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Retrospective chart review of surgical patients and chronic pain

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Thesis

RETROSPECTIVE CHART REVIEW OF SURGICAL PATIENTS AND CHRONIC PAIN

by

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DEDICATION

To my parents, whose sacrifices and unwavering support have made this journey possible, this achievement is as much yours as it is mine. I hope to continue making you proud.

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RETROSPECTIVE CHART REVIEW OF SURGICAL PATIENTS AND CHRONIC PAIN

ALEXIA ELBAZ

ABSTRACT

Background: Chronic postsurgical pain (CPSP) affects 10-30% of surgical patients and is associated with prolonged suffering, which may lead to a diminished quality of life (QOL). Thus, efforts to mitigate the incidence of CPSP have expanded, focusing on identifying risk factors and using new medical inventions. One recent advancement focuses on using functional near-infrared spectroscopy (fNIRS) as a brain biomarker to assess nociception during surgery. The goal of this technique is to help guide perioperative pain management strategies to mitigate CPSP. However, there are still many gaps in our understanding of what risk factors have direct effects on CPSP, requiring further exploration of its complexities and identification of the factors influencing its occurrence. This thesis aims to explore the multifaceted nature of CPSP by creating a retrospective chart review of surgical patients to understand standard demographics, preexisting health conditions, and surgical factors that may increase the incidence of CPSP.

Methods: This study focused on exploring the incidence of CPSP in two distinct groups: patients who underwent a hernia surgery and patients who underwent a cardiac surgery. A total of 100 patients were selected, and within each surgical cohort, 50 patients were included and divided into CPSP or No CPSP groups based on self-reported new or worsened pain that persisted for three or more months following their surgical procedure.

The CPSP and No CPSP groups for each surgical type were then compared against each other using prevalence rates and statistical measures based on three variables: demographics, preexisting conditions, and surgical factors. To ensure a comprehensive analysis, outliers were identified and removed. Thus, 41 hernia surgical patients (n= 11 CPSP, n= 30 No CPSP) and 50 cardiac surgical patients (11 = CPSP and 39 = No CPSP) were included in the final analysis.

Results: The prevalence rates of CPSP for the cardiac surgical group and hernia surgical group was 11 and 17 patients, respectively. After removing outliers from the hernia surgical group, the prevalence rate for the CPSP group was 11 patients. Among the hernia surgical group, the prevalence of pre-existing pain, surgical history, cardiovascular, and cancer conditions seemed to be greater for those with CPSP. Specifically, the odds of someone developing CPSP with a history of cancer was 4.1 times greater than someone without a prior cancer diagnosis ($\chi^2(1,41) = 3.617$, $p=0.057$, Odds ratio=4.1). Additionally, patients with three or more prior conditions were 6.2 times at greater odds of developing CPSP than those without these conditions ($\chi^2(1,41) = 6.05$, $p=0.01$, Odds ratio=6.2). When analyzing the cardiac surgical group, data revealed that both the pre-operative and postoperative pain levels on average were greater for the CPSP group (2.9 ± 2.5 and 3.3 ± 3.2, respectively) when compared to the No CPSP group (1.7 ± 2.1 and 1.8 ± 2.2, respectively). This data was supported by a medium effect size for the preoperative pain levels ($t(48) = -1.61$, $p=0.112$, Cohen's $d=0.46$) and post-operative pain levels ($t(48) = -1.73$, $p=0.08$, Cohen's $d=0.499$). Similarly, though the results were not statistically significant for preexisting pain ($p=0.823$) and prior surgeries ($p=0.494$),

the prevalence was greater for both variables in the CPSP group compared to the No CPSP group. Further comparing the total number of pre-existing conditions per patient showed no notable differences between the CPSP and No CPSP groups ($t(48) = 0.22$, $p=0.826$, Cohen's $d=0.078$).

Conclusion: We observed significant relationships between the incidence of developing CPSP and pre-existing conditions, such as cancer and having three or more premorbid conditions. Thus, highlighting the importance of addressing risk factors before surgical intervention. However, the study is limited by the small sample size thus future research with a larger sample pool may expand this relationship to provide more conclusive evidence as to which risk factors contribute to an increased risk of CPSP. Additionally, since this is a retrospective chart review, looking at longitudinal studies can help understand the transition from postsurgical acute to chronic pain development.

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LIST OF ABBREVIATIONS

BMI ..... Body Mass Index

CPSP ..... Chronic Postsurgical Pain

FC ..... Functional Connectivity

fNIRS ..... Functional Near-Infrared Spectroscopy

GIQLI ..... Gastrointestinal Quality Of Life Index

ICD-11 ..... International Classification of Diseases 11th Revision

ISAP ..... International Association for the Study of Pain

MATLAB ..... Matrix Laboratory

mFPC ..... Medial Frontopolar Cortex

QOL ..... Quality of Life

S1 ..... Somatosensory Cortex

SEM ..... Standard Error of Mean

INTRODUCTION

Background

In 1979, the International Association for the Study of Pain (ISAP) endorsed that pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage." (Raja et al., 2020) This definition of pain explains its multifaceted nature and highlights the importance of understanding the neurobiology of pain. Thus, many researchers and specialists have worked to categorize pain based on its variance and complexities. Pain is commonly classified based on its pathophysiological mechanisms, duration, etiology, and anatomical location. Pathophysiological mechanisms define three pathways in which pain can arise: the nociceptive pathway, which is triggered by tissue damage and typically leads to the activation of specific pain receptors; the neuropathic pathway, which results from damage to nerve cells in the peripheral and or central nervous system; or a combination of the two which is known as mixed pain. When referencing pain duration, it is most often deemed an acute or chronic form, each presenting challenges in research and clinical management. Acute pain typically occurs immediately following an injury and is a physiological response to tissue damage. In contrast, chronic pain persists for three months or longer and will often present itself with complex etiologies, requiring comprehensive treatment approaches. (Elsayed & Deer, 2019) By further investigating the field of pain neurobiology, researchers and clinicians can gain insights into the underlying mechanisms of pain and continue creating the development of targeted

interventions and novel therapies to alleviate patient suffering and improve long-term outcomes.

While many fields of medicine aim to remedy various forms of pain, a considerable amount of effort and research has been focused on understanding pain and its risk factors during and after surgery. (Rosenberger & Pogatzki-Zahn, 2022) Although acute pain following a surgical procedure is common, approximately 10-30% of patients experience a progression to moderate or severe pain known as CPSP. Within this cohort, nearly 25% of adults report requiring a referral to a pain clinic to manage their symptoms. The significance of CPSP is thus recognized due to its lasting effects on QOL, psychiatric and opioid-related morbidity, lasting beyond the expected timeframe for healing from surgery. (Sieberg et al., 2022) While the incidence of CPSP varies, the median incidence over six to twelve months after surgery is 20-30%, with a gradual decrease after that, either spontaneously or with medical/behavioral intervention. (Rosenberger & Pogatzki-Zahn, 2022)

The International Classification of Diseases 11th Revision (ICD-11) has outlined a list of criteria defining CPSP to establish a well-organized guideline within the medical and research communities. According to the ICD-11, CPSP is pain that develops or intensifies after a surgical procedure or tissue injury and persists for at least three months after the initial event. The revision also recognizes that CPSP can encompass neuropathic pain components, highlighting its complex pathophysiology. Most importantly, the ICD-11's classification of CPSP as a disease emphasizes the importance of recognizing it as more than just a symptom that can be ignored. (Rosenberger & Pogatzki-Zahn, 2022)

Therefore, encouraging proactive efforts to find treatments and preventions to address the pain itself can limit the subsequent costs of the disease.

