



ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ
ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ
ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ

ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ
«ΚΑΡΚΙΝΟΣ ΠΑΓΚΡΕΑΤΟΣ-από το Α ως το Ω»



Μεταπτυχιακή Διπλωματική Εργασία

***"Patient-Reported Outcome measures (PROMS) και
συμμόρφωση στα πρωτόκολλα Enhanced Recovery After
Surgery (ERAS) στην παγκρεατική χειρουργική"***

υπό

ΜΑΡΙΑΣ ΠΙΤΣΙΑΚΑΣ

Ειδικευόμενη Γενικής Χειρουργικής

Υπεβλήθη για την εκπλήρωση μέρους των
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Διπλώματος Μεταπτυχιακών Σπουδών
«ΚΑΡΚΙΝΟΣ ΠΑΓΚΡΕΑΤΟΣ-από το Α ως το Ω»

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Postgraduate Dissertation

***" Patient-Reported Outcome measures (PROMS) and
compliance to Enhanced Recovery After Surgery (ERAS)
protocols in pancreatic surgery"***

under

MARIA PITSILKA

Resident in General Surgery

Submitted in partial fulfillment of the
requirements for the attainment
of the Master's Diploma
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ΕΥΧΑΡΙΣΤΙΕΣ

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«...Πόσο μεγάλο γίνεται το τώρα, όταν με πάθος αγωνίζεσαι για το μετά;
Πόσο βαριά γίνεται η γραφίδα, όταν της ιστορίας μου τις μελλοντικές σελίδες γράφει;
Τώρα ξέρω, πως για να χτίσω της χαράς τη μέθη, πρέπει τον εαυτό μου να υποτάξω
στον ονείρου τη δύσβατη πορεία.
Πράξη πρώτη, πράξη ηρωική, απόσταγμα μιας δυνατής πορείας.»

Σαραϊλίδης Κώστας

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Περίληψη

Εισαγωγή

Σε σύγκριση με τα κλινικά αποτελέσματα φροντίδας, υπάρχει σημαντικά λιγότερη πληροφορία σχετικά με τα αποτελέσματα που αναφέρουν οι ίδιοι οι ασθενείς (PROs), όπως η ποιότητα ζωής, η συνολική υγεία και η λειτουργική κατάσταση, όπως αυτά βιώνονται και αναφέρονται από ασθενείς που υποβάλλονται σε ανοιχτή παγκρεατοδωδεκαδακτυλεκτομή (PD). Η μελέτη μας έχει ως σκοπό την αξιολόγηση της επιρροής των ποσοστών συμμόρφωσης στο πρόγραμμα ERAS στα αποτελέσματα που αναφέρουν οι ασθενείς.

Μεθοδολογία

Αυτή η προοπτική παρατηρητική μελέτη περιλαμβάνει ασθενείς που υποβλήθηκαν σε εκλεκτική ανοιχτή PD σε δύο κέντρα υψηλού όγκου καρκίνου στη κεντρική Ελλάδα. Όλοι οι ασθενείς ακολούθησαν ένα τυποποιημένο πρωτόκολλο ERAS. Τα Μέτρα Αποτελεσμάτων που Αναφέρουν οι Ασθενείς (PROMs), συγκεκριμένα το Ερωτηματολόγιο Υγείας EORTC QLQ-C30, χορηγήθηκαν έως και έξι μήνες μετά την επέμβαση. Συλλέχθηκαν δεδομένα σχετικά με τα PROMs, τη συμμόρφωση στο πρωτόκολλο ERAS και τα αποτελέσματα των ασθενών.

Αποτελέσματα

Τα δεδομένα μας δείχνουν μια πιθανή συσχέτιση μεταξύ των ποσοστών συμμόρφωσης στο ERAS και της Ποιότητας Ζωής (QoL). Τα ευρήματά μας υποδεικνύουν ότι υψηλότερα ποσοστά συμμόρφωσης σχετίζονται με καλύτερη ποιότητα ζωής στην 5η μετεγχειρητική ημέρα ($r=0.569$, $p<0.001$), στο πρώτο εξωτερικό ραντεβού ($r=0.24$, $p=0.039$) και στους έξι μήνες μετά την επέμβαση ($r=0.349$, $p=0.004$).

Συμπεράσματα

Ενώ αρκετές μελέτες έχουν αξιολογήσει την επίδραση της συμμόρφωσης στο ERAS στα κλινικά αποτελέσματα, καμία δεν έχει εξετάσει αν η συμμόρφωση στο ERAS επηρεάζει την ποιότητα ζωής όπως μετράται μέσω των PROMs. Η παρούσα μελέτη φαίνεται να είναι η πρώτη που δείχνει ότι υψηλότερα ποσοστά συμμόρφωσης στις αρχές ERAS βελτιώνουν την ποιότητα ζωής των ασθενών που υποβάλλονται σε ανοιχτή PD. Η μελέτη μας αναδεικνύει τις παραμέτρους που έχουν τη μεγαλύτερη σημασία για τους ασθενείς και συμβάλλει στην τεκμηρίωση που υποστηρίζει την εφαρμογή περιεγχειρητικών στρατηγικών για τη βελτίωση της εμπειρίας των ασθενών.

Λέξεις-κλειδιά: αποτελέσματα που αναφέρουν οι ασθενείς, ενισχυμένη ανάρρωση μετά από χειρουργική, παγκρεατοδωδεκαδακτυλεκτομή, ποιότητα ζωής

Abstract

Introduction

Compared to clinical care outcomes, there is significantly less information on patient-reported outcomes (PROs), such as quality of life, overall health, and functional status as experienced and reported by patients who undergo open pancreatoduodenectomy (PD). Our study aims to assess how PROs are affected by compliance rate to ERAS.

