general anaesthesia compared to spinal anaesthesia often leads to more daily intravenous consumption of morphine, is associated with higher postoperative pain and requires longer rehabilitation, in this study all participants received general anesthesia though length of rehabilitation is unknown to us [48].

There is a fine balance between choosing too little or too much opioid-based medications which lead to complications following surgery [3]. The

use of sparing or too much anesthesia is more common practice and explains the widespread need for initiatives such as the ERAS. However, due to short duration of this study, we are not able to foresee the long-term ramifications of choosing the different types of pain medication on pain levels or consumption of opioids. Hence, this study would require a follow-up for the re-evaluation of pain levels at day two post-operatively as well as 3 months after the surgery to find any associations.

There has been a legislative shift the past decades towards avoiding unnecessary pain and suffering. For example, the Italian law demands transparency with regards to pain therapy and records regarding the "characteristics of the monitored pain and its evolution during hospitalization, as well as the analgesic techniques and drugs, the relevant doses and the analgesic results achieved" [43]. This means that information collected from this study should be disseminated widely as possible so that pain research, specifically, the evidence-based administration of medication pre- and post-operatively could progress towards achieving that legislative goal.

In this study the 4 different types of pain medications post-operatively included epidural injection, local injection, transversus abdominal plane block and the combination of TAP and epidural injection. Oxycodone was chosen to supplement traditional pain medication post-operatively as mentioned. According to a recent meta-analysis investigating the differences between epidural and transverse abdominis plane block analgesia, it is suggested that most recent studies regarding pain outcomes and medications post-operatively have had low to very low quality of evidence [49]. Alternatively, the advancement in surgery techniques such as minimally invasive surgeries have allowed the use of TAP block. TAP block

analgesia is defined as a group of approaches that vary in needle insertion location; however, all approaches share the component of a local injection into the fascial plane between the internal oblique and the transversus abdominis muscle.

There is clearly a need for screening of patients prone to low blood pressure when choosing TAP as a post-operatively pain medication as opposed to epidural analgesia. TAP results in lowered hypotension following surgery and higher consumption of intravenous morphine in the first 24 hours following surgery which might have been missed in this study. In the meta-analysis previously described, the choice of medication did not seem to have a clinically meaningful differences on pain outcomes after abdominal surgery between TAP and epidural analgesia. This is especially important to consider as epidural analgesia is associated with adverse events of block failure, abscess, cardiovascular collapse, meningitis, spinal cord ischemia and haematoma. The results of the recent meta-analysis contrast with older studies that have suggested better analgesia, faster return of gastrointestinal function and lower incidence of pruritis with gastrointestinal patients [50].

On another note, regarding medications' adverse events, neither nausea nor sedation scores were reported in this study, contrary to recent recommendations [51]. The choice of low-dose oxycodone (opioid-based medication) in this study was based on the ability of the drug to attach to mu and kappa-opioid receptors as well as low post-operative nausea associated with its use compared to fentanyl; Oxycodone is similar to morphine and is considered a potent analgesic drug but is specifically indicated for visceral pain following open gastrointestinal surgery, its

weaknesses manifest in that it promotes respiratory depression, abnormally excessive sweating and diarrhea [52].

6.4 Expectation of pain, fear of pain related to the upcoming procedure and maximal post-operative pain levels

The results of the analysis regarding the expectation of pain and fear related to the pain post-operatively with maximal post-operative pain levels contradicted popular literature in the topic of pain suggesting a correlation[1,3,19].

Expectation of pain is often congruent with post-operative pain levels as studies regarding prediction of pain pre-operatively have suggested. A violation between the expected pain outcomes during the preoperative communication of expected pain by the healthcare practitioner results in lowered confidence in the surgeon and lowered patient satisfaction [28]. In this study there was no verbal suggestion as to the level of expected pain and this was not communicated at any point, though answers to participants questions and protocols post-operatively were included as is expected of any surgery. Expectation of pain is often measured in the literature using the NRS scale pre-operatively as participants are asked to predict the perceived level of pain post-operatively [28]. In this study a yes/no response was used that significantly limits the response of patients.