The burden of CPSP extends beyond physical discomfort, with profound implications affecting various aspects of a patient's life. (Guertin et al., 2018) Relative to other diseases and healthcare treatments, there is a positive correlation between individuals suffering from CPSP and an increased financial obligation. This cost association can be directly linked to increased medical expenses and heightened healthcare utilization to access proper treatment and management options. Depending on the type of pain and duration, many individuals are forced to seek out additional medical assistance aside from their original surgical procedure, such as pain physicians, surgeons, and or physical therapists, to be able to regain some pain relief to function in society. Indirect costs may also arise, such as decreased productivity at work due to absenteeism and disability. In 2010, it was estimated that the overall costs associated with all forms of chronic pain were between US$560 to US$635 billion annually and increased when considering cardiovascular diseases and cancer. (Guertin et al., 2018) A comprehensive analysis of a major city university hospital in Canada found that CPSP accounted for approximately CAN$2.5 million to CAN$4.1 million of their yearly costs, further highlighting the substantial economic impact of this condition. (Guertin et al., 2018)

Along with this financial strain, overall QOL has been shown to have a substantial negative impact on individuals who suffer from CPSP. When considering QOL for an individual with CPSP, it most often addresses their functional status and psychological well-being. A 2016 study focused on this phenomenon, specifically examining the

relationship between QOL and chronic pain after a small bowel obstruction surgery. QOL was measured using the gastrointestinal quality of life index (GIQLI), which is a 36-question survey that evaluates various aspects, including symptoms, physical status, emotions, social functioning, and the effect of medical treatment. Patients are asked to score each question on a scale from zero to four, with four indicating better functioning. Out of the 32 patients who completed the GIQLI, 19 of them reported CPSP, with 14 experiencing pain more than two days per week. The study found that patients reporting CPSP also had a lower GIQLI score in four out of the five domains, indicating a direct link between CPSP and decreased QOL. (Jeppesen et al., 2016)

A similar study in 2018 further supported these findings by reinforcing the relationship between QOL and CPSP, but this time focusing on patients who underwent an emergency laparotomy. Consistent with the data in the previous study, the GIQLI score among those experiencing CPSP was lower compared to patients with no report of CPSP. Among this patient population, 45% reported moderate to severe functional impairment, with the most significant factor associated with physical activity. (Tolstrup et al., 2019) Both these findings underscore the impacts of CPSP aside from the actual pain itself and encourage the continued importance of addressing risk factors of CPSP to find management strategies and interventions to address all components of this disease.

Known Risk Factors of Chronic Pain After Surgery

For many patients, the main goal of undergoing a surgical procedure is to alleviate and or manage their medical conditions with the hope of achieving a pain-free life after the surgery. However, a subset of these patients finds themselves experiencing new or

worsened CPSP months after the surgical site is healed. To understand this phenomenon and consequently prevent its development, it is crucial to recognize the wide array of risk factors associated with CPSP. Various factors, ranging from psychological, biological, and genetic to the nature of the surgical and anesthetic procedure itself, confers a risk for CPSP. A comprehensive guide linking these risk factors to CPSP is essential to optimize patient outcomes and allow healthcare providers to enhance the recovery period before the surgery.

Psychological Factors: Research has consistently shown that psychological variables can influence the experience of pain, recovery trajectory, and the likelihood of developing CPSP. (Chadwick et al., 2021) While psychological variables are abundant, this thesis will focus on the effects of anxiety and depression as a unit. On the surface, patients diagnosed with pain and anxiety generally have increased apprehensions and fears regarding their surgical procedure, putting them in a negative headspace from the onset. (Chadwick et al., 2021) However, these variables become much more complex, further analyzing why they are considered significant risk factors for CPSP. It is well known that patients with anxiety have a reduced analgesic response to opioids. (Chadwick et al., 2021) Hence, their rate of developing CPSP is increased as their responsiveness to opioid medications in relieving pain is diminished. Also, both anxiety and depression play a critical role in pain catastrophizing, which is when the patient magnifies the perceived threat of pain and becomes helpless. This is linked with patients becoming overwhelmed as they only focus on the worst possible outcomes. (Chadwick et

al., 2021) Such negative thought associations affect their postsurgical recovery and are why individuals with anxiety and or depression have a higher rate of developing CPSP.

Biological and Premorbid Factors: Understanding pain perception from a psychological standpoint is essential in assessing the long-term risk of developing CPSP. However, it is equally crucial to consider biological and genetic factors in this context. At the start of any medical intervention and before offering a diagnosis, healthcare professionals will ensure they have a complete understanding of the patient's prior medical history. This is required as many health complications, diseases, and surgical procedures can have different outcomes due to a person's innate biological and genetic makeup.

Prior research has estimated that up to 70% of differences in pain sensitivity result from individual differences in both a person's DNA sequence (genetics) and the structure of their genome (epigenetics). This also includes overall susceptibility to CPSP and associated responses to pain management. (Chadwick et al., 2021) This analysis also aids in understanding why certain individuals report different pain scores before and after a surgical procedure. Considering a person's biological framework allows research and medical professionals to identify health predispositions that may have exacerbated or led to developing CPSP. This can include comorbidities (preexisting medical and psychiatric conditions) and other premorbid factors such as age, sex, weight, and body mass index (BMI).

Surgical and Anesthetic Factors: Lastly, considering the components of the surgical procedure itself can be instrumental in understanding possible risk factors for

CPSP, this study includes an exploration into pre- and postsurgical variables associated with the incidence of CPSP. Along with the previous key pieces of physiological, biological, and genetic information, perioperative variables include type of surgical procedure, preemptive analgesia, anesthesia type, and pre-surgical pain levels. Conversely, post-operative factors include post-operative pain levels, surgery duration, postsurgical sensory disorders and reports of chronic pain. A thorough analysis of these measures can ultimately identify any incidence of CPSP. A study examining "Post-operative Pain in Ambulatory Surgery" found that one in ten patients under anesthesia for 90 minutes reported severe pain. (Chung et al., 1997) If the anesthesia lasted longer than 120 minutes, the incidence increased to one in five patients. Further analysis of their data proved to be critical in proving that the type of surgery could influence the likelihood of developing CPSP as: "orthopedic and neurosurgery patients were 17 times and 13 times, respectively, more likely to have severe pain, and gynecology and plastic surgery patients were thirteen times and nine times, respectively, more likely to have severe pain than were ophthalmology patients." (Chung et al., 1997)

Intraoperative factors contributing to the development of CPSP

Anesthetic Management: During surgical procedures, tissue damage typically can trigger the activation of nociceptor nerve fibers and/or inflammatory systems, which in turn stimulates nociceptive afferent signals. (Sieberg et al., 2022, Karunakaran et al., 2023) These signals have been shown to reach the brain even under general anesthesia, which "is a state of drug-induced unconsciousness with suppression of sensory perception and consists of both hypnotic and analgesic components" (Borsook et al., 2010),

ultimately activating the pain pathways. Thus, even with vigilant monitoring, types of anesthesia and adjustments by anesthesiologists throughout the procedure, there is evidence that inadequate analgesia can affect the brain's neuroplasticity and overall function, leading to CPSP. (Borsook et al., 2010)

One of the ways in which research is aiming to address this problem is by focusing on the development of multimodal analgesic techniques to mitigate the increased risk perioperative pain poses in the development of long-term pain. (Fregoso et al., 2019) These various techniques target the nociceptive pathways crucial in the prevention of CPSP. For instance, a study evaluating the risks of CPSP stated that one analgesic technique involves using local anesthetics during the perioperative period. This approach would lessen acute postoperative pain, thereby potentially reducing the risk of CPSP development. Another approach focuses on the benefits of regional anesthesia, which was found to reduce the development of CPSP in breast surgery, thoracic surgery, and caesarean sections. Therefore, the use of multimodal analgesic techniques during the preoperative, intraoperative, and postoperative surgical periods can reduce the activation of nociceptor nerve fibers and decrease the incidence of CPSP. Nevertheless, while these forms of anesthesia hold promise to reduce the effect of CPSP there is still much to understand regarding the transition from acute to chronic pain leading to CPSP. (Fregoso et al., 2019)

Peripheral and Central Inflammation Exposure to noxious stimuli triggers repetitive nociception that occurs due to prolonged activation of neuropathic responses and inflammatory systems. This elicits a chain of events resulting in changes within various

pain pathways, ultimately leading to peripheral and central sensitization. (Fregoso et al., 2019) Studies indicate that approximately 10-40% of patients who develop nerve damage during a surgical procedure experience abnormal pain process, further contributing to sensitization. (Borsook et al., 2013) Moreover, the inflammatory process that promotes the transition from acute to chronic pain can be exacerbated by additional surgical factors, such as the introduction of surgical materials like mesh and chronic nerve stretching. (Fregoso et al., 2019) Consequently, these alterations in a patient's central nervous system manifest as shooting pains, sensory loss, and other symptoms associated with CPSP. (Borsook et al., 2013)

Utilization of Neurophysiology and Neuroimaging to Explore Pain Pathways

Pain assessments are typically limited by their reliance on self-reported measures (which are unavailable during surgery), and as such has led to an increased interest in further investigating brain or physiology-based measures to develop a more comprehensive analysis and predictor of pain. These discoveries have helped advance the interest in the utilization of electrophysiological and brain imaging techniques to advance pain analysis. Identifying the biological markers associated with pain can more accurately analyze assessments of pain and treatment efficacy and decrease the factors that lead to pain development after a surgical procedure. However, majority of the current physiology-based measures do not provide enough specificity, while imaging-based measures are either impractical or inaccessible for clinical use let alone in the operating room—a highly dynamic environment.