Methodology

This prospective observational study includes people that underwent elective open pancreatoduodenectomy at two high-volume cancer centers in central Greece. All patients followed a standardized ERAS pathway. Patient-reported outcome Measures (PROMs), specifically the EORTC QLQ-C30 Health Questionnaire, were administered up to six months post-operation. We collected data on PROMs, ERAS protocol compliance, and patient outcomes.

Results

Our data show a potential association between ERAS compliance rates and Quality of Life (QoL). Our findings indicate that higher adherence rates correlate with better QoL on postoperative day 5 ($r=0.569$, $p<0.001$), at the first outpatient appointment ($r=0.24$, $p=0.039$), and at six-month mark after surgery ($r=0.349$, $p=0.004$).

Conclusion

While several studies have examined the effects of ERAS compliance on clinical outcomes, no research has explored whether ERAS compliance affects quality of life as measured by PROMs. This study appears to be the first study to indicate that higher adherence rates to ERAS principles enhance the Quality of Life for patients undergoing open PD. Our study illuminates QoL parameters that are most important to the patients and contributes to the evidence supporting the implementation of perioperative strategies that enhance patient experiences.

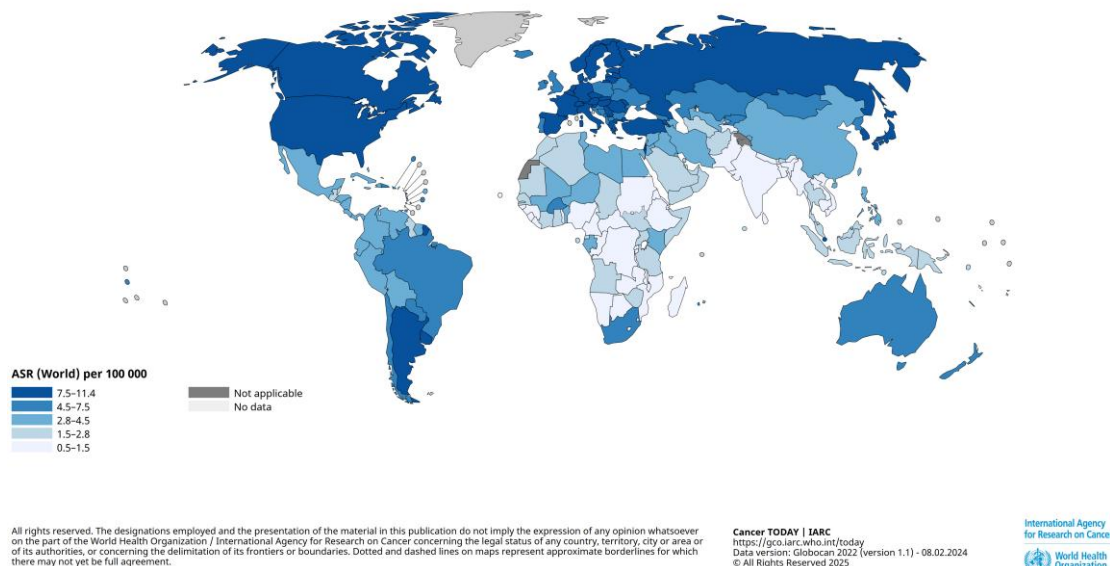
Keywords: patient-reported outcomes, enhanced recovery after surgery, pancreatoduodenectomy, quality of life

Chapter 1 Introduction

1.1 Pancreatic cancer and surgery

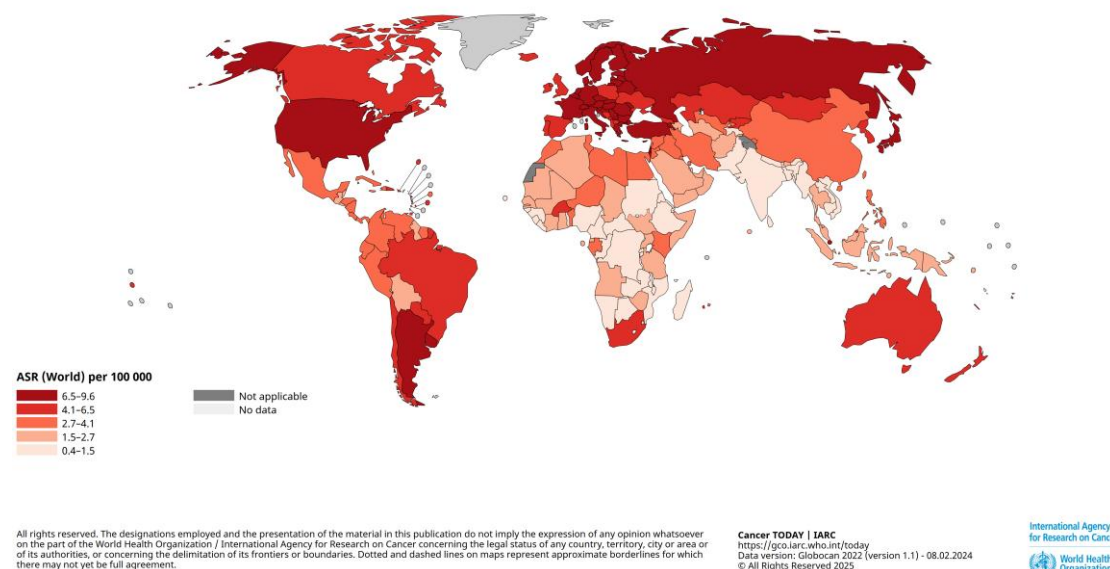
Pancreatic cancer is the third leading contributor to cancer mortality in the United States and is predicted to become the second leading cause of cancer-related death in some regions.¹ The five year survival rate in patients that underwent a surgical procedure is about 17.4%, but for non-resected tumors remains low, around 0.9% meaning that we have more to provide to those patients in the future.² The most common type of pancreatic tumors is Pancreatic ductal adenocarcinoma (PDAC). New cases are most commonly diagnosed in individuals aged 65-74, with the median age at diagnosis being 70 years.³ Additionally, the highest percentage of deaths occurs within the same age group, with the median age at death being 72 years.²

