Miinalainen, S., Löyttyniemi, E., Jyrkkiö, S., Akrén, O., 2025. Assessing Quality of Life in Patients with Pancreatic Cancer in a Prospective Single-Center Observational Study. Journal of Palliative Medicine.

DOI: https://doi.org/10.1177/10966218251383708

Abstract

Background and purpose: Patients with pancreatic cancer have an extensive symptom burden and a modest quality of life (QoL). Our aim was to evaluate three QoL questionnaires in clinical practice and monitor patients' symptoms over a 4-month follow-up period. *Material and methods:* The study included 54 patients with pancreatic cancer in a single-center University Hospital in Finland. The QoL questionnaires involved were the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C15-PAL, QLQ-C30, and QLQ-PAN26. Patients completed the questionnaires at baseline and at 2 and 4 months. *Results:* All three questionnaires served as a tool for facilitating dialogue between patient and physician. No relevant changes were observed in reported symptoms, concerns, or QoL during the follow-up period. However, the amount of missing data increased over time due to patients' declining health or death. The main reported concern was worry about future health. *Conclusion:* The shorter 15-question survey seemed to capture an adequate picture of patient well-being. The QLQ-PAN26 added valuable insight, as it focuses on pancreatic cancer-related symptoms. The information gathered from these QoL questionnaires can be used both to emphasize patients' concerns and to support decision making.

Key message: QoL questionnaires can provide a comprehensive overview of a patient's well-being, facilitate dialogue, highlight key patient concerns, and support decision making, especially in patients with a heavy symptom burden such as those with pancreatic cancer.

Keywords: Pancreatic cancer, quality of life, palliative care, QLQ-C30, QLQ-C15-PAL, QLQ-PAN26

Introduction

Pancreatic cancer is the third leading cause of cancer-related deaths in Finland, with 1266 deaths recorded in 2022.[1] The disease course is often aggressive with a poor prognosis. Most pancreatic cancer patients are beyond curative care, with <20% eligible for surgical intervention.[2] The prognosis remains poor even after resection. The 5-year overall survival (OS) rate of 5–12%[2,3] has remained unchanged for decades.[4] Patients with pancreatic cancer often carry a substantial symptom burden of anorexia, cachexia, abdominal pain, and fatigue. For many, QoL is modest at best.[5-7] The primary goal of care is to alleviate symptoms. Palliative care should be integrated into the management of all patients with chronic, progressive illnesses that impair QoL due to significant symptom burden or psychosocial support needs. This is particularly critical in pancreatic cancer, given its aggressive clinical course, substantial symptom burden, and the often intensive nature of anticancer therapies. As a result, preserving and improving QoL becomes a central concern in the care of these patients.[8,9] Assessment of symptoms is recommended to be introduced at an early stage.[10] QoL itself is a broad concept encompassing subjective perceptions of physical, psychological, and social well-being, and can be measured with different questionnaires. QoL assessment is also important for guiding decision making. Several tools have been developed to evaluate the QoL of cancer patients. EORTC has developed multiple symptom assessment questionnaires to measure various aspects of

QoL in cancer patients, including physical, emotional, and social functioning. These have been used in numerous studies. Although there are many investigations of the QoL in pancreatic cancer patients,[7,8,11] combined use of the questionnaires has not been extensively studied. The Edmonton Symptom Assessment System (ESAS) is a simple, widely used palliative care tool for tracking symptoms over time. It has been used in our clinic for several years in pancreatic cancer patients. However, it is unclear which questionnaire is most suitable for such patients in a clinical setting. Subsets to the general QoL core questionnaires include a survey specifically designed for pancreatic cancer patients, QLQ-PAN26.[12] It has been widely used, translated, and validated internationally.[13] While a Finnish version exists, it has not yet been validated.

The questionnaires play a role in patient care from cancer diagnosis through the palliative phase. The palliative care decision is made by the oncologist and marks the shift from life-prolonging anticancer treatment to symptom-focused care, marking the start of the palliative phase.

This study aimed to explore the usability of three multifaceted QoL questionnaires for pancreatic cancer patients in a prospective setting. Additionally, it examined whether a change in reported symptoms could be observed over time and used to inform decision making in symptom management and cancer care.

Material and methods

Cohort selection. This prospective, single-center study was conducted at Turku University Hospital, the sole provider of cancer care in the region, with around 100 new pancreatic cancer diagnoses annually. All adult patients with a clinical, radiological, or pathological diagnosis of pancreatic cancer referred to the Department of Oncology at Turku University Hospital were invited to participate. The recruitment target was 75–100 patients over 2 years. All patients with a sufficient general condition to complete the questionnaires, independently or with assistance, were included. The only exclusion criterion was feeling too ill to participate as judged by the patient, clinician, or nurse. The number of excluded patients was not recorded. Informed consent was obtained from all participants.