To mitigate this limitation, a series of studies explored the utility of fNIRS as a tool to evaluate brain function during pain/nociception. (Karunakaran et al., 2021, Peng et al., 2018, Peng et al., 2021, Kussman et al., 2016, Karunakaran et al., 2022) fNIRS is a noninvasive imaging technique with moderate spatial resolution and temporal resolution that is superior to functional MRI but comparable to electroencephalography. Recent studies using fNIRS during experimental pain have demonstrated the ability to quantify cortical activity associated with nociception and its reversal following opioids (analgesia). (Aasted et al., 2016, Peng et al., 2018) These studies consistently report the recruitment of regions previously reported by fMRI studies (Wager et al., 2013), involving the prefrontal cortex regions (specifically the medial frontopolar cortex (mFPC) and lateral prefrontal cortex), responsible for cognitive and emotion processing, and the primary somatosensory cortex (S1), which is associated with nociceptive processing. Such advancements have led to further research utilizing machine learning approaches with the goal to enhance clinical practices and objectively measure pain using cortical signatures. (Fernandez Rojas et al., 2019, Fernandez Rojas et al., 2024, Lopez-Martinez et al., 2019)

Importantly, recent studies have shown that even when patients are unconscious and are unable to experience conscious pain, surgical procedures continue to activate similar nociceptive pathways in the cortex as conscious individuals. (Peng et al., 2021, Green et al., 2022) Interestingly, the magnitude of the cortical response to surgery was correlated to the post-operative pain levels (Karunakaran et al., 2023), further suggesting that the brain continues to activate even under standard anesthetic protocol. A subsequent

study focusing on patients undergoing cardiac ablation corroborated this relationship, reporting that surgery-induced activation of cortical areas was diminished in patients with continuous infusion of opioids but not in patients with the placebo. (Karunakaran et al., 2022) Fundamentally, these studies provide evidence for brain activity that potentially initiates the process of central sensitization leading to CPSP. Importantly, they highlight the utility of using fNIRS as a device to measure nociception/pain to mitigate the effects of nociceptors and brain systems that have been implicated in CPSP development. This can hopefully then lead to using fNIRS as a brain biomarker and control pain while a person is in an unconscious state (anesthesia), limiting CPSP and increasing medical interventions.

Need for Improved Treatments

Postsurgical pain has been identified as one of the most common symptoms experienced by patients after surgery. As of 2010, about 10 million patients had a major surgical operation, and as the global population grows, so does the incidence of post-operative pain. (Coppes et al., 2020) However, pain is subjective, highlighting the importance of finding effective ways to predict and manage pain prior to and during surgical intervention. Current approaches and techniques for pain assessments in conscious individuals rely mainly on patient's self-reports. Whereas pain assessment during unconscious states relies entirely on clinical indicators such as heart rate, blood pressure, respiratory rate, etc. The downside, however, is that these physiological/autonomic changes are highly variable, unreliable, and intermittent proxies of pain. These methods lack objectivity and increase the risk of inadequate or inappropriate perioperative care. (Ip et al., 2009) Electrophysiological methods such as

the bispectral index have proven effective for intraoperative use, however, it only indicates the depth of anesthesia and does not reflect nociception or the conscious perception of pain. (Shi et al., 2022) Hence, there is an urgent need for reliable, immediate, and objective assessments of pain under anesthesia.

The nerve damage resulting from surgery can lead to both peripheral and central sensitization, causing neuropathy and CPSP in the post-operative state. These factors can also be coupled with a cascade of negative long-term factors such as depression, underscoring the importance of proper pain management in the post-operative period. (Borsook et al., 2013) Without proper management, high levels of post-operative pain have also been linked to adverse outcomes such as delirium, increased hospital stays, increased opioid use, and, most commonly, CPSP. Several studies have consistently shown a positive correlation indicating that one of the most common predictors of post-operative pain is pre-operative pain. Hence, individuals who report high levels of pre-operative pain also have increased post-operative pain scores and analgesic consumption. (Coppes et al., 2020)

Given the high prevalence of CPSP, it is imperative to develop better treatments to improve QOL for patients and reduce the burden that is associated with a poor surgical outcome. However, developing treatments will only be possible with ongoing research to identify objective measures of pain. Innovations such as fNIRS, which can measure pain in both conscious and unconscious states, could achieve this goal and revolutionize the ways in which patients experience post-operative pain. This approach may enable research scientists and healthcare professionals to identify pre-operative risk factors and

or block pain signals produced during the surgical procedure, ultimately reducing the incidence of CPSP. Without continued efforts in this direction, patient well-being, economic burdens, and satisfaction are at a continued risk of further decline, accompanied by an increased strain on healthcare resource utilization due to persistent long-term pain sensations and discomfort.

SPECIFIC AIMS

This paper seeks to explore the effects different risk factors have on determining if a patient will develop CPSP or No CPSP. It investigates the relationship by looking at three different levels of analysis to find significant relationships within the respective surgical groups.

Aim 1: Evaluate the incidence of chronic pain based on demographic variables (age, sex, and BMI).

Aim 2: Evaluate the incidence of chronic pain based on preexisting health conditions (psychiatric disorder, cardiovascular abnormality, report of pain, previous surgeries, and cancer diagnosis).

Aim 3: Evaluate the incidence of chronic pain based on surgical factors (preoperative pain score, postoperative pain score, surgical duration).

Aim 4: Understand how the results from the CPSP and No CPSP patients compare and contrast between the cardiac and hernia surgical group.

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METHODS

Sample and Setting

This chart review delved into exploring the correlation between surgical procedures, specifically, hernia surgery and cardiac surgery, and CPSP. A total of 100 patient records on EPIC were examined, comprising the first 100 records from a physician in each surgical group. The first surgical group consisted of 50 hernia surgery patients who underwent procedures at Massachusetts General Hospital (MGH) between May 2018 and February 2023. These patients were selected from seven randomly chosen surgeons at MGH who specialize in hernia repair, and all variations of hernia surgeries were categorized together for analysis. Similarly, 50 patients who underwent cardiac surgery under six randomly chosen cardiac surgeons at MGH between March 2018 and July 2023 were included in the chart review under the same parameters. All records were accessed via EPIC following IRB approval, and strict confidentiality was ensured through the allocation of alphanumeric study numbers to each patient.

During initial analytical review, 9 patients from the hernia surgical group were classified as outliers which was defined as any value greater than 3 scaled Median Absolute Deviation from the median. Hence when calculating prevalence and performing subsequent statistical analyses using Matrix Laboratory (MATLAB) only 41 out of the 50 hernia surgical patients (n= 11 CPSP, n= 30 No CPSP) were included.

Measures

For both surgical groups the information collected was identical to develop a comprehensive review. Information collected from the patient's pre-operative assessments included: age, sex, weight, BMI, surgery date, type of surgical procedure, and pre-surgical pain levels. Additionally, a patients' comorbidities (preexisting medical or psychiatric conditions), cardiovascular health, and smoking habits were recorded. Post-operative variables included post-operative pain levels, surgery duration, anesthesia type, post-surgical sensory disorders, and incidence of chronic pain. Pre- and post-surgical pain levels were self-reported by patients on a scale from zero to ten, where zero indicated no pain and ten signified extreme pain. Patients previously diagnosed with chronic pain were also included in the data collection process.

Descriptive Analysis

There was a total of three levels of analysis: demographics, preexisting conditions, and surgical factors. Descriptive statistics were employed for analysis, focusing on the frequency of chronic pain following surgical procedures in both groups. Within the subset of patients with CPSP and No CPSP, preoperative variables were examined to identify common risk factors associated with persistent post-surgical pain. The analysis primarily aimed at identifying prevalent preexisting conditions and surgical factors among patients reporting pain following their surgical intervention. This information was analyzed against the sample of patients who did not report incidence of chronic pain following the surgical procedure to create a comprehensive incidence report among both surgical groups.

Cardiovascular health encompassed any significant cardiac procedures, surgeries or abnormalities reported before the hernia or cardiac surgery. Preexisting medical conditions followed a similar methodology, comprising of major procedures or diagnoses that could impact chronic pain severity post-surgery. These factors were determined at the discretion of the examiner. Any specific preexisting health risks reported more than five times were individually listed. This included: cardiovascular abnormalities, previous surgeries, psychiatric diagnosis, reports of significant pain/ pain disorder and cancer diagnosis. All other variables were grouped as a collective. Psychiatric factors were defined as any report or prior diagnoses of anxiety and/or depression.

Demographic data such as age, sex and BMI were also considered in analysis to determine plausible relationships and increased risk factors.

Chronic pain was defined as:

- Pain occurring on or related to the surgical site, persisting for three or more months following the surgical procedure.
- Pain that existed prior to surgical intervention but worsened after the surgery.
- Pain reported in other areas (away from the surgical site) for at least three months after the surgical procedure.