Age-Standardized Rate (World) per 100 000, Incidence, Both sexes, in 2022
Pancreas



Figures 1 Map showing estimated age-standardized rates of incidence for pancreatic cancer worldwide in 2022, including both sexes and all ages. Copyright

Age-Standardized Rate (World) per 100 000, Mortality, Both sexes, in 2022
Pancreas



Figures 2 Map showing estimated age-standardized rates of mortality for pancreatic cancer worldwide in 2022, including both sexes and all ages. Copyright ©International Agency for Research on Cancer 2021. Published by World Health Organization.

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Cancer of pancreas can be located at pancreatic head, body or tail. Regarding the distribution of pancreatic cancer within the pancreas, approximately 78% of cases occur on the pancreatic head, 11% on the body and 11% on the tail.⁵ The most frequent symptoms include fatigue, weight loss, anorexia, and abdominal or back discomfort. Tumors that exist at the head of the pancreas or neck are often linked to pruritus and jaundice due to biliary obstruction, while those on the pancreatic body or tail typically present with pain.⁶

The treatment of PDAC remains challenging because by the time of diagnosis it is usually a systemic disease. Moreover, diversity of the biological behavior of the tumor creates an even bigger obstacle for doctors and a resistance to chemotherapy. For the resectable tumors, surgery is still the king of the treatment options. Depending on where the tumor is located we can either undergo traditional pancreatoduodenectomy (PD), Pylorus preserving pancreaticoduodenectomy (PPPD) and distal pancreatectomy (DP).⁷

Pancreatic resection remains one of most technically challenging procedures that is accompanied by difficult complications. The most common are delayed gastric emptying, pancreatic fistula, and bleeding. DGE happens in 20% to 50% of patients, PF occurs in 10 to 15% and bleeding in 4 to 16%.⁸ These situations are not only delaying recovery but also increase morbidity. The mortality in expert centers remains < 3%.

Enhanced Recovery After Surgery (ERAS) is a multidisciplinary, evidence-based approach centered on the patient, aiming to enhance surgical outcomes through the application of structured clinical pathways. This concept encompasses thorough preparation and education of the patient before surgery, along with a well-organized postoperative follow-up conducted by specialized healthcare professionals. Research has demonstrated that ERAS significantly improves key factors such as reducing hospital stay duration, minimizing complications, and lowering readmission rates.⁹ Besides the surgical outcome, other ways to evaluate the standard of medical care and surgical procedures provided to the patients, are the patient-reported outcome measures (PROMs). The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) is a worldwide used PROM designed to evaluate the quality of life in patients that suffer from cancer. It consists of 30 items covering multiple domains, including physical, emotional, cognitive, and social functioning, as well as symptoms like fatigue, pain, nausea. The questionnaire provides valuable insights into patients' well-being, helping clinicians and researchers monitor treatment effects, personalize care, and improve overall patient outcomes.¹⁰

1.2 PROMs and pancreatic surgery

Enhanced Recovery After Surgery (ERAS) is an evidence-based, multidisciplinary approach designed to improve patient outcomes and accelerate recovery following surgery. Henrik Kehlet introduced the concept in 1997, proposing that while individual modifications in perioperative practice may have little effect on their own, combining multiple changes could lead to a significant improvement in patient outcomes.¹¹ In a 2017 review published in JAMA Surgery, Ljungqvist, Scott, and Fearon outline key ERAS principles, emphasizing preoperative, intraoperative, and postoperative strategies that collectively minimize surgical stress and complications.¹² Preoperative measures focus on patient education,

nutritional optimization, and carbohydrate loading to reduce insulin resistance. Intraoperative strategies prioritize minimally invasive techniques, optimal fluid management, and the avoidance of unnecessary tubes and drains to limit surgical trauma. Postoperatively, ERAS encourages early mobilization and utilizes multimodal pain control strategies with minimal reliance on opioids, and early oral nutrition to support faster recovery. By challenging traditional perioperative practices, ERAS protocols have demonstrated significant reductions in hospital stays and postoperative complications, making them a transformative approach in modern surgical care.¹²

