

Medical Science

To Cite:

Krygowska AM, Sieradocha K, Śledziewska AM, Zagajewska A, Cyrkler M, Słupik D, Reda A, Giba A, Wąsik M. Multimodal approach in pain management in pancreatic cancer. *Medical Science* 2025; 29: e66ms3546 doi: <https://doi.org/10.54905/disssi.v29i158.e66ms3546>

Authors' Affiliation:

¹Military Institute of Medicine - National Research Institute, Szaserów 128, 04-141 Warsaw, Poland, Orcid: <https://orcid.org/0000-0002-6860-9942>; Email: amkrygowska@gmail.com

²University Clinical Hospital in Poznań, Przybyszewskiego Str. 49, 60-355 Poznań, Poland Orcid: <https://orcid.org/0009-0006-1952-0139>; Email: sieradochakamila@gmail.com

³Military Institute of Medicine - National Research Institute, Szaserów 128, 04-141 Warsaw, Poland, Orcid: <https://orcid.org/0009-0006-3782-9201>; Email: masledziewska@gmail.com

⁴Infant Jesus Clinical Hospital in Warsaw, Williama Heerleina Lindleya 4, 02-005 Warsaw, Poland, Orcid: <https://orcid.org/0009-0001-8610-0234>; Email: aleksandra.zagajewska@gmail.com

⁵Military Institute of Medicine - National Research Institute, Szaserów 128, 04-141 Warsaw, Poland, Orcid: <https://orcid.org/0009-0003-5721-6945>; Email: mcyrkler@tlen.pl

⁶Military Institute of Medicine - National Research Institute, Szaserów 128, 04-141 Warsaw, Poland, Orcid: <https://orcid.org/0009-0006-1818-2684>; Email: slupikdorota@gmail.com

⁷Military Institute of Medicine - National Research Institute, Szaserów 128, 04-141 Warsaw, Poland, Orcid: <https://orcid.org/0009-0006-2339-0568>; Email: aleksandra.reda1@gmail.com

⁸Military Institute of Medicine - National Research Institute, Szaserów 128, 04-141 Warsaw, Poland, Orcid: <https://orcid.org/0009-0003-2384-1662>; Email: giba.aleksandra99@gmail.com

⁹Military Institute of Medicine - National Research Institute, Szaserów 128, 04-141 Warsaw, Poland, Orcid: <https://orcid.org/0009-0007-8163-4265>; Email: michal.michal.w@wp.pl

*Corresponding author

Aleksandra Małgorzata Krygowska, Military Institute of Medicine - National Research Institute, Szaserów 128, 04-141 Warsaw, Poland; Email: amkrygowska@gmail.com

Peer-Review History

Received: 07 January 2025

Reviewed & Revised: 16/January/2025 to 03/May/2025

Accepted: 09 May 2025

Published: 16 May 2025

Peer-review Method

External peer-review was done through double-blind method.

Medical Science

pISSN 2321-7359; eISSN 2321-7367



© The Author(s) 2025. Open Access. This article is licensed under a [Creative Commons Attribution License 4.0 \(CC BY 4.0\)](https://creativecommons.org/licenses/by/4.0/), which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/>.



Multimodal approach in pain management in pancreatic cancer

Aleksandra Małgorzata Krygowska^{1*}, Kamila Sieradocha², Aleksandra Maria Śledziewska³, Aleksandra Zagajewska⁴, Magdalena Cyrkler⁵, Dorota Słupik⁶, Aleksandra Reda⁷, Aleksandra Giba⁸, Michał Wąsik⁹

ABSTRACT

Pancreatic cancer is often associated with significant pain, affecting approximately 75% of patients at the time of diagnosis. This type of pain is frequently the first symptom prompting medical consultation, leading to extended diagnostic pathways and ultimately resulting in delayed detection and poorer prognoses due to the formation of metastases. Managing cancer-related pain by integrating many treatment options, such as pharmacological interventions and interventional procedures, is called a multimodal approach and is being discussed in this article. Healthcare providers should coordinate the aforementioned multimodal approaches to ensure cooperation in the process and the patient's safety. Furthermore, hope remains in targeted therapies, which focus on the molecular pathways of pain signaling. There is also an opportunity for more personalized strategies that affect the microenvironment of the cancer. Implementing coordinated multimodal pain management strategies should be a caregiver's priority.