Fear in the pre-operative phase is often due to lack of control during the inpatient hospital settings or results due to lowered confidence in the surgeon or healthcare system in general. One suggestion is that the subjective experience of other participants of elective GI participants prior

to surgery perhaps should be shared with elective GI surgery candidates to increase confidence [28,53]. In this study, expectation of pain resulted in slightly higher median maximum pain levels post-operatively (e.g., 0.5 points more on the NRS) than the group both expecting pain and fearful of the pain related to the upcoming procedure.

6.5 Level of invasiveness and fear related to post-operative pain

The relationship between the level of invasiveness of the surgical procedures and the fear related to pain post-operatively was explored. The results of the study indicated no correlation between the level of invasiveness and the fear related to the post-operative pain. The classification of surgeries based on their respective level of invasiveness proved challenging, requiring a thorough literature investigation of each of the surgeries performed in this study.

After the creation of a table classifying the level of invasiveness, the supervisor of this study was contacted as to obtain a professional critic of the classification. The supervisor of this thesis arranged a meeting between the operating room manager who was present during the study at Turku University Hospital Henry Suhonen and the author of this study. Communication resulted in the final classification and expert opinion.

The highly invasive operations included in this study were only few (5/50) compared to the minimally invasive procedures (45/50) based on the classification.

Minimally invasive procedures result in lower pain levels compared with open surgeries, result in shorter recovery times, and are cost efficient (Meissner et al., 2015). The scientific exploration of the relationship between fear related to the pain post-operatively and level of invasiveness is challenging. In the case of laparoscopic surgery, patients and clinicians are not necessarily knowledgeable regarding the magnitude of the surgery they are about to undergo preceding the operation (e.g., a case where following laparoscopy demands an excision). Measuring of the patient's fear related to the pain post-operatively results in a somewhat arbitrary result as the true extent of the operation is not guaranteed. Therefore, the classification is almost impossible to verify due to its arbitrary nature and should be divided based on open or laparoscopic surgery. Another alternative could include some sort of scoring system to determine the differences between the operations. The scoring system should involve strict criteria with yes or no answers and if possible, include the patient records. Such scoring system is beyond the scope of this thesis and requires the validation of its reliability in the classification of elective gastrointestinal patients. Lastly, participants could have also been classified based on an organ of interest or quadrant that was involved in the surgery.

6.6 Differences in maximum pain levels post-operatively

Maximum pain levels post-operatively were slightly higher for those expecting pain post-operatively than the mixed group who were both fearful of pain related to the upcoming procedure and expecting pain post-operatively. The results of this analysis are quite surprising in the sense that individuals who were both fearful of pain related to the upcoming

operation and expecting pain are hypothesized to experience greater levels of pain as catastrophizing is associated with higher pain levels [47]. The results can be explained by group size differences where 30/50 participants experienced compared to only 19/50, though a difference of 0.5 in the median of maximal pain levels measured, is clinically insignificant.

6.7 The effect of the administration of pain medication and the amount of pain medications given in the recovery room on post-operative pain

The multivariate regression analysis suggested that the administration of pain medication and the amount of pain medications administered post-operatively were significant predictors of maximum post-operative pain. The results of this analysis were significant as p values were below .001.

In essence, the more pain the participant experienced following the operation, the more Oxycodone, the supplemental drug for post-operative pain relief, was administered. It can be explained due to the natural inclination to administer pain medication post-operatively when pain levels remain high. In this study, participants asked for additional rescue analgesia when maximum pain levels were high, with the hope that pain medication will decrease the severity of pain, though literature suggest some groups do not respond linearly [4]. Using opioids post-operatively at high doses can cause tolerance which may impede the recovery process in later stages after hospital discharge, alternatively, choosing NSAIDS for supplemental pain medication is associated with adverse events following gastrointestinal operations[3].

Considering that 30 participants consumed between 1-4 supplemental pain medications within 2 hours suggests that pain levels were well maintained, except for one participant who received 6 times supplemental pain medication.

The medical staff was available throughout the study. Many variables included were removed from the multiple regression analysis because they did not prove relevant or had a high level of collinearity. The study did not include logarithmic transformation as it would severely comprise the results of the analysis, however, this study could have used sophisticated statistical bootstrapping techniques to simulate the regression. The literature review in this study supports and further reinforces the results of the multivariate analysis. Severe pain is often treated with more pain medication post-operatively, however, certain population suffer from severe post-operative pain regardless of pain medication administered and the multivariate is too limited to provide the whole picture as previously discussed [4].