The PROMs (TABLE 1) have not been sufficiently studied so far, especially in pancreatic cancer surgery. A limited number of publications address this particular topic, which, however, appears to be of utmost importance for improving the overall provision of medical services to surgical patients. The study titled "Patient-Reported Outcome and Experience Measures (PROM/PREM) in Patients Undergoing Liver Surgery with Enhanced Recovery after Surgery (ERAS®) : An Exploratory Study" explored patient-reported outcomes and experiences in individuals undergoing liver surgery within an Enhanced Recovery after Surgery protocol. Conducted in Austria, it assessed 30 patients through clinical data, including postoperative complications, hospital stay length, and self-reported measures of recovery (QoR-15) and satisfaction (EORTC IN-PATSAT32). The findings showed a 20% complication rate with no mortality, median hospitalization of 7 days, and consistently high recovery scores. Patients expressed strong satisfaction, particularly regarding medical care and information provided. The study concluded that incorporating patient-reported measures into ERAS® protocols is both feasible and beneficial, enhancing personalized care and optimizing recovery outcomes in liver surgery.¹³

Traditional clinical criteria, such as days of hospitalization, contrary to PROMs, do not fully show what is of most importance in patients during recovery.¹⁴ In the late 1990s, a specialized questionnaire module for pancreatic cancer was created to supplement the EORTC core cancer module (QLQ-C30).¹⁵ A systematic review of Ashika D. Maharaj et al. evaluated the use of patient-reported outcome measures (PROMs) in pancreatic cancer (PC) by analyzing 170 studies. It assessed the psychometric properties and applicability of 70 patient-reported outcome measures (PROMs) in pancreatic cancer. It found that tools like the EORTC QLQ-C30 (Figure 3) with QLQ-PAN26, and FACT-HEP were the most widely used, though

only a few were validated specifically for PC. The review highlighted challenges in data collection methods and suggested that no single tool captured all necessary domains. It recommended the use of QLQ-PAN26 with its core PROM, QLQ-C30, which when used in conjunction, they capture about 35 of the 50 scales. It also recommended specific PROMs for different stages of the disease and emphasized the need for further validation and standardization.¹⁶ Arja Gerritsen et al. aimed to identify a set of 17 PROs that are considered most important by both patients and healthcare professionals. The selected PROs cover a wide range of aspects, including overall quality of life, physical functioning, capacity to carry out daily activities, medication usage, pancreatic enzyme replacement therapy, appetite, weight fluctuations, fatigue, emotional health, fear of cancer recurrence, and relationships with family and caregivers. The findings revealed a notable difference between patients and HCPs, with healthcare professionals giving higher importance to physical PROs like pain, nausea, and jaundice, which are often more prominent during the diagnostic and perioperative phases of the disease. On the other hand, patients, particularly those in palliative care, focused more on their current health status and psychosocial factors, such as coping mechanisms and their relationships with loved ones. These differences highlight the diverse perspectives of patients and professionals in assessing the impact of pancreatic cancer and underscore the importance of considering both physical and emotional aspects in patient care and research.¹⁷

RROMs	Question Number
<u>Global health status / QoL</u>	
Global health status/QoL	29,30
<u>Functional scales</u>	
Physical functioning	1-5
Role functioning	6-7
Emotional functioning	21-24
Cognitive functioning	20,25
Social functioning	26,27
<u>Symptom scales / items</u>	

Fatigue	10,12,18
Nausea and vomiting	14,15
Pain	9,19
Dyspnoea	8
Insomnia	11
Appetite loss	13
Constipation	16
Diarrhoea	17
Financial difficulties	28

Table 1 EORTC QLQ-C30 version 3.0, PROMs explained

ENGLISH



EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials:

Your birthdate (Day, Month, Year):

Today's date (Day, Month, Year): 31

ENGLISH

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a <u>long</u> walk?	1	2	3	4
3. Do you have any trouble taking a <u>short</u> walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4
During the past week:				
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

Please go on to the next page

During the past week:

17. Have you had diarrhea?

18. Were you tired?

19. Did pain interfere with your daily activities?

20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?

21. Did you feel tense?

22. Did you worry?

23. Did you feel irritable?

24. Did you feel depressed?

25. Have you had difficulty remembering things?

26. Has your physical condition or medical treatment interfered with your family life?

27. Has your physical condition or medical treatment interfered with your social activities?

28. Has your physical condition or medical treatment caused you financial difficulties?

Not at All A Little Quite a Bit Very Much

1 2 3 4

1 2 3 4

1 2 3 4

1 2 3 4

1 2 3 4

1 2 3 4

1 2 3 4

1 2 3 4

1 2 3 4

1 2 3 4

1 2 3 4

1 2 3 4

1 2 3 4

1 2 3 4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1 2 3 4 5 6 7

Very poor Excellent

30. How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7

Very poor Excellent

© Copyright 1995 EORTC Quality of Life Group. All rights reserved. Version 3.0

Figure 3 EORTC QLQ-C30 version 3.0

Chapter 2 Methodology

2.1 Aim

The primary objective of the research is to identify how compliance with ERAS influences PROs in PD.

In our study we measure PROs using the health questionnaire EORTC QLQ-C30¹⁸. This questionnaire is specifically developed to assess health-related quality of life in oncology patients. It comprises of 30 questions that examine the functional , emotional , cognitive and social components of life ,as well as symptoms, such as pain and insomnia, that may affect the quality of daily activities. The items included in the questionnaire can be found in Table 1. The questionnaire also asks the patients to self-evaluate their overall health and quality of life. Patients will be requested to fill out the questionnaires at the following time points within 7 days preoperatively, POD5, first appointment post-discharge, 30 days and 6 months follow-up.