Keywords: pancreatic cancer, pain management, celiac plexus block, analgesia, multimodal therapy.

1. INTRODUCTION

Pancreatic cancer has an aggressive biology, predisposition for late-stage diagnosis, and limited therapeutic options. Therefore, it remains a big oncological challenge. In this disease, pain is a frequent and debilitating symptom. It significantly reduces the well-being and functional capacity of those afflicted. Pain is even more critical to treat due to the relatively short survival expectancy of pancreatic cancer patients. Effective pain management is also an ethical imperative due to the relatively short time of survival. This review will summarize the area of pancreatic cancer-related pain and a multimodal approach that integrates various methods like pharmacological treatments, interventional

techniques, and comprehensive support systems. This approach seems to optimize pain control and enhance patient outcomes.

Pathophysiology of Pancreatic Cancer Pain

The mechanisms underlying pain in pancreatic cancer are complex and multifactorial, involving a combination of nociceptive and neuropathic components (Lohse and Brothers, 2020). Nociceptive pain arises from the tumor mass directly invading or compressing surrounding tissues, including the pancreatic parenchyma, adjacent organs, and nerve structures (Coveler et al., 2021). This process is further exacerbated by inflammation and the release of chemical mediators, such as prostaglandins and cytokines, which sensitize peripheral pain receptors and contribute to the pain experience. Visceral pain, stemming from the internal organs, is a critical feature in pancreatic cancer due to the tumor's location. It impacts the function and anatomy of the digestive system, frequently resulting from ductal obstruction and pancreatic enzyme insufficiency.

Neuropathic pain, on the other hand, results from direct injury or dysfunction of the nerves themselves, often due to tumor invasion or compression of nerve plexuses, such as the celiac plexus (Coveler et al., 2021). This type of pain may consist of shooting, burning, or electric-like sensations and can be particularly challenging to manage with conventional analgesics (Coveler et al., 2021). The presence and severity of pain in pancreatic cancer patients are correlated with pancreatic cancer prognosis and an adverse tumor microenvironment, suggesting that a more toxic cancer environment correlates with increased nerve damage (Lohse and Brothers, 2020). The celiac plexus, which innervates the upper abdominal organs, is frequently infiltrated by tumor cells along the connective tissue nerve sheaths due to the anatomical proximity of the pancreas (Lee et al., 2021).

Perineural invasion, the infiltration of tumor cells around and within nerve fibers, is a common feature of pancreatic cancer and contributes significantly to neuropathic pain. That process leads to nerve damage, tissue remodeling, and elevated pain signaling (Lee et al., 2021). Patients often present with vague and nonspecific abdominal pain, sometimes radiating to the back, indicating involvement of retroperitoneal nerves (Lee et al., 2021). Therefore, this type of pain presentation can lead to delayed diagnosis and treatment.

Pancreatic cancer, characterized by its dismal prognosis, often presents at advanced stages, limiting resectability to a mere 12%-20% of cases upon diagnosis (Pérez-Aguado et al., 2021). Surgical resection remains the sole curative option, yet its applicability is hindered by late diagnoses and the propensity for rapid disease progression (Cheng et al., 2020). Survival statistics say that over half of affected individuals succumb to the disease within the first year, culminating in an overall five-year survival rate of less than 10% (Cheng et al., 2020).

A significant proportion of patients, approximately 75%, experience pain at the time of diagnosis, which significantly reduces their quality of life (Lohse and Brothers, 2020). Pancreatic cancer is notoriously resistant to conventional chemotherapy and radiotherapy, which means scientists need to find new treatments urgently (Kalli et al., 2022). The insidious nature of pancreatic cancer, often dubbed the "silent killer," stems from its paucity of early-stage symptoms, resulting in delayed diagnoses and compromised prognoses due to metastasis to adjacent organs (Lohse and Brothers, 2020).