Questionnaires. This study used three EORTC QoL questionnaires: QLQ-C15-PAL, QLQ-C30, and QLQ-PAN26. The first two are general core questionnaires, while the latter is a supplement to the QLQ-C30. The QLQ-C30 includes two seven-point global health and QoL items, along with 28 four-point items covering five functional scales (physical, role, emotional, cognitive, social functionality), three symptom scales (fatigue, nausea and vomiting, pain), and six single-item scales (dyspnea, insomnia, loss of appetite, constipation, diarrhea, financial aspects). The QLQ-C15-PAL is a shortened version of the QLQ-C30, designed for palliative cancer patients. Although not all participants were in the palliative phase, it was used because pancreatic cancer patients often require palliative care early in the disease trajectory. The QLQ-PAN26 is a complement to the QLQ-C30 and cannot be used independently. It comprises 26 questions concerning pancreatic cancer-related symptoms, treatment side-effects, and emotional issues (12). The QLQ-PAN26 includes both symptom scales and single items. Multi-item scales cover pain, digestive symptoms, altered bowel habits, hepatic symptoms, body image, satisfaction with health care, and sexuality. Question 46 (Did you have frequent bowel movements?) was excluded due to a translation error in the Finnish version. Question 47 (Did you feel the urge to move your bowels quickly?) alone was retained to reflect bowel habits. Scoring followed EORTC guidelines, with raw scores converted to a scale of 0 to 100. Higher scores indicate better functioning, global health, and QoL, while high symptom scores reflect a greater burden of symptoms/concerns. Likewise, in the QLQ-PAN26, higher scores indicate more severe symptoms, except for the health-care satisfaction subscale, where higher scores denote greater satisfaction.

Questionnaires were completed at diagnosis, along with background information (living conditions [living alone or with family], occupation, use of pain medication, smoking, and alcohol consumption). The surveys were repeated at 2 and 4 months. Participants were asked for permission to access their electronic medical records, which were used to gather follow-up data. Alongside the questionnaires, data on received treatments (surgery, chemotherapy, chemoradiation), pain medication use, palliative care interventions, and survival were collected manually from the electronic patient records. Data on pain medication use were obtained both from patient-reported forms and medical records. Since patient-reported information on the use of pain medication was incomplete, we used the information from medical records. Questionnaires were completed on paper. Since the QLQ-C15-PAL items are included in the QLQ-C30, patients did not need to complete it as a separate questionnaire.

Statistical analysis. Patient characteristics were reported using descriptive statistics, with counts and percentages for categorical variables and medians with lower (Q1) and upper (Q3) quartiles or ranges for continuous variables. Data analysis was conducted by a biostatistician in accordance with EORTC guidelines.

None of the questionnaires yield a total score; instead, they use different subscales. Questions 29 and 30 (global health and overall QoL status) were omitted from this comparison analysis as they use a scale from 1 to 7, whereas all other questions use 1 to 4. Time series analysis of the questionnaires data was not performed, as missing data were non-random and primarily due to poor health or death. Cronbach's alpha was calculated for each questionnaire at every timepoint to examine internal consistency, and Pearson correlation coefficients were used to examine associations between scores. The association between palliative care decisions and number of treatment lines was analyzed using Fisher's exact test. The statistical reporting for this paper was generated using SAS software, Version 9.4 of the SAS System for Windows (SAS Institute Inc., Cary, NC, USA).

Results

Descriptive statistics. The study cohort included 54 patients of median age 70 years (range 51–80 years), with an equal distribution of men and women. The patient characteristics are presented in Table 1.

The follow-up time was from November 2019 to April 2023. Anticancer treatment with a life-prolonging intent was administered to 72% (n=39/54) of the patients. No systemic anticancer therapy was initiated in 20% of the patients, the goal of care being palliative from the outset. Of those who started non-curative anticancer treatment, 85% (n=33/39) died during follow-up, compared to 91% (n=10/11) of those who did not start any anticancer therapy.

For most of the patients (76%, n=41/54), a palliative care decision was made during the disease course. In cases without such decision, the most likely reason was continuation of anticancer treatment. The time intervals are presented in Table 2.

Age had no impact on the timing of the palliative care decision, nor did the number of treatment lines influence the likelihood of such a decision ($p=0.94$). Among patients who underwent surgery, only 27% received a palliative care decision during follow-up.