The complete data collection involved a detailed analysis of each patient in which demographic variables (age, sex, BMI), preexisting health conditions (psychiatric disorder, cardiovascular abnormality, previous surgeries, reports of pain and cancer diagnosis) and surgical factors (surgical duration, preoperative pain score and postoperative pain score) could be organized into a comprehensive review. To determine

the differences between the CPSP and No CPSP group prevalence rates (%) were calculated and displayed on bar charts using the standard error of mean (SEM). Standard deviations were also calculated for each category and is the value included within the results section.

Statistical Analysis

All statistical analysis for both the hernia and cardiac surgical group to determine the differences between the CPSP and No CPSP patients was calculated independently using MATLAB. There was a total of three levels of analysis: demographics, preexisting conditions, and surgical factors. An independent sample t-test was calculated within each of these variables to compare the means of the two groups regarding the variables with continuous numerical data.

To determine the association between the CPSP and No CPSP groups regarding categorical variables a chi-square test was implemented. If the p- value was less than .05, the result was considered statistically significant. If the p- value was greater than .05, the result was considered statistically insignificant. To accompany the results of the t-test, Cohen's d was calculated to determine effect size. Based on standard calculations, effect size was determined as either: small (d = 0.2), medium (d = 0.5), or large (d = 0.8).

A box whisker plot was also generated to show the total number of pre-existing conditions and average surgery duration in the CPSP and No CPSP groups. Additionally, the odds ratio among certain variables, as detailed in the results section, was manually calculated to determine the probability of CPSP occurring or not occurring depending on the comorbidity.

RESULTS

Data from 100 participants who underwent cardiac and hernia surgical procedures between March 2018 and July 2023 were analyzed to determine prevalence rates and further statistical analysis.

Hernia Surgical Group

Among the 50 patients who underwent hernia surgery, 34% (n=17) reported CPSP, while 66% (n=33) had No CPSP. Further dividing the patient factors based on CPSP prevalence rate, patients in this group had a higher, mean duration of surgery, mean preoperative and mean postoperative pain scores. Additionally, the prevalence of pre-existing conditions was greater in the CPSP group for all categories (cardiovascular abnormality, cancer diagnosis, report of pain, and previous surgeries), expect for a previous diagnosis of a psychiatric disorder, which was equal in the CPSP and No CPSP groups. (Table 1)

Table 1: Descriptive Statistics for the Hernia Surgical Group. The population included CPSP (n=11) vs. No CPSP (n=30). The mean values are defined for the continuous variables. Percent calculations are used to describe prevalence rate.

Patient Factors	CPSP (No. of patients)	No CPSP (No. of patients)
Age	68.9	65
Males	9	19
Females	2	11
	CPSP (Average score)	No CPSP (Average score)
Body Mass Index	27.3	27.9
Pre- OP Pain Score (0 -10)	2.91	1.72
Post- OP Pain Score (0 -10)	2.82	2.37
Surgery Duration (min)	115.4	90.1
	Prevalence Rate (%) within CPSP group (n=11)	Prevalence Rate (%) within No CPSP group (n=30)
Previous Surgery/ Procedures	82.0%	60.0%
Report of Pain	64.0%	40.0%
Cancer Diagnosis	45.0%	17.0%
Cardiovascular Abnormality	82.0%	60.0%
Psychiatric Disorder	27.0%	27.0%

During initial investigation, 9 patients from the hernia surgical group were classified as outliers based on either age, duration of surgery or BMI. An outlier was defined as any value greater than 3 scaled Median Absolute Deviation from the median. Hence, when performing subsequent statistical analysis using MATLAB, there were 41 hernia surgical patients (n= 11 CPSP, n= 30 No CPSP). All data was organized into three levels of analysis, demographics, preexisting conditions, and surgical factors, to determine the variables associated with incidence of CPSP after surgery.

Demographics:

Of the 41 patients included in the analysis there were 13 females and 28 males. Two out of the 13 females and 9 out of the 28 males reported CPSP. A chi-square test of independence showed that the proportion of patients with CPSP or No CPSP after surgery did not statistically differ based on sex ($\chi^2(1,41) = 1.270$, $p=0.259$). (Table 2) The mean ± SD age for individuals with CPSP was 68.9 ± 1.5 years old and No CPSP was 65.0 ± 1.8 years old. The mean ± SD BMI for these patients was 27.3 ± 5.3 for those with CPSP and 27.9 ± 5.2 for those with No CPSP. (Figure 1) There were no significant differences between the two groups based on age ($t(39) = -1.23$, $p=0.223$) or BMI ($t(39) = 0.335$, $p=0.738$).

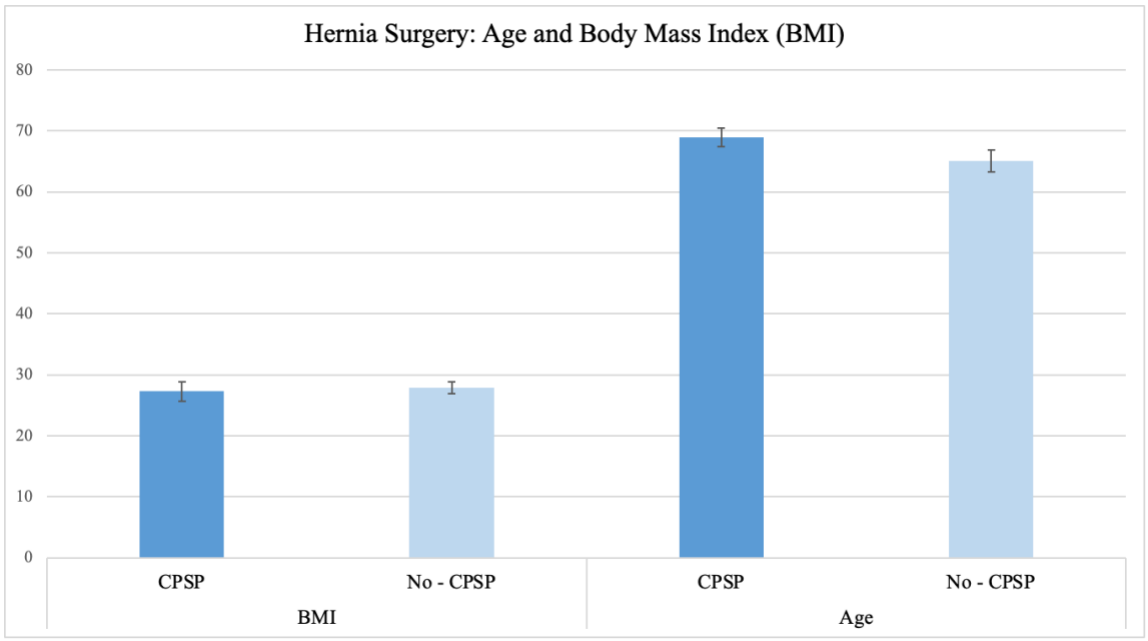

Figure 1: BMI and Age-related effects comparing CPSP and No CPSP (Hernia). In this analysis the CPSP group on average has a slightly lower BMI value (27.3) and higher age (68.9) compared to the No CPSP groups BMI (27.9) and age (65). Error bars indicate the SEM for each variable.

Pre-existing conditions:

Among the five preexisting conditions investigated, the CPSP group had a higher incidence rate in four of the variables and was equal to the No CPSP group for one of the variables. (Figure 2) In both the CPSP and No CPSP group, 27% of the patients had a previously diagnosed psychiatric disorder. A previous cardiovascular abnormality was found in 82% of the patients who developed CPSP while 60% for those with No CPSP. Of the patients with CPSP 45% had a previous cancer diagnosis before the surgical procedure and the value decreased to 17% for those with No CPSP. The fourth variable examined was a previous report of pain which was found in 64% of patients in the CPSP group and among 40% of the patients with No CPSP. Lastly, 82% of patients with CPSP had a previous surgical procedure while that number was 60% for patients with No CPSP. (Figure 2)

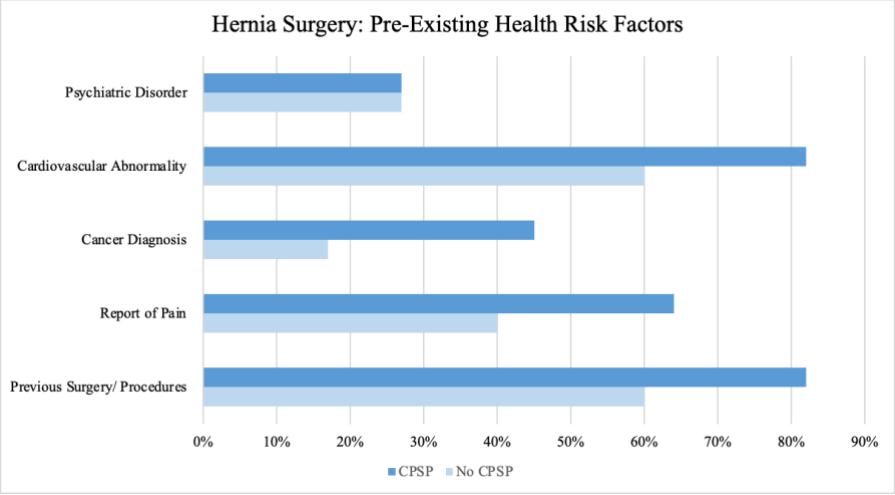

Figure 2: Prevalence (%) of the preexisting risk factors in the Hernia Surgical Group. This analysis compared preexisting conditions for CPSP and No CPSP patients who had undergone a hernia surgery. Each variable was totaled and divided by the total number of patients in their respective group; CPSP (n= 11) and No CPSP (n=30). This figure shows that the CPSP group has a higher prevalence rate for four out of the five variables.