Pharmacological Interventions: A Comprehensive Analysis of Analgesic Options

Pain, a frequent and debilitating symptom in advanced pancreatic cancer, afflicts 70%-90% of patients due to perineural invasion by tumor cells, necessitating intricate medical management (Lohse and Brothers, 2020; Pérez-Aguado et al., 2021). Traditional pain management protocols typically commence with non-opioid analgesics, escalating to opioids in refractory cases; however, opioids can participate in the occurrence of adverse effects, including nausea, constipation, urinary retention, and drowsiness (Pérez-Aguado et al., 2021).

Current research is hopefully unravelling the complexities of the pancreatic cancer microenvironment, particularly the dense tumor-associated stroma characterized by extracellular proteins such as collagen I and hyaluronan. Furthermore, understanding the pathogenesis of pancreatic cancer has revealed potential targets for effective therapy, including metabolic inhibitors or antimetabolites, which have been part of cancer therapy for over five decades (Gupta et al., 2021). Recent findings suggest that pancreatic stellate cells secrete increased levels of exosomes containing inflammatory cytokines and active proteins that contribute to the tumor's resistance to gemcitabine.

Interventional Pain Management Techniques: Advanced Approaches for Targeted Pain Relief

Interventional pain management techniques offer targeted approaches to alleviate pain in pancreatic cancer patients when conventional analgesics prove insufficient. Celiac plexus neurolysis involves the injection of neurolytic agents, such as alcohol or phenol, into the celiac plexus to disrupt pain signals (Al-Jumah et al., 2020). This procedure can provide pain relief, reduce opioid consumption, and improve life quality for patients with abdominal malignancies. Early celiac plexus neurolysis has demonstrated superior pain control and reduced opioid requirements compared to delayed intervention. Furthermore, studies suggest that pre-emptive celiac plexus neurolysis, performed before significant pain escalation, may prevent the establishment of chronic pain pathways and improve long-term outcomes.

Endoscopic ultrasound-guided celiac plexus neurolysis enables precise visualization and targeting of the celiac plexus, thereby minimizing the risk of complications. Celiac plexus radiotherapy is a novel approach that utilizes a single, precisely targeted high dose of stereotactic ablative radiotherapy aimed at the celiac plexus. This treatment targets the entire length of the affected nerves, rather than just a specific area, to provide patients with more effective pain relief (Lawrence et al., 2024).

Modulation of the Tumor Microenvironment

The tumor microenvironment significantly contributes to cancer progression and pain development. To influence the course of symptoms and disease development, one must modulate its composition and signalling pathways. Targeting the stroma surrounding pancreatic cancer cells, which promotes tumor growth and hinders the delivery of drugs, is under intensive investigation (Coveler et al., 2021). Agents that disrupt stromal elements, such as hyaluronan and collagen, can improve the penetration of chemotherapeutic drugs. Additionally, strategies that hold promise for enhancing the efficacy of the treatment are methods that inhibit cancer-associated fibroblasts, which contribute to stromal remodelling and immunosuppression. Modulating the tumor microenvironment to enhance immune responses against cancer cells remains an area of active research.

The management of pain in pancreatic cancer requires a multidisciplinary approach, integrating interventional techniques, pharmacology, and modulation of the tumor microenvironment (Lee et al., 2021). Ultimately, doctors should integrate an overall pain management strategy also to address other symptoms like bleeding, jaundice, and gastrointestinal system obstruction. Further research should identify novel therapeutic targets that can revolutionize the treatment landscape for pancreatic cancer and alleviate the suffering of those affected by cancer (Lee et al., 2021). Microenvironment normalization represents a promising avenue, with agents like losartan showing potential in clinical trials by targeting the transforming growth factor beta pathway (Kalli et al., 2021).