2.2 Inclusion/exclusion criteria

Inclusion Criteria:

- Over 18 years old
- Fluent in Greek
- Engaged in enhanced recovery protocol
- Undergoing elective open pancreaticoduodenectomy (PD)

Exclusion Criteria:

- Under 18 years old
- Unable or unwilling to participate
- Other pancreatic surgeries
- Missing data
- Lost to follow-up

2.3 Study design

Ethics approval

The research protocol has received endorsement from the ethics committee associated with the Faculty of Medicine at the University of Thessaly. Additionally, authorization has been conferred by the Institutional Review Board of IASO Thessalias Hospital and the Scientific Board of the Larissa University Hospital.

Study design

This study is a prospective observational cohort that adheres to STROBE reporting guidelines¹⁹. We utilize the RECOVER Checklist²⁰, which provides a standardized framework for reporting studies related to Enhanced Recovery After Surgery (ERAS).

Study setting

The investigation was conducted at two medical institutions: the Larissa University Hospital, an academic facility, and IASO Thessalias Hospital, a private center for oncology surgery. A stable group of surgeons and anesthesiologists was involved throughout the study. Participants undergoing elective open PD between June 2022 and January 2025 were recruited for the research.

All patients were enrolled in a prospective manner after providing written informed consent. Throughout the preoperative, intraoperative, and postoperative phases, these individuals strictly followed the ERAS protocol, specifically designed for pancreatic surgeries. This protocol is based on guidelines from the ERAS Society, aimed at promoting faster recovery after pancreatoduodenectomy.

To systematically monitor each patient's progress, the study utilized a comprehensive checklist of ERAS criteria (Table 2).

ERAS Criterion	Description
1. PREOPERATIVE COUNSELING	Information by surgeon Information by anesthetist Educational patient leaflet
2. PREHABILITATION (5 days preop)	Physical exercise (30 min walk twice a day) Respiratory exercises with three-flow device Nutritional supplements

3. PREOPERATIVE ASSESSMENT	Smoking cessation Alcohol cessation Patient optimization
4. PREOPERATIVE NUTRITION	Assessment with NRS-2002 Nutritional support if BMI<18.5 or weight loss >15%
5. FASTING & CARBOHYDRATE LOADING	6h for solids 2h for clear liquids Carbohydrate loading
6. PRE-ANESTHETIC MEDICATION	No long-acting sedatives on day of surgery Paracetamol 1g 2h preop Gabapentinoid 2h preop
7. ANTITHROMBOTIC PROPHYLAXIS	Preop LMWH Postop LMWH TED stockings
8. ANTIMICROBIAL PROPHYLAXIS & SKIN PREPARATION	Antibiotics <60min before incision Additional dose every 3–4h Intraop bile culture Postop antibiotics per culture result (stop if negative unless needed)
9. MULTIMODAL ANALGESIA (INTRA & POSTOP)	Analgesia bundle 1-4 Other
10. PONV PROPHYLAXIS	Based on risk factors
11. AVOIDING HYPOTHERMIA	Active warming Temp >36°C intraop and in PACU
12. POSTOPERATIVE GLYCEMIC CONTROL	Target 80–150 mg/dL
13. NASOGASTRIC INTUBATION	Remove by POD1
14. FLUID BALANCE	GDFT intraop Fluid load <30ml/kg Postop fluids 3ml/kg/day, adjusted per 24h balance Stop IV fluids once drinking >1.5L by POD5
15. PERIANASTOMOTIC DRAINAGE	Number of drains Drain amylase <5000U/L on POD1 Early removal on POD3
16. URINARY CATHETER	Remove when patient ambulating independently by POD5

17. DELAYED GASTRIC EMPTYING (DGE)	Cilroton + Primperan
18. STIMULATION OF BOWEL MOVEMENT	Chewing gum
19. POSTOPERATIVE NUTRITION	Diet protocol followed Parenteral if needed
20. EARLY & SCHEDULED MOBILIZATION	Out of bed in chair Walking Mobilization protocol followed

Table 2 Local ERAS protocol for pancreatic surgery

Data on adherence to these established criteria were collected using a secure Excel spreadsheet, which served as an electronic database for systematic collection of prospective data.