6.8 Instruments and validity

Electrocardiograms were used in this study for the measurement of heart rate but not heart rate variability and were not included in the analyses performed. According to a small-scale yet innovative study the use of HRV and heart rate as a measurement of autonomic nervous system activity is a suitable and potentially reliable adjunct for pain intensity assessment [6]. There appears to be a positive correlation between ECG reports and pain intensity when using an ECG (i.e., higher perceived pain results in higher activity on the ecg). Emotional states also have a significant impact on the

ECG such as post-operative stress or anxiety and are important to measure for improved pain management as previously discussed.

The use of the Empatica E4 on the patient's wrist was recorded during the research. The Empatica E4 contains four sensors: an electrode measuring electrodermal activity, 3-axis accelerometer, a temperature sensor and a photoplethysmography. The purpose of monitoring the electrodermal activity is to allow the identification of changes in skin electrical conductivity (e.g., sympathetic nervous system response that promotes the excretion of sweat) which should reflect changes related to pain [54]. Skin electrical conductivity can also suggest other states such as stress, fatigue, and other. The emotional state of the participant is measured by using the sensitive plethysmograph sensor which relies on light signals reflected from blood vessels to the sensor and blood volume pulse signal is calculated, thereby measuring the participants heart rate and inter-beat interval. The estimation of heart rate variability is more difficult when participants are moving and other challenges arise when the device is not worn tightly enough, or pressure is introduced, resulting in data loss. The Empatica E4 is considered a reliable wearable technology for heart rate measurement at rest [55].

Non-verbal pain expressions can be communicated voluntarily and non-voluntarily to others [6]. In this study, electromyography was placed on the frontalis muscle during phase II of the study to measure pain expression. Brown lowering, nose wrinkling, lip raising, orbit tightening, and eye closure were all associated with pain. The increased activity of corrugator supercilli muscle was specifically suggested as a reliable indicator of the pain response. Nevertheless, anatomical differences in facial muscles such as aging related changes, skinfold thickness as well as other soft tissue

variations may challenge the feasibility of the specific electromyography tool.

7. Conclusion

The study adds value in the prospective research of gastrointestinal pain management pre, intra and post-operatively. The expectation of pain and fear of pain related to elective gastrointestinal surgery was common and suggests two domains of possible intervention of a multidisciplinary team. The suggestions included in this study are both relevant for the patient as well as surgical teams. Future elective gastrointestinal participants' pain management programs should integrate the use of detailed patient education followed by a confirmation of correct interpretation of those same programs. In addition, the analysis of pain should always include a variety of assessment tools that encompass the biopsychosocial prism to manage patient expectation and fear. Opioid-sparing initiatives should be well known in hospitals conducting major surgery to improve patient outcomes but also prevent the development of adverse events such as opioid addiction or the further proliferation of chronic pain.

Indubitably, most participants (i.e., 32/50) in this study expected pain post-operatively compared to all groups, but the correlation between the expectation of pain with maximal pain levels was negligible. Fear related to the pain post-operatively was less prevalent (i.e., 13/50) than expectation of pain among that same population and showed a negligible correlation with maximal pain levels following elective gastrointestinal surgery. Maximal pain levels post-operatively were slightly higher for those expecting pain post-operatively than those who were both expecting pain and fearful of the pain related to the upcoming procedure (i.e., Median of

0.5 higher). The management of participant expectation is therefore a crucial area of intervention pre-operatively.

Furthermore, the relationship between the level of invasiveness of the surgical procedures and the fear related to pain post-operatively did not show any association.

The choice of pain medication post-operatively did not show a significant effect on post-operative maximal pain levels measured on the NRS when controlling for pre-operative pain levels. Continuous infusion of epidural at 5ml/h was the most prevalent choice of pain medication post-operatively. These presented results contradict current pain literature as discussed in previous chapters.

The administration of pain medications post-operatively and the amount of administered pain medications post-operatively are significant predictors of maximal post-operative pain as expected. The relationship is self-explanatory and requires no further investigation.