Complementary approach

A holistic approach in modern-day medicine also includes physical therapy, psychological consultations, and lifestyle modifications. Conventional treatments sometimes have their limitations, and the need for improved patient outcomes has spurred the exploration of alternative and complementary therapies, including herbal medicines, acupuncture, and mind-body techniques. Some studies suggest benefits of specific herbal formulations to alleviate cancer-related pain. Identifying novel pain mitigation strategies that minimize adverse effects and enhance the quality of life for pancreatic cancer patients (Lee et al., 2021).

The role of healthcare professionals in recognizing, understanding, and treating cancer-associated pain through education and skill acquisition is pivotal (Damm et al., 2020). Palliative care approaches should be integrated early in the disease trajectory to address pain and other distressing symptoms. Moreover, the aggressive nature of pancreatic cancer, combined with advanced patient age and intensive treatment regimens, makes pain management particularly challenging (Lohse and Brothers, 2020).

Pancreatic cancer-related pain is commonly managed pharmaceutically with analgesics, opioids, and anti-inflammatory drugs, but these can have serious side effects (Lohse and Brothers, 2020). Developing targeted therapies that address the molecular pathways implicated in pain signalling holds promise for more effective and personalized pain management strategies. The presence and severity of pain in pancreatic cancer patients exhibit a strong correlation with prognosis and an adverse tumor microenvironment, implying that a more toxic cancer environment is associated with increased nerve damage (Lohse and Brothers, 2020). Addressing the underlying causes of pain in pancreatic cancer patients is crucial, given that current treatments often exacerbate pain and rely almost exclusively on opioids, which have significant side effects (Lohse and Brothers, 2020).

Nurses in palliative care can make medications more accessible on demand and stay up-to-date on treatments and symptom management. A multidisciplinary team for managing pancreatic cancer pain can coordinate medical interventions, interventional procedures, and psychosocial support (Lee et al., 2021).