A chi-square test of independence showed that the proportion of patients with CPSP or with No CPSP after surgery did not statistically differ based on premorbid conditions. (Table 2) However, the results for the cancer comorbidity were marginally significant (p=0.057) and the prevalence of patients with a prior cancer diagnosis was greater in the CPSP group than the No CPSP group (45% of patients in CPSP had prior cancer as opposed to 16.6% in No CPSP group). Using Relative Risk as an effect size, we observed patients who developed CPSP are .45/.16 = 2.80 times more likely to have a prior cancer diagnosis than the No CPSP group. In other words, the odds of a person with prior cancer diagnosis developing CPSP is 5 to 5 or 1 i.e., 50%. The odds of a person without a prior cancer diagnosis developing CPSP is 6 to 25 or 0.24. This means that the odds of someone developing CPSP with a history of cancer are 1/0.24 = 4.1 times (odds ratio) greater than someone without a prior cancer diagnosis ($\chi^2(1,41) = 3.617$, p=0.057, Odds ratio=4.1).

Additionally, comparing the total number of pre-existing conditions per patient between the two groups using an independent sample t-test showed that the CPSP group had greater number of pre-existing pain-related, surgical, or medical conditions (t (39) = -2.74, p=0.009, Cohen's d=0.966 (large effect)). Figure 3 is a box whisker plot showing the distribution of data within each group. Seventy-five % of data in the CPSP group is above 2.2 (i.e., 1st quartile) whereas 75 % of data in the No CPSP group is below 3 (3rd quartile). Specifically, the proportion of patients with 3 or more presurgical conditions (pain, prior surgery, cardiovascular abnormality, psychiatric disorder) in the CPSP group was significantly greater than the No CPSP group ($\chi^2(1,41) = 6.05$, p=0.01, Odds ratio=6.2).

This suggests that patients with three or more prior conditions have 6.2 times the odds of developing CPSP than those without these conditions.

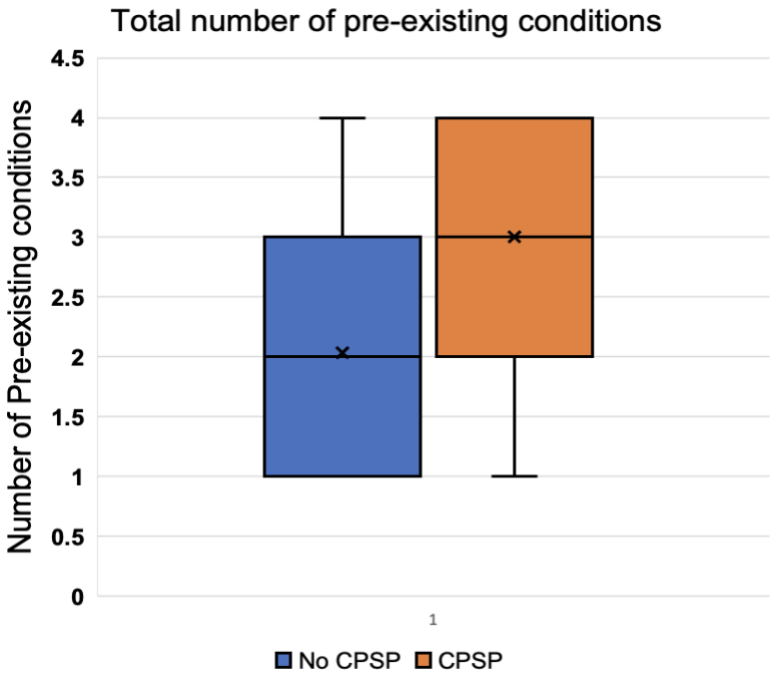

Figure 3: Box whisker plot showing the total number of pre-existing conditions in the CPSP and No CPSP group (Hernia). Independent sample t-tests comparing the two groups showed a significantly higher number of pre-existing conditions in CPSP group vs. the No CPSP group (t (39) = -2.74, p=0.009, Cohen's d=0.966).

Table 2: Results of Chi-square test of independence for Hernia Surgical Group. The chi-square value (χ^2) and p value are used to evaluate the relationship between CPSP incidence and premorbid factors.

Variable	χ^2 (1,41)	P value
Sex	1.270	0.259
Previous Surgery	0.422	0.515
Prior Pain	1.808	0.178
Cancer Diagnosis	3.617	0.057
Cardiovascular Abnormalities	0.422	0.515
Psychiatric Conditions	0.001	0.969

Surgical Factors Analysis:

The complete surgical duration for patients who reported CPSP was 115.4 ± 55.8 minutes and 90.1 ± 49.6 minutes for those with No CPSP. (Figure 4-Left**)** Although, the CPSP group has a greater average duration of surgery by over 15 minutes, independent sample t-tests comparing the two groups showed no statistical difference (t (39) = - 1.39, p= 1.70, Cohen's d=0.477 (medium effect)). However**,** excluding two suspected outliers, identified as data points > 1.5 interquartile range from 3rd or 1st quartile—shown in Figure 4-Left, resulted in (t (37) = -2.80, p= 0.04, Cohen's d=0.68), indicating a medium effect. The preoperative and postoperative pain scores for individuals with CPSP was 2.9 ± 2.9 and 2.8 ±1.8, respectively. For those who had No CPSP their pain scores were1.7 ± 2.4 in the preoperative state and 2.4 ± 2.4 in the postoperative condition. (Figure 4-Right). There were no statistically significant differences between the two groups based on pre-operative (t (39) = -1.23, p=0.223, Cohen's d=0.45 (small to medium effect)) or post-operative pain scores (t (39) = 0.335, p=0.738, Cohen's d=0.188 (small effect)).

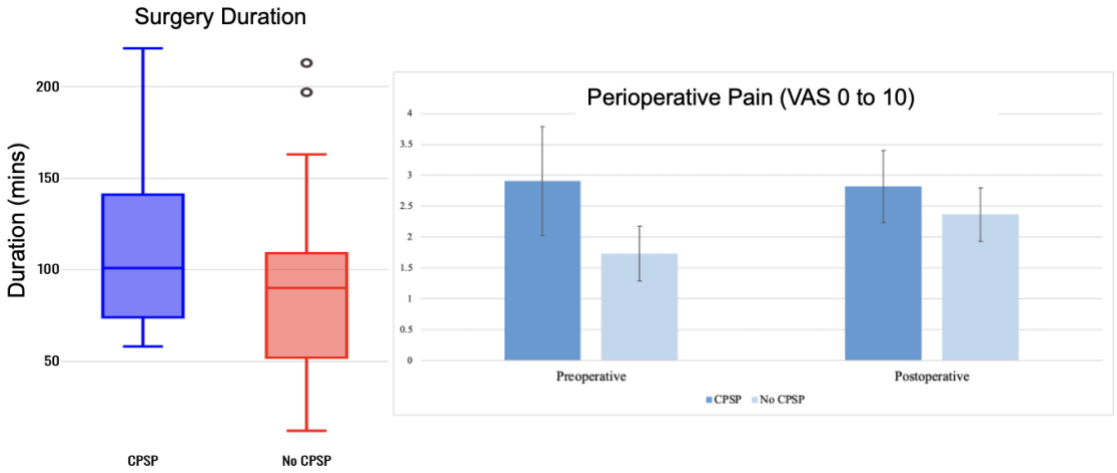

Figure 4: Average surgery duration (left panel) and average preoperative and postoperative pain scores (right panel). This analysis for the hernia surgical group measured the three surgical factors for patients with CPSP and those with No CPSP. Error bars represent SEM. Black circles on the box whisker plot indicate suspected outliers (i.e., >1.5 interquartile range above the 3rd quartile). On average the CPSP group had higher preoperative (2.9) and postoperative pain scores (2.8) compared to the No CPSP groups preoperative (1.7) and postoperative (2.4) pain scores. The surgical duration for the CPSP group was also longer than that of the No CPSP group.