Future research should include a larger sample, focus on other variables than maximal post-operative pain levels which may cloud the results, measure pain at different points in time for all participants of the study and be conducted in different countries for better generalizability.

8. Limitations

This study has briefly introduced the SPA project goals and provides additional descriptive information and statistical analysis of the results following phase II of the project. The results included in this study are of the correlations between previous pain experiences, administration of pain medication and pain intensity should be interpreted with caution as

consistent statistically insignificant results and negligible correlations do not support or negate a relationship, thereby no generalization can be made from this study.

The researcher of this study was separate from that who collected the statistical raw data and all inaccuracies or challenges that were faced during the research could have not been brought up during the communication between the researcher involved with the collection of data in Turku university Hospital and the author of this study. The main limitation as in many descriptive and comparative studies is the availability and accuracy of the medical records. This study was expanded to a rapid literature review and creating a PEO chart was very difficult as the purpose of the review and this study are not to evaluate a distinct intervention.

The weakness of this study is in that it cannot indicate causation. In this case, even if associations were found they are not immediately applicable in the clinical context. Such studies often include the method of modelling to control for confounding effects. Modelling is the computation of adjusted effects based on characteristics among subjects before and after the implementation of the intervention using sophisticated statistical techniques such as logistic regression [39].

Another limitation is that the post-operative pain assessment using the numeric rating scale was continued for only 2 hours post-operatively. The research nurse requested pain levels using the NRS every 10 minutes or when participants communicated with the study nurse. The assessment of pain for 2 hours post-operatively was decided due to the limited funding and the study design. The author of this thesis was not included in the decision-making process.

In this study, the exploration of pain intensity focused on a unidimensional variable (i.e., NRS) and disregards response bias which may have altered the responses given by participants to the two nurses conducting the study. Response bias pertains to the tendency of participants to inaccurately respond to questions presented by the researcher, in this case, the pain questionnaire that was administered by the study nurse. There is always the risk that the participant desired to be a good experimental participant and provide socially desirable responses that may affect the response somehow [56]. Moreover, there were 8 patients who continued sleeping after the surgery and whose results are missing from the statistical analysis. The weakness of this study design may occur due to lack of control group that is often used in interventional studies and strong publication bias, favouring positive results. External validity may lack as the population chosen may not be representative or generalizable and convenience sampling and selection bias were observed since there was a lack of follow-up time out of study as well as the careful selection of participants based on strict exclusion criteria already established in the study design of Phase II.

This rapid literature review study had well-defined questions and relied on questions of relevance to the statistical analysis. The data abstractors who coded the charts given to the author of this study, played a critical role in the quality of the data. No training of the coder was carefully indicated preceding the study to the best of the authors knowledge. Research indicates that discrepancies in code should be review by other researchers and discussed with regards to the clarification of issues such as inter-rater reliability measured by using Cohen’s kappa. Moreover, the data abstractor should be blinded to the purpose of the study and a small pilot test should

be used prior to the actual study [57]. The study design did not include the above recommendations.

The inclusion criteria for Phase II of the study excluded those with mental disorders and resultingly could have influenced the outcomes. The exclusion resulted in a more homogeneous population that is less fearful or expecting pain post-operatively to begin with compared to the general population undergoing elective gastrointestinal surgeries. The relationship between depression, anxiety and higher catastrophizing scores have already been discussed in this study with regards to their potential influence on severe post-operative pain.

The participants of this study were all Finnish individuals. The reader should bear in mind that the study of pain relies on participants openly discussing about their pain experiences and recognizes the perceptual difference between different cultures and ethnicities in relation to dealing with pain. The generalizability of the results of this study may differ between cultures, as some cultures may under or over predict pain which literature has already suggested influences pain outcomes [28]. All in all, the standardization of post-operative protocols and experience of anesthesiologists as well as specialized nurses included in this study could have also influenced the observed outcomes of this study, as experienced clinicians are more aware of initiatives to reduce pain levels and the importance of proper dosing of opioid-based medications.