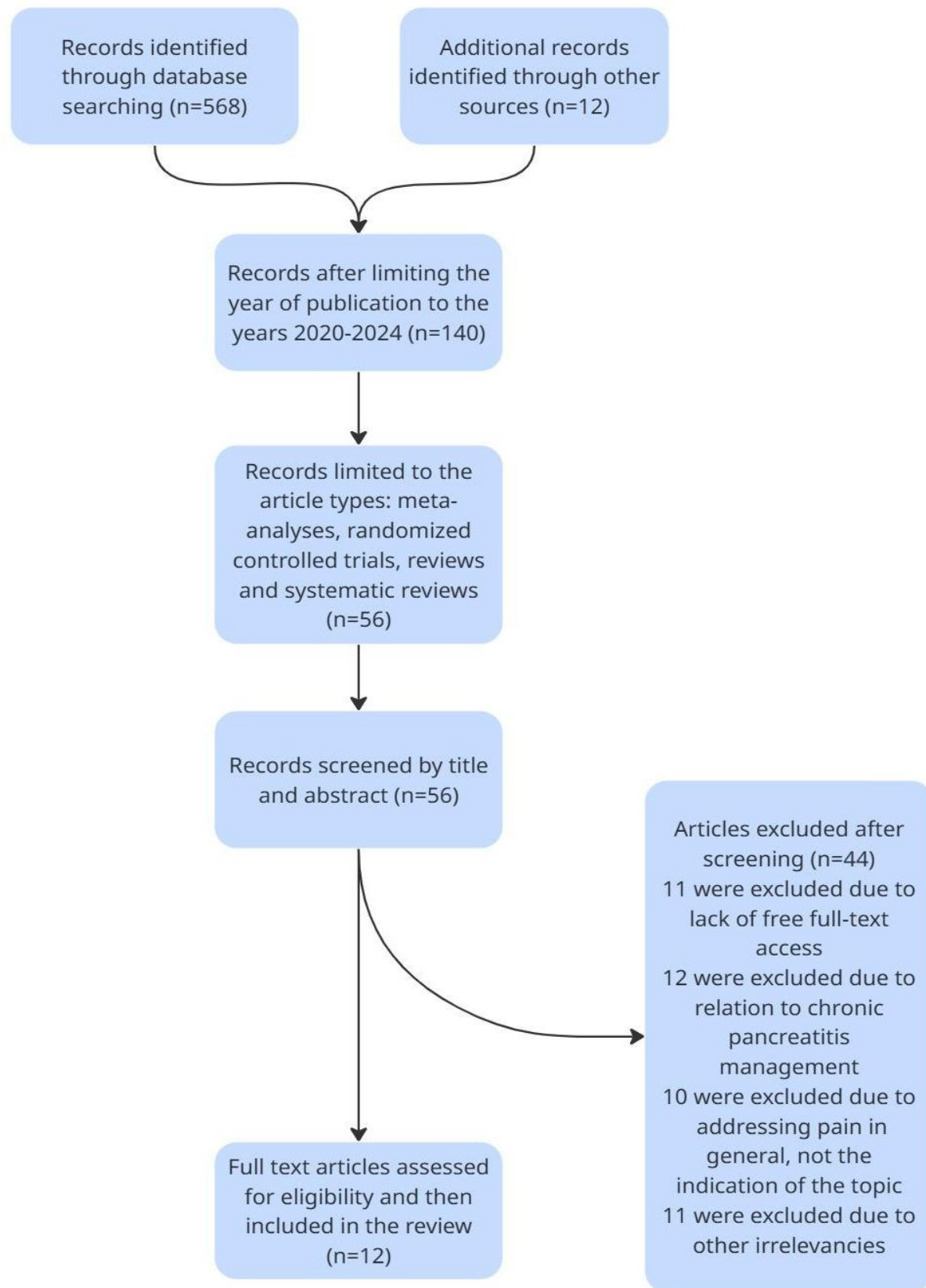


Figure 1: Summary of the research and the processing of information

Furthermore, chronic pancreatic pain is associated with impairment not only of physical, but also mental health, leading to a higher prevalence of depression, anxiety, sleep disturbance, and physical disability (Nicoletti et al., 2024). Ultimately, a multifaceted approach that combines analgesics, nerve blocks, and potentially tumor-modifying therapies may offer the best hope for comprehensive pain relief and improved quality of life for pancreatic cancer patients (Lohse and Brothers, 2020).

In certain instances where the pain is intractable and all other measures have failed, a last resort to alleviate the pain can be a palliative sedation that helps minimize suffering in the late stages of the disease (Surges et al., 2024). In resource-constrained environments, numerous cancer patients receive care from healthcare professionals who may lack the necessary pain assessment skills because their training did not include palliative care.

Further research is needed to complete the limited data on pain management in pancreatic cancer and optimize treatment strategies and improve patient outcomes (Coveler et al., 2021). The complex and multifactorial pathophysiology of pain in pancreatic cancer highlights the importance of comprehensive pain management to influence life quality and survival (Coveler et al., 2021). Comprehensive pain management programs integrating pharmacological, interventional, and psychosocial modalities can enhance pain relief and improve overall well-being (Coveler et al., 2021).

2. METHODOLOGY

The search used the medical database PubMed. The following keywords were used to find relevant articles: ("Pancreatic Cancer" OR "Pancreatic Neoplasms") AND ("Pain Management" OR "Pain Relief"). The articles included in the research were Clinical Trial, Meta-Analysis, Review, Systematic Review, and Multicentre Study. The publication range was limited to the years 2020 to 2024. In the beginning, 56 articles were identified that met the criteria. After further analysis based on relevance and quality, 12 articles were chosen for inclusion. Figure 1 provides a summary of the research and the processing of information. Based on the obtained strategy, the most important literature in this field was identified using the authors' expertise on the subject of cancer and the quality of life associated with the disease.

3. RESULTS AND DISCUSSION

"Multimodal" encompasses more than just medical and interventional techniques. Psychological interventions, physical therapy, and complementary and alternative medicine can play a role (Coveler et al., 2021). The use of a multimodal approach, including pharmacological interventions, nerve blocks, and psychological support, has demonstrated promising outcomes for individuals who have pancreatic cancer, such as:

Pharmacological Interventions: This includes opioids, non-opioid analgesics (like NSAIDs and acetaminophen), adjuvant medications (such as antidepressants and anticonvulsants for neuropathic pain), and corticosteroids to reduce inflammation and nerve compression.