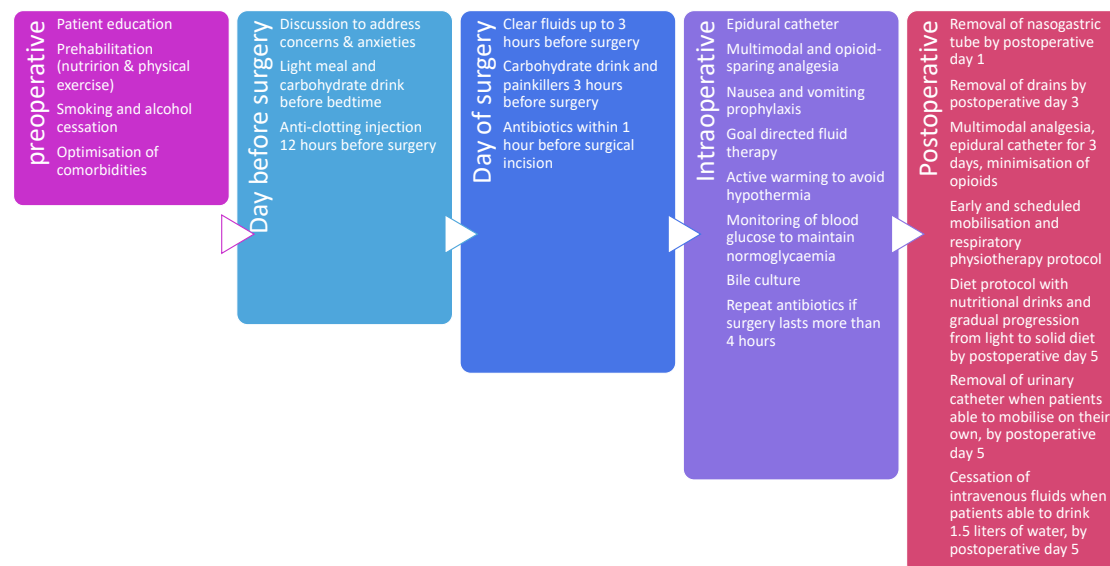


Figure 4 Local ERAS protocol

We also gathered information on complications, which included cardiovascular and respiratory issues, and infectious complications like surgical site infections, chest infections, urinary tract infections, intra-abdominal abscesses, and sepsis. Anesthetic complications were documented, including severe pain, delirium, and cognitive decline. Functional complications were noted as well, including functional decline, new use of mobility aids, pressure ulcers, and discharge to nursing or rehabilitation facilities. Other complications included renal failure, ileus, reoperation, hospital readmission, and mortality.

Furthermore, information were collected on the days of hospitalization and complications specific to PD, such as delayed gastric emptying, hemorrhage, and pancreatic fistula formation.

After anonymization, local investigators prospectively uploaded all data to a secure database and included them in a spreadsheet for analysis.

2.4 Definitions

Postoperative complications were considered as those arising within a 30-day period after the surgical procedure, with their severity classified based on the Clavien-Dindo system²¹. Complications were classified into minor (Grades I-II) or major (Grades III-IV).

The International Study Group of Pancreatic Surgery indicates that delayed gastric emptying (DGE) is defined as either the requirement for nasogastric tube (NGT) reinsertion beyond the third day after surgery or the inability to resume oral intake by postoperative day seven.²² The ISGPS further categorizes DGE into three severity grades: A, B, and C.

Moreover, a postoperative pancreatic fistula (POPF)²³ is characterized by the presence of measurable fluid from a surgical drain on or after the third postoperative day, containing amylase levels exceeding three times the normal upper serum limit. The ISGPF classifies POPF into three severity grades: A, B, and C.

Postoperative hemorrhage (PPH)²⁴ was determined based on ISGPS guidelines as either early (<24 hours) or late (>24 hours) intraluminal or extraluminal bleeding, categorized as mild, moderate, or severe. PPH is classified into 3 grades based on severity and clinical impact.

Length of hospital stay is defined as the time from the day of surgery until the day of discharge.

Readmission is defined as any hospital admission occurring within thirty days after discharge.

2.5 Statistical analysis

Statistical analysis was carried out with the use of R statistical environment software (R Core Team (2024). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>) and JASP (University of Amsterdam).

The influence of factors like BMI, sex, age, ASA classification, and compliance was evaluated. Adherence was calculated by dividing the number of fulfilled interventions by the total of 20 ERAs interventions. The primary outcome analysed was the global EORTC-30 score.

Quantitative data were presented as mean $\pm$ standard deviation (SD), median, and range, while categorical data were expressed as percentage frequencies. Univariate analysis was performed to evaluate the association between each factor and the outcome variables. For continuous variables (such as age, EORT-C30 score, and ERAS compliance), correlations were assessed using Pearson's or Spearman's test after testing for normality with the Kolmogorov–Smirnov test. A P-value < 0.05 was considered statistically significant.

Chapter 3 Results

3.1 Patient characteristics

Based on research criteria, 82 consecutive patients that underwent an elective pancreatoduodenectomy for pancreatic cancer under the ERAS protocol were part of the study (Figure 5). The mean age was calculated at 67.2 (11.5) years and 45 (55.5%) of them were male. The mean BMI was 26.2 and each participant had an ASA score II or III. Moreover, the average compliance rate was calculated at 72% (15.9).

3.2 Synthesis of outcomes

The mean and standard deviations (SD) values of EORT-C30 score at preoperative day, 5th postoperative day (POD5), the first follow-up visit, first month and at six months postoperative are displayed on Table 3. It is worth noting that the mean score at six months after the surgery was notably increased at 84.53% compared with the mean 67.73% preoperative value.

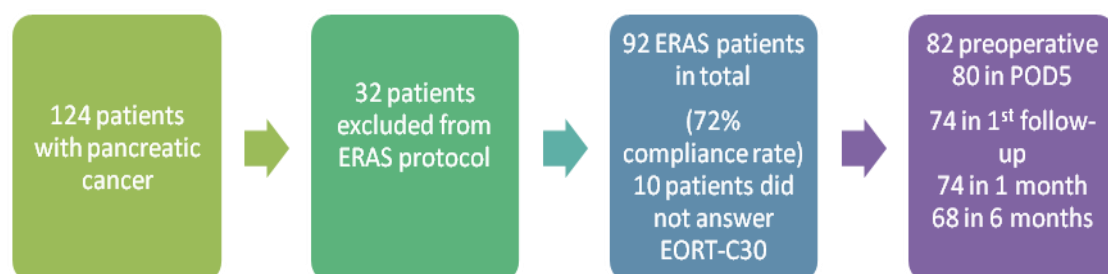


Figure 5 Flow chart.