Cardiac Surgical Group

In the 50 patients who underwent cardiac surgery, 22% (n=11) reported CPSP, while 76% (n=39) reported No CPSP. Similar to the hernia group, we found greater mean BMI, mean duration of surgery, mean preoperative and post-operative pain scores in the CPSP group when compared to the No CPSP group. Regarding preexisting conditions, only prior surgeries, and prior reports of pain were greater in the CPSP group compared to the No CPSP group. Table 3 shows a summary of all patient factors between the two groups, CPSP and No CPSP.

Table 3: Descriptive Statistics for the Cardiac Surgical Group. The population included CPSP (n=11) vs. No CPSP (n=39). The mean values are defined for the continuous variables. Percent calculations are used to describe prevalence rate.

Patient Factors	CPSP (No. of patients)	No CPSP (No. of patients)
Age	63.1	68
Males	9	23
Females	2	16
	CPSP (Average score)	No CPSP (Average score)
Body Mass Index	29.7	28.6
Pre- OP Pain Score (0 -10)	2.90909091	1.69230769
Post- OP Pain Score (0 -10)	3.272727273	1.820512821
Surgery Duration (min)	301.545455	286.512821
	Prevalence Rate (%) within CPSP group (n=17)	Prevalence Rate (%) within No CPSP group (n=33)
Previous Surgery/ Procedures	72.7%	69.2%
Report of Pain	72.7%	56.4%
Cancer Diagnosis	18.1%	25.6%
Psychiatric Disorder	9.0%	23.0%

*Prior cardiovascular abnormalities were not included as it is expected to be present across all patients undergoing cardiac surgery.

No outliers were found in the cardiac surgical group when evaluating age, duration of surgery and BMI. Hence, when performing subsequent statistical analyses using MATLAB, there were 50 cardiac surgical patients (n= 11 CPSP, n=39 No CPSP). All data was organized into three levels of analysis to determine the factors associated with incidence of CPSP after surgery.

Demographics:

Of the 50 patients included in the analysis there were 18 females and 32 males. Two out of the 18 females and 9 out of the 32 males reported CPSP. A chi-square test of independence showed that the proportion of patients with CPSP or No CPSP after cardiac surgery did not statistically differ based on sex. (Table 4) The average age for individuals

with CPSP was 63.1 ± 7.1 years old and No CPSP was 68.0 ± 8.5 years old. The average BMI for these patients was 29.8 ± 6.4 for those with CPSP and 28.7 ± 5.0 for those with No CPSP. (Figure 5) There were no significant differences between the two groups based on age (t (39) = 1.75, p=0.08) or BMI (t (39) = -0.598, p=0.552).

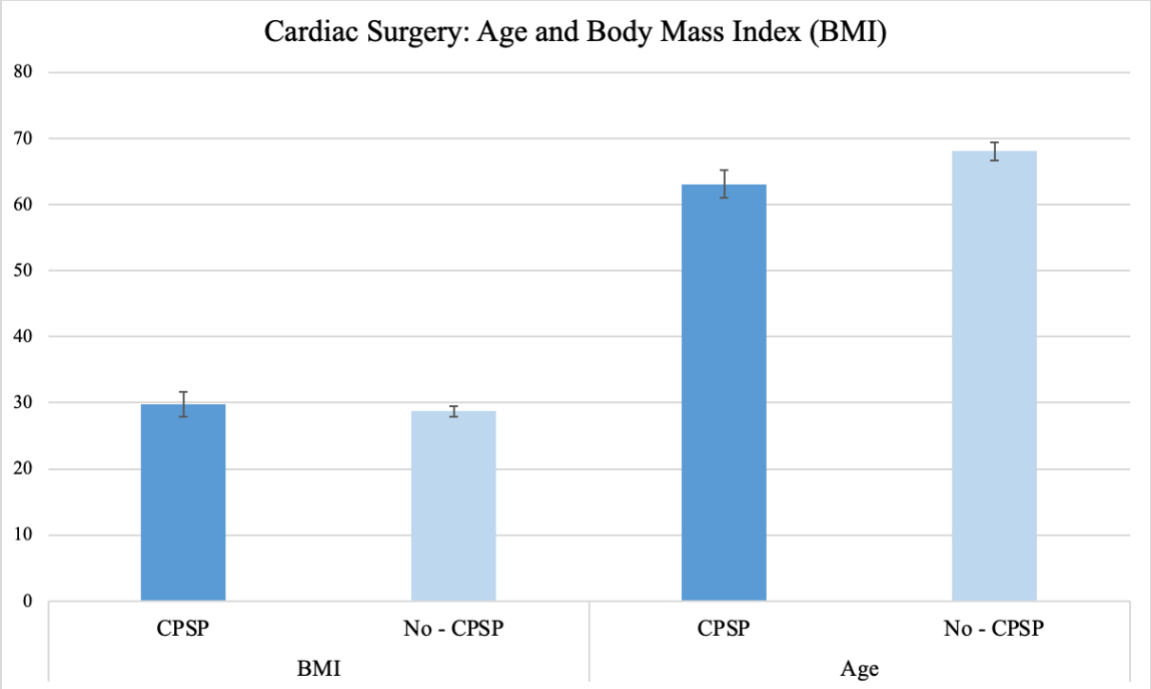

Figure 5: BMI and Age-related effects comparing the CPSP and No CPSP groups (Cardiac). In this analysis, the CPSP group on average had a slightly higher BMI value (29.8) and lower age range (63.1) compared to the No CPSP groups BMI (28.7) and age (68). Error bars indicate SEM for each variable.

Pre-existing Conditions:

Overall, patients with CPSP had a higher incidence rate in two of the variables looking at preexisting conditions and was equal to the No CPSP group for one of the variables. Prior to the surgical procedure, a psychiatric disorder was diagnosed in 9% of the patients who later developed CPSP and in 23% of the patients with No CPSP. All the patients (100%) in both the CPSP and No CPSP group had been diagnosed with a previous cardiovascular abnormality. (Figure 6) Among the patients with CPSP, 18% had a previous cancer diagnosis, whereas 26% of the patients with No CPSP had a prior cancer diagnosis. Previous reports of pain were reported in 73% of the patients with CPSP and in 62% of those with No CPSP. Lastly, 73% of patients with CPSP had a previous surgical procedure and the value slightly decreased to 69% in the No CPSP group. (Figure 6)

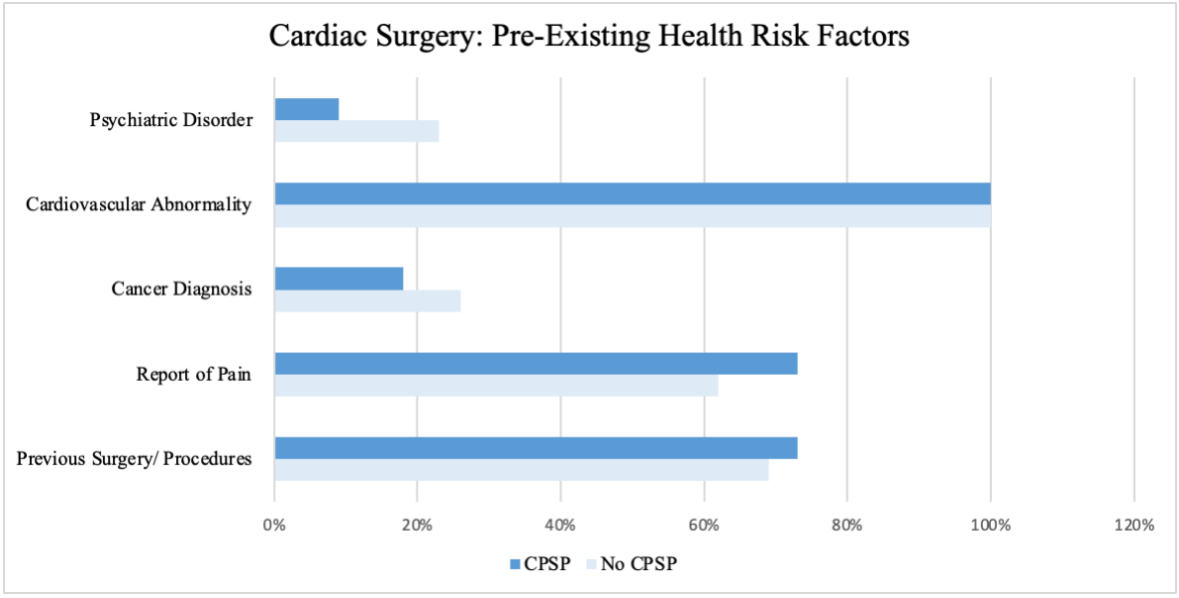

Figure 6: Prevalence (%) of the preexisting risk factors in the Cardiac Surgical Group. This analysis compared preexisting conditions for CPSP and No CPSP patients. Each variable was totaled and divided by the total number of patients in their respective group; CPSP (n= 11) and no CPSP (n=39). This figure shows that the CPSP group has a higher prevalence rate for two out of the five variables. The CPSP and No CPSP group had the same prevalence rate for cardiovascular abnormalities.