Interventional Procedures: Celiac plexus neurolysis, splanchnic nerve blocks, and radiofrequency ablation can disrupt pain signals transmitted through nerves in the abdomen (Al-Jumah et al., 2020). Discuss these techniques. EUS-guided CPN has been reported in (Pérez-Aguado et al., 2021).

Psychological Support

Psychological support allows patients to cope with the emotional burden of their diagnosis and the challenges of living with chronic pain. Cognitive Behavioral Therapy: CBT helps in identifying and changing negative thought patterns that are a product of pain and distress. It equips patients with coping mechanisms to manage pain flare-ups, reduce anxiety and depression, and improve sleep quality. Mindfulness and Relaxation techniques can help patients reduce muscle tension and improve their overall sense of well-being. Support Groups and Counselling: Connecting with other patients who face similar misery can offer emotional support and alleviate feelings of isolation. Individual counselling can address specific emotional and psychological needs. These can be beneficial to the patient, as psychological well-being is usually not included in the treatment roadmap for pain management. Table 1 provides a visual summary of the main conclusions regarding multimodal pain management.

Table 1: Summary of multimodal pain management strategies in pancreatic cancer

Category	Key summary points
Multimodal approach	Combines pharmacological, interventional, psychological, physical therapy, and complementary therapies for improved pain management in pancreatic cancer. Targets multiple pain pathways, potentially leading to better relief than single modalities. It can decrease opioid use and associated side effects. Enhances overall quality of life by addressing physical, emotional, and functional aspects of pain.
Interventional techniques	Celiac Plexus Neurolysis (CPN): Injection of neurolytic agents into the celiac plexus to disrupt pain signals. EUS-guided CPN offers improved precision. Splanchnic Nerve Blocks: Temporary injection of local anesthetics near splanchnic nerves to block pain; can be diagnostic. Radiofrequency Ablation (RFA): Uses heat to damage pain-transmitting nerve fibers.
Psychological support	Crucial for coping with emotional burden and chronic pain. Cognitive Behavioral Therapy helps change negative thought patterns and develop coping mechanisms. Mindfulness and relaxation techniques reduce tension and improve well-being. Support groups and counseling offer emotional support and address specific needs. Often overlooked in traditional pain management.
Challenges in pain management	Despite multimodal approaches, optimizing pain control remains challenging. Pain may persist even with tumor response to chemotherapy. Lack of specific treatment guidelines and side effects of available treatments limit options. Undertreatment of cancer pain is widespread due to regulatory barriers, knowledge deficits, poor communication, and negative attitudes toward opioids. Inadequate pain control is linked to poorer clinical outcomes.
Importance of effective pain management	Essential for patient care, as pain significantly lowers quality of life and can impact overall survival in pancreatic cancer. Requires considering both biological and psychological factors. A coordinated effort among stakeholders is necessary to ensure optimal pain and symptom control.
Future directions	Future research should focus on identifying more therapeutic targets and developing innovative pain management strategies for pancreatic cancer. Epigenetic modulation shows potential as a new avenue for pain management.

Physical Therapy and Rehabilitation: Exercise, stretching, and other physical therapy modalities can improve mobility and reduce muscle tension. *Complementary and Alternative Medicine:* Some patients find relief through acupuncture, massage, and complementary and alternative medicine therapies. However, more research is needed to establish their effectiveness (Coveler et al., 2021).

By a multimodal approach, one can obtain:

Improved pain control by combining many different modalities allows targeting multiple pain pathways and potentially leads to better pain relief than any single approach used individually. The need for a multidisciplinary approach is vast due to the limited treatment options.