Timepoint	Mean	Std. Deviation
Preoperative	67.73%	20.633
5 th postoperative day	59.05%	18.661
1 st follow-up	63.11%	12.228
1 month	74.32%	11.678
6 months	84.53%	15.084

Table 4 EORT-C30 mean values

3.3 Quality of life and ERAS compliance.

On Table 4 are displayed the correlation between EORT-C30 scores and compliance rate. In particular, statistically significant positive correlations were observed between EORT-C30 and ERAS compliance rate at POD5, 1st follow-up visit and at six months ($p < 0.001$, $p = 0.039$ and $p = 0.004$ respectively), meaning that a higher compliance rate is linked with better postoperative quality of life.

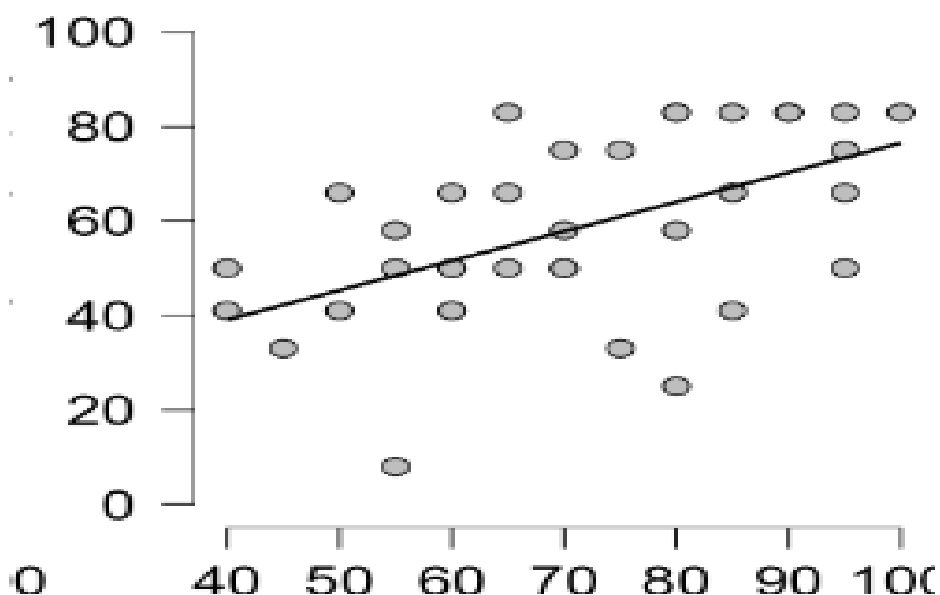


Figure 6 Correlation between EORT-C30 on 5th postoperative day and ERAS compliance

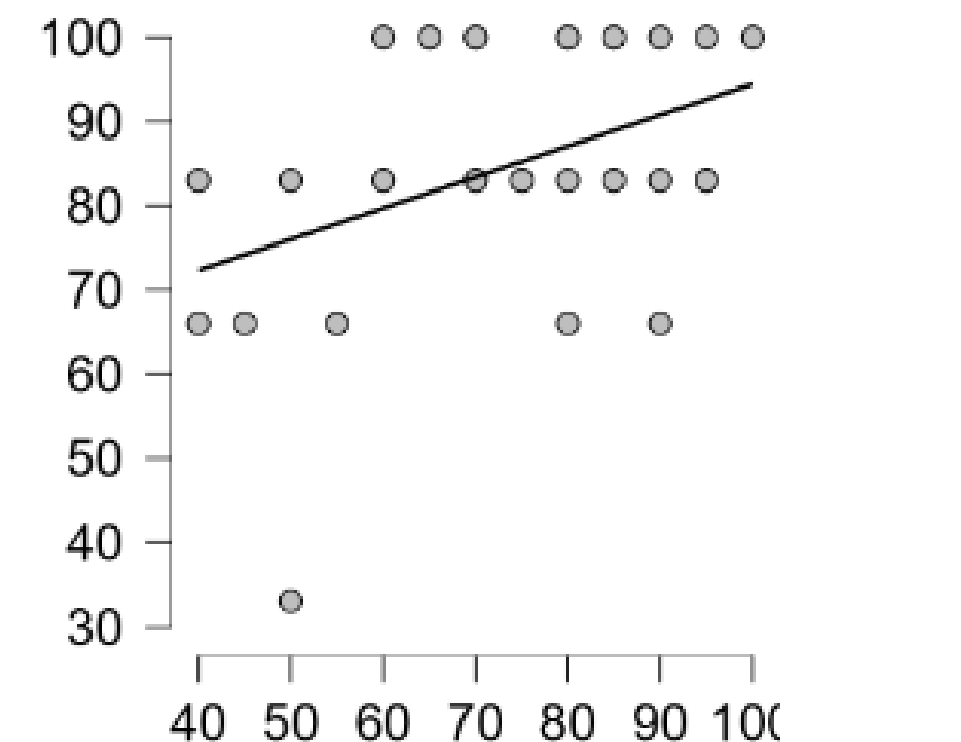


Figure 7 Correlation between EORT-C30 at six months postoperative and ERAS compliance.

Timepoint		Preoperative	5th postoperative day	1st follow-up	1 month	6 months
ERAS COMPLIANCE (%)	Spearman's rho	0.009	0.569	0.240	-0.022	0.349
	p-value	0.938	<0.001	0.039	0.854	0.004

Table 4 Correlations between EORT-C30 and ERAS compliance rate.