A chi-square test of independence showed that the proportion of patients with CPSP or No CPSP after cardiac surgery did not statistically differ based on premorbid conditions. (Table 4) Additionally, comparing the total number of pre-existing conditions per patient between the two groups showed no notable difference (t (48) = 0.22, p=0.826, Cohen's d=0.078). (Figure 7)

Table 4: Results of Chi-square test of independence for the Cardiac Surgical Group. The chi-square value (χ^2) and p value are used to evaluate the relationship between CPSP incidence and premorbid factors.

Variable	χ^2 (1,50)	P value
Sex	1.943	0.163
Previous Surgery	0.466	0.494
Prior Pain	0.050	0.823
Cancer Diagnosis	0.216	0.608
Psychiatric Conditions	0.634	0.425

*Prior cardiovascular abnormalities were not compared as it is expected to be present across all patients undergoing cardiac surgery.

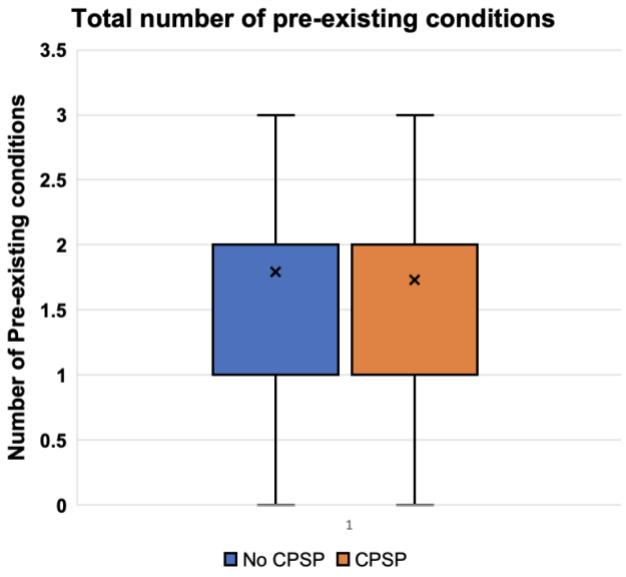

Figure 7: Box whisker plot showing the total number of pre-existing conditions in the CPSP and No CPSP groups (Cardiac). Independent sample t-tests comparing the two groups showed no notable differences (t (48) = 0.22, p=0.826, Cohen's d=0.078).

Surgical Factors:

The surgical duration for patients who reported CPSP was 301.5 ± 135.6 minutes and 286.5 ± 92.7 minutes for those with No CPSP. An independent sample t-test comparing the two groups showed no significant differences (t (48) = -0.426, p=0.671, Cohen's d=0.1). The preoperative and postoperative pain scores for individuals with CPSP was 2.9 ± 2.5 and 3.3 ± 3.2, respectively. The preoperative pain score for individuals with No CPSP was 1.7 ± 2.1 and the postoperative pain score was 1.8 ± 2.2. (Figure 8) There were no statistically significant differences between the two groups based on pre-operative pain levels (t (48) = -1.61, p=0.112, Cohen's d=0.46 (Medium effect)) and post-operative pain levels (t (48) = -1.73, p=0.08, Cohen's d=0.499 (Medium effect)). However, the greater pain in the CPSP group, when compared to the No CPSP group, had a Cohen's d >0.45, suggestive of a medium effect.

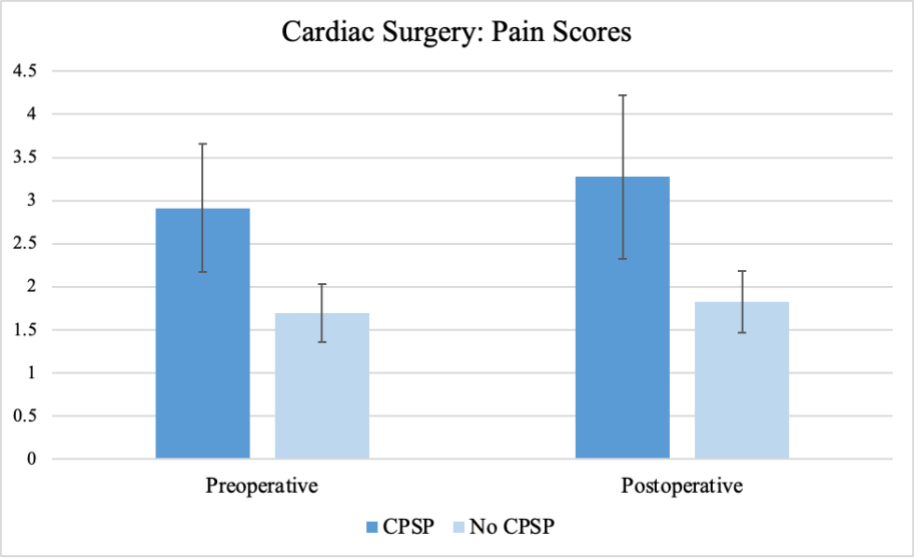

Figure 8: Average preoperative and postoperative pain scores (Cardiac). On average the CPSP group had higher preoperative (2.9) and postoperative pain scores (3.3) compared to the No CPSP groups preoperative (1.7) and postoperative (1.8) pain scores. Error bars indicate SEM for each variable.

DISCUSSION

The effects of CPSP have been extensively examined across a multitude of different surgical procedures. However, the influence of specific variables remains largely unexplored. Thus, the purpose of this analysis was to further evaluate the incidence of CPSP based on several variables following a hernia and cardiac surgical procedure. This retrospective chart review has shed light on this relationship by exploring three different potential factors (demographic, preexisting health conditions and surgical factors) that may contribute to the development of CPSP or No CPSP.

Hernia Surgical Group

Demographic comparisons between the CPSP and No CPSP groups revealed no substantial differences in age or BMI which was further supported by statistical analysis indicating insignificance between the two groups. Contrary to initial hypothesis and existing literature which suggests a correlation between advanced age and higher BMI incidence, the findings in this analysis of hernia surgical patients challenges these assumptions. Thus, suggesting that while BMI and age are often considered risk factors for CPSP, they may not be a measure that can predict a patient's postsurgical outcome and risk of developing CPSP.

In general, when evaluating preexisting conditions, the prevalence rates (%) for the preexisting pain, surgical, cardiovascular and cancer variables were greater in the CPSP group than in the No CPSP group even though, further analysis proved these relationships to be insignificant. Specifically, despite statistical insignificance, the observed odds ratio of 4.1 in the hernia surgical group underscores a potential association

between cancer history and CPSP development, emphasizing the urgency for heightened vigilance in patients who have previous malignancies undergoing further surgical intervention. Research has found evidence suggesting that chronic inflammation is associated with many health conditions including cancer progression and is defined “by sustained tissue damage, damage-induced cellular proliferation, and tissue repair.” (Singh et al., 2019) Thus, when patients undergo subsequent procedures such as a hernia repair their inflammation symptoms may become heightened as nerve damage during surgery often induces nociceptor nerve fibers and inflammatory systems leading to both peripheral and central sensitization increasing their susceptibility for CPSP. (Borsook et al., 2013)

As hypothesized, when analyzing the total number of preexisting conditions per patient between the CPSP and No CPSP group there was a statistical significance. Suggesting, that patients with three or more prior conditions are at 6.2 times increased odds of developing CPSP than those without these conditions. While considering the preexisting conditions on an individual basis showed no significant effects this data showed that the more preexisting medical conditions an individual has the higher the probability, they will develop CPSP. This underscores the importance of all patients undergoing a comprehensive preoperative assessment to identify high risk patients (that have three or more of these preexisting conditions) and implement preoperative and postoperative interventions to mitigate CPSP risk.