This study included the databases of PubMed, Embase and Web of Science. The literature review includes only three databases and was limited. The search words used in the search strategy could have been further expanded. The author of this thesis recognizes that the study should

have included more databases as to provide an even wider perspective and different viewpoints into the literature review itself to reflect from. The search words could have been further expanded as well as the 10-year article publication criteria which was part of the inclusion criteria. Future studies warrant the use of a knowledgeable librarian to further broaden the search which could prove essential.

The sample size of this study was considerably low, even though the goal was not to find meaningful effect size differences (50 participants). This is a considerable limitation due to the funding of the study but also was based on the receiver operator curve that was calculated before the beginning of the study. The goal of the study was to find significant correlations and this study did in fact find weak positive or negative correlation that could significantly have been amplified if more participants were added to the study group. The lack of power analysis a prior could have resulted in missed probabilities and relationships between the variables which may have required a different sample size.

This rapid literature review was conducted with only one reviewer that had to report the bias assessment using the PRISMA checklist for abstracts. The amount of work and objectivity is therefore questionable, even though state-of-the art tools were used and implemented during the writing of the review.

Future studies should include a sample size of over 100 individuals and follow the patients post-operatively for at least 6 days to 3 months as acute pain is often dramatically reduced during this period. The SPA project has received limited funding from The University of Turku which is also another limitation. Finally, the nursing researchers received little equipment during

the study time based on availability for the study, and equipment had to be transferred from one patient to another which may have influenced the quality of the study.

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10. Appendices

Appendix A

SPA CRF – Demographics and pain history - Preoperative

Date (dd.mm.yyyy): _____._____._____ Subject ID: SPA_____

Researcher: _____

BASIC INFORMATION

Date of birth (dd.mm.yyyy): _____._____._____

Sex M / F

Dominant hand L / R

QUESTIONNAIRE ON PAIN HISTORY

1.Do you expect to feel pain in relation to the forthcoming procedure? no / yes

2.Are you afraid of the possible pain related to the procedure? no / yes

3.1Have you ever had continuous pain? no / yes

3.2 Where was it located (The pain map on the next page can be used to localize the pain)

3.3 For how long did it last?

_____

4.1 Do you remember any other previous pain experiences? no / yes

4.2 What was your pain like then? (The pain map on the next page can be used to describe the pain)

_____

After instructing the NRS pain scale to the patient:

PREOPERATIVE ASSESSMENT OF PAIN NRS (X.x)

___.___

Subject ID:

SPA_____

SPA CRF – The assessment of pain - Postoperative

Date (dd.mm.yyyy): _____._____._____ Subject ID:

SPA:_____

Researcher:_____

Anesthetic record nro: _____

Procedure code: _____

Anesthesia code: _____

If discontinued, reason: _____

Peripheral IV line L / R / missing

Equipment setup / checked / circle the correct hand:

EKG checked

SpO2 L / R / missing

finger / ear / missing

Blood pressure Cuff / IA / missing

Warming of the body none / Bair Hugger / warming blanket

Empatica E4 L / R

Button on the side of [thumb / little finger]

EMG checked

SPA EKG checked

SPA EMG version v1n1 / v2n4 / v2n5 / v___n___

Start time of the recording: _____:_____:_____

End time of the recording: _____:_____:_____

Time mark nro:_____ time: _____:_____:_____ – TM:_____ time: _____:_____:_____

NRS (X.x) ___.___ location: _____

notes:_____ _____

Appendix B

International classification of diseases 10 clinical manual: TABULAR LIST of DISEASES and INJURIES

Table of Contents:

Certain infectious and parasitic diseases (A00-B99)

Neoplasms (C00-D49)

Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50-D89)

Endocrine, nutritional and metabolic diseases (E00-E89)

Mental, Behavioral and Neurodevelopmental disorders (F01-F99)

Diseases of the nervous system (G00-G99)

Diseases of the eye and adnexa (H00-H59)

Diseases of the ear and mastoid process (H60-H95)

Diseases of the circulatory system (I00-I99)

Diseases of the respiratory system (J00-J99)

Diseases of the digestive system (K00-K95)

Diseases of the skin and subcutaneous tissue (L00-L99)

Diseases of the musculoskeletal system and connective tissue (M00-M99)

Diseases of the genitourinary system (N00-N99)

Pregnancy, childbirth and the puerperium (O00-O9A)

Certain conditions originating in the perinatal period (P00-P96)

Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99)

Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (R00-R99)

Injury, poisoning and certain other consequences of external causes (S00-T88)

External causes of morbidity (V00-Y99)

Factors influencing health status and contact with health services (Z00-Z99)

Instructional Notations

Includes:

The word 'Includes' appears immediately under certain categories to further define or give examples of the content of the category.