By addressing pain through multiple mechanisms, caregivers can decrease opioid use and therefore minimize the risk of side effects like constipation, nausea, and dependence (Gupta et al., 2021). Enhanced quality of life is achieved through a multimodal approach that improves patients' overall well-being by targeting physical, emotional, and functional aspects of pain. These findings underscore the effectiveness of multimodal approaches; however, several challenges remain in optimizing pain management for pancreatic cancer. Although tumor response to chemotherapy may occur, pain control may still be necessary (Coveler et al., 2021). There are still areas in the treatment of pain associated with pancreatic cancer that need further investigation. Future research should focus on identifying more therapeutic targets and developing innovative strategies to improve pain management in pancreatic cancer (Coveler et al., 2021).

Effective cancer pain management is essential to patient care, as pain significantly lowers quality of life, and overall survival in pancreatic cancer patients is often short; therefore, efficient pain treatment is necessary (Coveler et al., 2021; Nicoletti et al., 2024). Effective pain management also requires considering biological and psychological factors. Unfortunately, medical management alone often fails to alleviate chronic pain or improve the emotional impacts and disability that come with it. The undertreatment of cancer pain is a widespread issue that has many contributing factors, including, but not limited to, regulatory barriers, knowledge deficits, poor communication, and negative attitudes toward opioid use.

Inadequate pain control is significant not only for its adverse effects on patient mood, function, and quality of life but also for its correlation with poor clinical outcomes, including higher overall mortality (Coveler et al., 2021). A coordinated effort involving many stakeholders, like government agencies, regulatory bodies, educational institutions, patients, and healthcare professionals, is necessary to ensure that all patients suffering from pain receive appropriate therapies to achieve and maintain optimal pain and symptom control. The absence of specific treatment guidelines and the side effects associated with available treatments limit pain management options for effective pancreatic cancer pain treatment (Lohse and Brothers, 2020).

Recent research suggests that modifications to the epigenome play a role in developing acute and chronic pain, indicating that epigenetic modulation could offer a new avenue for pain management in pancreatic cancer (Lohse and Brothers, 2020).

4. CONCLUSIONS

The real key is individualization. What works best for one patient may not work for another. Developing clear clinical guidelines and improved assessment tools to tailor multimodal strategies to individual cases is the next step toward maximizing pain management effectiveness in pancreatic cancer. A proper pain management is crucial for the quality of life and even the survival of cancer patients. The study has demonstrated that a multimodal approach can improve well-being through pain relief. Psychological interventions empower patients to participate in managing their illness. Adding behavioral and environmental management strategies to the treatment plan of a patient with chronic pain has been demonstrated to improve functional outcomes.

Proper pain management is crucial, given the short life expectancy of pancreatic cancer patients. The use of percutaneous image-guided celiac plexus block and neurolysis as part of a multimodal approach can help decrease pain, improve function, and reduce opiate dependence in patients with abdominal malignancy. Celiac plexus neurolysis can provide pain relief to a significant percentage of people living with cancer. The issue of cancer pain is complex, encompassing medical, legal, moral, and ethical dimensions.

Acknowledgments

Not applicable

Author's Contribution:

Aleksandra Krygowska: Conceptualization, Investigation, Writing - review and edition, Supervision

Aleksandra Maria Śledziowska: Methodology, Resources, Writing - review and edition

Aleksandra Giba: Conceptualization, Resources, Investigation

Aleksandra Zagajewska: Methodology, Conceptualization, Writing - rough preparation

Magdalena Cyrkler: Formal analysis, Supervision

Dorota Szupik: Resources, Investigation, Writing - rough preparation

Aleksandra Reda: Methodology, Resources, Writing - rough preparation
 Michał Wąsik: Methodology, Writing - rough preparation
 Kamila Sieradocha: Formal analysis, Data curation, Writing - review and edition
 All authors have read and agreed with the published version of the manuscript.

Informed Consent

Not applicable.

Ethical approval

Not applicable.