Chapter 4 Discussion

Overview of findings

Our study sought to assess the effect of ERAS protocol compliance on postoperative quality of life in patients undergoing surgery for cancer of pancreas. In this study of 82 consecutive patients, significant improvements in quality of life were observed over the postoperative period, alongside a positive association between ERAS compliance and patient-reported outcomes. The cohort had a mean ERAS compliance rate of 72%. The EORTC-C30 scores, reflecting global quality of life, increased progressively, from a preoperative mean of 67.73% to 84.53% at six months postoperatively. Moreover, higher ERAS compliance rates were correlated with improved EORTC-C30 scores at the 5th postoperative day($p<0.001$), first follow-up visit($p=0.039$), and six months postoperatively ($p=0.004$). These findings highlight the potential benefits of improving ERAS adherence to enhance both short- and long-term quality of life outcomes in patients undergoing major pancreatic surgery.

Interpretation in the context of other evidence

As noted before, although the implementation of ERAS protocols has been extensively studied for many types of surgeries, there is a striking shortage of studies specifically examining a relationship between protocol adherence and patient-reported outcomes (PROs) in pancreatic surgery. However, our findings align with and expand upon previous research demonstrating the benefits of ERAS protocols in improving postoperative outcomes. Daniela Rappold, et al. showed that liver surgery patients within the ERAS pathway experienced low complication rates, high satisfaction with care, and consistently strong recovery scores, demonstrating the value of PROMs and PREMs in capturing patient-centered outcomes. Davin Martin, et al.²⁵ found that patient-centered measures in pancreatic cancer surgery are diverse and inconsistently reported, emphasizing the urgent need for standardized PROMs/PREMs to better capture what truly matters to these patients. Other studies such as Ashika D. Maharaj et al. and Arja Gerritsen et al. focus on the need of finding more specific PROs for pancreatic cancer and highlight the necessity for additional validation and the establishment of standardization. Notably, our study is among the first to demonstrate

a statistically significant correlation between higher ERAS compliance and improved quality of life as measured by the EORTC QLQ-C30.

Implications for practice

Unfortunately, even modern medicine still has considerable progress to make in addressing the broader dimensions of patient health. Contemporary clinical practice often remains focused on measurable clinical parameters—such as vital signs, symptoms, and laboratory results—when evaluating postoperative recovery, while overlooking the fact that the patient is a multidimensional being whose recovery experience encompasses far more than physiological metrics alone. Therefore, it is crucial to incorporate the systematic assessment of factors that reflect broader aspects of quality of life into routine clinical culture. The present study represents a step toward this goal, demonstrating that validated tools for such assessment do exist, and that their successful implementation in clinical practice requires not only a shift in mindset but also the promotion of quality improvement initiatives.

Implications for future research

While the existing research has shown remarkable results between higher compliance to ERAS and better postoperative quality of life, there are still many questions rising about their implementation in patients with severe medical issues such as pancreatic cancer. To begin with, more specific and precise questionnaires should be created for this purpose. Therefore, well-designed multicenter prospective cohort studies may be more appropriate in order to identify the exact factors we should evaluate in those patients regarding their quality of life. Furthermore, longitudinal studies with larger patient cohorts and extended follow-up periods are warranted to assess the sustainability of QoL improvements over time and to determine whether similar associations can be observed across diverse surgical populations and healthcare settings.

Limitations

This study is prospective, observational cohort study. Conducting multicenter studies with ERAS can be challenging due to the difficulty of maintaining consistent quality across different centers. Additionally, unlike randomized controlled trials (RCTs), observational studies may be better suited for evaluating the effects of a multimodal

approach, such as the ERAS program, on patient outcomes. The follow-ups at one month and six months were conducted by telephone, which may introduce selection bias. To mitigate this issue, the person making the phone calls was a secretary who was not otherwise involved in the study.

Chapter 5 Conclusion

According to this study higher compliance to ERAS protocols in patients that undergo open pancreatoduodenectomy, is associated with better results in PROs and improved quality of life in specific postoperative timelines. This study is among the first to interrelate ERAS adherence with short and long-term quality of life in pancreatic surgery. Further research is needed in this field to confirm these results and standardize the use of PROMs in this population.

Thesis synopsis

This study explores the relationship between compliance to the Enhanced Recovery After Surgery (ERAS) protocol and patient-reported outcomes (PROs) in individuals undergoing open pancreatoduodenectomy (PD) for pancreatic cancer. Although the ERAS program has been widely adopted for its role in improving clinical recovery, there has been little investigation into how closely following this protocol might influence how patients themselves experience their recovery, especially in complex surgeries like PD.

The research was conducted as a prospective cohort study at two major hospitals in central Greece: the University Hospital of Larissa and IASO Hospital. Eighty-two patients undergoing elective open PD were enrolled and followed within a standardized ERAS framework. Their quality of life was assessed using the EORTC QLQ-C30 questionnaire, administered before surgery and at several points after: on the fifth postoperative day, at the first follow-up appointment, one month later, and again six months postoperatively.

These results revealed a clear trend: patients who had higher compliance with the ERAS protocol tended to report better quality of life, with statistically significant

improvements noted particularly at day 5 ($p<0.001$), the first outpatient follow-up ($p=0.039$), and six months post-surgery ($p=0.004$). The results indicate that the level of adherence to ERAS principles can meaningfully influence to the physical recovery and also the overall patient experience.

To date, very little studies have examined this connection in the context of pancreatic surgery. This work contributes new evidence showing that greater ERAS compliance may be associated with improved patient-reported outcomes over time. The findings support the broader use of PROMs in surgical care and highlight the importance of viewing recovery not just through clinical metrics, but also through the patient's own perspective.

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