Excludes Notes:

The ICD-10-CM has two types of excludes notes. Each note has a different definition for use but they are both similar in that they indicate that codes excluded from each other are independent of each other.

Excludes 1:

A type 1 Excludes note is a pure excludes. It means 'NOT CODED HERE!' An Excludes1 note indicates that the code excluded should never be used at the same time as the code above the Excludes1 note. An Excludes1 is used when two conditions cannot occur together, such as a congenital form versus an acquired form of the same condition.

Excludes 2:

A type 2 excludes note represents 'Not included here'. An excludes2 note indicates that the condition excluded is not part of the condition it is excluded

from but a patient may have both conditions at the same time. When an Excludes2 note appears under a code it is acceptable to use both the code and the excluded code together.

Code First/Use Additional Code notes (etiology/manifestation paired codes):

Certain conditions have both an underlying etiology and multiple body system manifestations due to the underlying etiology. For such conditions the ICD-10-CM has a coding convention that requires the underlying condition be sequenced first followed by the manifestation. Wherever such a combination exists there is a 'use additional code' note at the etiology code, and a 'code first' note at the

manifestation code. These instructional notes indicate the proper sequencing order of the codes, etiology followed by manifestation.

In most cases the manifestation codes will have in the code title, 'in diseases classified elsewhere.' Codes with this title are a component of the etiology/ manifestation convention. The code title indicates that it is a manifestation code. 'In diseases classified elsewhere' codes are never permitted to be used as first listed or principal diagnosis codes. They must be used in conjunction with an underlying condition code and they must be listed following the underlying condition.

Code Also:

A code also note instructs that 2 codes may be required to fully describe a condition but the sequencing of the two codes is discretionary, depending on the severity of the conditions and the reason for the encounter.

Appendix C

An updated guideline for reporting systematic reviews:

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	9-14
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	15-19
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	24
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	23
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	22
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	24
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report	25

Section and Topic	Item #	Checklist item	Location where item is reported
		retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	25
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	25-27
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	25-27
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	25-27
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	N/A
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	25-27
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	25
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	25
Study characteristics	17	Cite each included study and present its characteristics.	N/A
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	25-27
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	N/A
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	40
	23b	Discuss any limitations of the evidence included in the review.	40
	23c	Discuss any limitations of the review processes used.	40
	23d	Discuss implications of the results for practice, policy, and future research.	40
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	21

Section and Topic	Item #	Checklist item	Location where item is reported
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	N/A
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	55,121-122
Competing interests	26	Declare any competing interests of review authors.	N/A
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Acknowledgements and dedication

Many people have supported me in the making of this thesis during the past year when I first began conducting this study. I wish to express my deepest

and sincere gratitude to all of them even though I may miss some individuals who took part in helping with this study and were part of the Phase 2 study of the SPA project.

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This study relied on a previous study conducted at Turku university hospital by the department of Nursing Sciences at Turku University. I would like to first and foremost thank my supervisor Professor Sanna Salanterä who was continuously available through the making of this study and provided the data of this study as well as interesting perspectives to be considered from start to finish. Professor Salantera has continuously arranged required meetings with other professionals for the making of this thesis with the goal of verifying and validating this study's results. It has also been a privilege to work with Professor Cheng Yun of Fudan University which has given me new perspectives regarding the quality of this study and mentioned differences between post-operative pain management differences between China and Finland. I also wish to thank doctoral candidate of Turku university, Riitta Mieronkoski for her dealing with the raw data but also for her continuous support and criticism of this study which has encouraged me and motivated me by agreeing to frequent meetings which have allowed me to grow professionally as a researcher and reach my goals one step at a time.

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Thanks to Ruwang Han my friend I was able to translate the title and abstract of this thesis. Finally, I wish to thank my parents for supporting me throughout the writing of this master's thesis and their never-ending encouragement to keep educating myself.

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