Funding

This study has not received any external funding.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES

- Lohse I, Brothers SP. Pathogenesis and treatment of pancreatic cancer related pain. *Anticancer Res.* 2020;40(4):1789–96. doi: 10.21873/anticancer.14133
- Coveler AL, Mizrahi J, Eastman B, Apisarnthanarax SJ, Dalal S, McNearney T, Pant S, Precision Promise Consortium. Pancreas cancer-associated pain management. *Oncologist.* 2021;26(6):e971–82. doi: 10.1002/onco.13796
- Lee KG, Roy V, Laszlo M, Atkins KM, Lin KJ, Tomassian S, Hendifar AE. Symptom management in pancreatic cancer. *Curr Treat Options Oncol.* 2021;22(1):8. doi: 10.1007/s11864-020-00801-4
- Pérez-Aguado G, de la Mata DM-A, Valenciano CM-L, Sainz IF-U. Endoscopic ultrasonography-guided celiac plexus neurolysis in patients with unresectable pancreatic cancer: An update. *World J Gastrointest Endosc.* 2021;13(10):460–72. doi: 10.4253/wjge.v13.i10.460
- Cheng B, Wang Q, Song Y, Liu Yanna, Liu Yanyan, Yang S, Li D, Zhang Y, Zhu C. MIF inhibitor, ISO-1, attenuates human pancreatic cancer cell proliferation, migration and invasion in vitro, and suppresses xenograft tumour growth in vivo. *Sci Rep.* 2020;10(1):6741. doi: 10.1038/s41598-020-63778-y
- Kalli M, Li R, Mills GB, Stylianopoulos T, Zervantonakis IK. Mechanical stress signaling in pancreatic cancer cells triggers p38 MAPK- and JNK-dependent cytoskeleton remodeling and promotes cell migration via Rac1/cdc42/myosin II. *Mol Cancer Res.* 2022;20(3):485–97. doi: 10.1158/1541-7786.MCR-21-0266
- Gupta VK, Banerjee S, Saluja AK. New pharmacological approaches for pancreatic cancer therapy: A light at the end of the tunnel?. *Clinical Pancreatolgy for Practising Gastroenterologists and Surgeons.* Wiley; 2021; 564–72. doi: 10.1002/9781119570097.ch69
- Lawrence YR, Miszczyk M, Dawson LA, Diaz Pardo DA, Aguiar A, Limon D, Pfeffer RM, Buckstein M, Barry AS, Meron T, Dicker AP, Wydmański J, Zimmermann C, Margalit O, Hausner D, Morag O, Golan T, Jacobson G, Dubinski S, Stanescu T, Fluss R, Freedman LS, Ben-Ayun M, Symon Z. Celiac plexus radiosurgery for pain management in advanced cancer: a multicentre, single-arm, phase 2 trial. *Lancet Oncol.* 2024;25(8):1070–9. doi: 10.1016/S1470-2045(24)00223-7
- Nicoletti A, Vitale F, Paratore M, Quero G, Negri M, Nista EC, Alfieri S, Gasbarrini A, Zileri Dal Verme L. Neuropancreatolgy: The nervous system and pain management in pancreatic diseases. *Life (Basel).* 2024;14(3):299. doi: 10.3390/life14030299
- Surges SM, Brunsch H, Jaspers B, Apostolidis K, Cardone A, Centeno C, Cherny N, Csikós À, Fainsinger R, Garralda E, Ling J, Menten J, Mercadante S, Mosoiu D, Payne S, Preston N, Van den Block L, Hasselaar J, Radbruch L, Revised European Association for Palliative Care (EAPC) recommended framework on palliative sedation: An international Delphi study. *Palliat Med.* 2024;38(2):213–28. doi: 10.1177/02692163231220225

11. Al-Jumah R, Urits I, Viswanath O, Kaye AD, Hasoon J. Radiofrequency ablation and alcohol neurolysis of the splanchnic nerves for a patient with abdominal pain from pancreatic cancer. *Cureus*. 2020;12(10):e10758. doi: 10.7759/cureus.10758
12. Damm M, Weniger M, Kölsch A-K, Lampert C, Ceyhan GO, Beer S, Schorn S, Moir J, Michl P, Rosendahl J. The quality of pain management in pancreatic cancer: A prospective multi-center study. *Pancreatology*. 2020;20(7):1511–8. doi: 10.1016/j.pan.2020.08.017