An intriguing finding in the hernia surgical group was the longer average surgical duration among the CPSP group compared to the No CPSP group. Notably, on average

the over 15-minute long disparity in surgical duration between the two groups highlights the impact of prolonged surgical procedures on CPSP development. Although, statistical significance was not attained $p>0.05$ ($p=1.70$), by excluding two suspected outliers the Cohen's d effect size showed a medium effect $d>0.45$ ($d=0.68$), indicating a potential clinical relevance. This underlines the need for adequate perioperative pain management as some patients may require enhanced anesthetic and analgesic control due to the nature of surgery, longer durations of surgery, increased risk of sensitization, or a combination of all the above. Perhaps, the deployment of objective pain assessments using brain imaging or autonomic measures may supplement existing clinical proxies of pain and enable the ability to provide precision analgesia.

Hyperalgesia, which is a postsurgical factor leading to an "increased painful sensation caused by a noxious stimulus" is indicative of nerve damage during the surgical procedure. (Rosenberger & Pogatzki-Zahn, 2022) Furthermore, opioids used during surgical procedures, such as fentanyl, morphine, and hydromorphone, can produce certain effects on the brain, increasing neuropathic pain due to an increase in hyperalgesia. (Borsook et al., 2013) This suggests that a longer surgical duration may be the contributing factor to increased nerve damage and greater acute postoperative pain. Additionally, the continues pain signaling that occurs during the postoperative stage (hyperalgesia) may initially act as a protective mechanism, however, due to a cascade of changes in the brain, immune system, etc., along with other risk factors, it may cause pain to persist for a period longer than normal leading to patients developing CPSP. Hence, in

accordance with our hypothesis, this relationship supports that longer surgical procedures may lead to greater risk of CPSP development.

Cardiac Surgical Group

The statistical analysis conducted for the cardiac surgical group revealed that variables such as BMI and sex had no significant effects between the CPSP and No CPSP group. Like the hernia surgical group, these data findings go against our original hypothesis and may suggest the importance of emphasizing the other variables to determine the risk factors of CPSP. However, the average age was slightly higher by about 5 years in the No CPSP group compared to the CPSP group. Nevertheless, the observed p value of 0.163 indicated that these results were not statistically significant, suggesting that age may not be a decisive factor in CPSP incidence.

Exploration of preexisting conditions among the cardiac surgical group revealed consistent trends. While previous reports of pain and prior surgical intervention exhibited greater prevalence in the CPSP group than in the No CPSP group, statistical analysis failed to show significance. Most notably, unlike the hernia surgical group, the total number of preexisting conditions per patient was similar between the CPSP and No CPSP group suggesting no significance. Though this analysis goes against the original hypothesis and data collected from the hernia surgical group, it may contribute to the understanding that different factors may have a greater or less impact in the development of CPSP based on surgery type. This is supported by a study in 2009, that collected incidence of chronic pain across eleven different surgery types. They found that 85% of

patients following an amputation developed CPSP while the incidence decreased to 1% after a cataract surgery. (Akkaya & Ozkan, 2009)

A significant finding emerged when examining surgical factors in relation to CPSP development following a cardiac procedure. Similar to the observations in the hernia surgical group, the CPSP group exhibited an average 15 minute longer surgical duration compared to the No CPSP group, though statistical significance was not obtained ($p= 0.671$). As mentioned in the hernia surgical group analysis, longer surgical durations likely result in increased nerve injury causing greater postoperative pain and overall CPSP development.

Interestingly, while the CPSP group had a higher average pain score in the preoperative and postoperative states, there was no statistically significant differences between the CPSP and No CPSP groups ($p=0.112$ and $p=0.08$, respectively). However, Cohens d analysis revealed that both preoperative and postoperative pain levels had a medium effect size for the CPSP group compared to the No CPSP group. This suggesting that a larger sample size would be needed to accurately capture these differences in pain levels between the two groups, as they may play a key role in predicting if a patient will develop CPSP.

Both Surgical Groups

While understanding the differences between the cardiac and hernia surgical groups is crucial to determine the factors contributing to the incidence of CPSP, it is also important to compare them as a unit. Within these two surgical groups, we see that while

overall the prevalence rates for the risk factors are higher in the CPSP group than in the No CPSP group, they vary in which data prove to be statistically significant.

Several factors, such as hospital stay duration, surgical duration and greater number of preexisting conditions, are all indicative that typically cardiac procedures are much more invasive than hernia surgical procedures. On average, open-heart surgeries require a hospital stay of about four to five days, while many patients undergoing hernia surgery are discharged the same day or the following day. In our statistical analysis, we found that the average hernia surgery duration was 115.4 minutes, while the cardiac surgery duration was 293.5 minutes. This data would assume that since the invasiveness of cardiac surgical procedures is greater, than the incidence of CPSP reported would be higher in the cardiac group. However, only 22% of these patients reported CPSP while that number increased to 34% for the hernia surgical group. While this may be due to a low sample size, it is important to consider the possibility that pain is underreported for reasons such as self-treatment or the patient views pain as a natural consequence of an invasive procedure. Furthermore, while exact research has not been conducted, it can be inferred that the parts of the body affected during these procedures plays a role in the development of CPSP.

A 2022 study looked at how the effects of remifentanil administration during cardiac ablation would affect a patient's cortical hemodynamics when they are under general anesthesia. Their analyses found that during the cardiac procedure, there was brain activity unless the patients were continuously injected with the opioid, indicating that the dose of the remifentanil is what contributed to the brain's response to the painful

cardiac surgical procedure. (Karunakaran et al., 2022) When looking at our data, among the cardiac surgical group, 10 out of the 11 patients reported CPSP in the shoulder, chest, and back areas, and 5 out of the 11 patients reported CPSP in the leg and foot areas. This relationship indicates that undergoing an invasive procedure such cardiac surgery infers that there is increased surgical trauma in the brain which has its own cascade of events. As such, this is why most of the patients with CPSP in the cardiac surgical group had pain localized to regions near the site of surgical intervention. For the five patients who experienced leg pain, this is also a common co-occurrence. A study examining leg pain after a cardiac procedure found that out of 644 patients, 139 patients reported chronic chest and leg pain, while 100 reported chronic chest pain only and 86 reported leg pain only. (Bruce et al., 2003)

On the other hand, it can be inferred that during less invasive surgeries, such as the hernia surgical procedures, the impact on the brain may be reduced, and the incidence of CPSP is heightened by an increase in pre-existing health conditions, amongst other factors. This is consistent with the results found in the study, as a greater total number of preexisting conditions was correlated with an increased risk of developing CPSP. This was supported by further analysis which found that the patients with three or more prior conditions are at 6.2 times greater odds of developing CPSP than those without these conditions. On the other hand, for the cardiac surgical group, the total number of pre-existing conditions per patient was similar between the two groups and was statistically insignificant.

Ultimately, highlighting that the more invasive surgical procedures play a larger role in brain responses, and CPSP is more localized to the site of injury. In contrast, the less invasive surgical procedures have a greater incidence of CPSP when the patient has multiple presurgical comorbidities.

Limitations of the Study

There are several limitations which need to be taken into consideration when interpreting the results of this study. Firstly, data collection relied on the discretion of the examiner, which may introduce a level of subjective bias or lack of knowledge when determining the importance of certain preexisting health conditions. Although strict guidelines were implemented, minor deviations may have occurred during data collection. Additionally, the characterization of preexisting conditions, including the number and type of surgical procedures, pain localization, and cancer diagnoses, may not have been exhaustive. In the future, developing a more comprehensive analysis that considers the number of times these variables were reported (not only a yes or no) may enhance the understanding of CPSP development.

Another limitation in the study involves the reliance on self-reported pain measures in the preoperative and postoperative states, which may introduce biases. Since pain is subjective, these scores may have been skewed and could contribute to discrepancies in the data. However, this further emphasizes the importance of the development and incorporation of new devices such as fNIRS to determine pain severity more accurately and strive to find ways to mitigate the incidence of CPSP among all surgery types. Additionally, when pain is not reported in surgical history, it may be due to

the patients self-treating their symptoms or consulting with their general physician instead of with the surgeon or a pain specialist. This introduces another limitation to the study, as the compressive medical records of patients may be missing.

Most notably, the small size of the data pool for the hernia and cardiac surgical groups limits the extent of associations within these findings. Having a larger data set may establish a more predictive analysis for the effect size and significance between the variables examined and the incidence of CPSP.

Future Advancements

This retrospective chart review has provided critical analysis between the demographic, preexisting and surgical factors that may lead to the development of CPSP or No CPSP. Thus, paving the way for future research to investigate larger cohorts of patients, variables, and surgery types with the goal to change clinical practices and optimize patient outcomes. Hence, future analysis should use these preliminary findings to expand their data sets, refine their data collection methods and explore other surgical nuances.

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