Evaluation of QoL questionnaires

Mathematically, the questionnaires are not directly comparable, since one is disease-specific while another is a subscale of the core questionnaire QLQ-C30. To evaluate the association between the questionnaire responses, we calculated the mean values for all four-level questions. Unsurprisingly, the correlation between the QLQ-C30 and QLQ-C15-PAL mean values was extremely high ($r \geq 0.96$ for all timepoints, $p<0.0001$). Likewise, the mean values of the QLQ-PAN26 items correlated strongly with both the QLQ-C30 and QLQ-C15-PAL mean values ($r \geq 0.76$ for all timepoints, $p<0.0001$). When comparing the mean scores between the QLQ-C30 and QLQ-C15-PAL, the greatest mean difference was 0.05, which is considered clinically insignificant. Additionally, when all subscales of the QLQ-C30 and QLQ-C15-PAL were compared, only minor

differences were observed, with 100% agreement across almost every subscale.
Missing data is informative in this type of study population, as many patients pass away during the course of the study. Consequently, the conventional statistical linear mixed model for repeated measurements is not suitable for this analysis.

Reported symptoms and QoL during follow-up. There were no clinically meaningful changes in reported symptoms or concerns during the follow-up period. Anticancer therapy did not appear to affect the number or severity of symptoms reported. The seven-level item scores on overall QoL remained stable during follow-up for the whole study cohort (Figure 1, Overall QoL at baseline and follow-up) and were unaffected by the number of anticancer therapy lines received.
The most frequently reported concern was worry about future health. Most patients were satisfied with the support provided by health care professionals. The most commonly reported moderate or severe symptoms are shown in Table 3.

Data from the remaining questions revealed only a few disturbing symptoms, with no notable changes observed over time. These data are included as supplementary material (Suppl 1). During follow-up, the number of patients completing the surveys dropped, as most of them (n=43, 80%) passed away. OS was more than twice as long for patients receiving at least one line of anticancer treatment. In contrast, OS was poor for patients who did not receive life-prolonging anticancer therapy, with a median survival of 2.1 months and mean 4.7 months. A significant dropout was observed in this group: of the

15 patients enrolled, only eight completed the questionnaire at 2 months and six at 4 months. The need for regular pain medication did not impact OS.

Discussion

The aim of this study was to gain real world data on the use of three QoL questionnaires in pancreatic cancer patients. A further objective was to evaluate whether changes in symptoms or QoL could be observed over time. Evaluating QoL in patients with a heavy symptom burden is crucial, as patient-reported outcomes are increasingly used but it remains unclear how best to benefit from them in clinical practice. The demographics and OS of the study population were consistent with those in previous studies.[5,6,8,14,15]

QoL questionnaires can provide a comprehensive overview of a patient's well-being. All three questionnaires used in this study performed similarly and provided largely overlapping information. Comparison of the questionnaires is limited, as the QLQ-C15-PAL is a subset of the broader QLQ-C30. Nevertheless, we recommend the QLQ-C15-PAL, as a shorter tool is more convenient in clinical use. Although the QLQ-PAN26 is not a stand-alone tool, it adds valuable insight by focusing on symptoms specific to pancreatic cancer. Patient feedback on their experiences completing the questionnaires was not collected, as the primary objective of this study was to evaluate the questionnaires from the physician’s perspective - specifically, their utility in clinical practice.

The initial recruitment target was not met, reflecting the difficulty of recruiting patients with an aggressive disease. Several patients declined participation due to weakness and feeling unwell. However, as the primary aim of the study was not to assess between-group differences, the smaller sample size is not expected to significantly affect the validity of the findings. During the study, some patients experienced rapid disease progression and withdrew due to clinical deterioration or death. Patient dropout was attributable to rapid disease progression and clinical deterioration, rather than any issues related to the questionnaires themselves. We could not report the patients' ECOG performance status as the questionnaires were completed outside the outpatient clinic setting, and information regarding patient dropout was obtained either by telephone contact or through nursing staff. Furthermore, some patients did not complete all the questionnaire items. It is worth noting an existing sampling bias, as only patients who felt well enough took part in the study. The short life expectancy associated with pancreatic cancer was confirmed in this study. As observed in previous studies,[16] OS is poor in patients who do not receive life-prolonging treatment. Since only a single week's symptoms were reported, the benefit of the surveys is limited. Results obtained with the QLQ-C15-PAL have demonstrated that patients with pancreatic cancer experience worse global health and a greater symptom burden compared to the general population,[5] with pain, fatigue, appetite loss, and insomnia being the most severe symptoms. In this study, symptom control, including pain management, was generally adequate for patients who remained alive during follow-up. However, it is possible that patients with the worst symptoms were those who dropped out of the study. The major concern reported was worry about future health, which is understandable given the aggressive nature of the disease. It should be noted that during the study period, social restrictions due to the COVID pandemic placed further limitations on the social life of patients.

Anticancer treatments for pancreatic cancer are often administered with the goal of ameliorating symptoms and improving QoL. Previous studies confirm that anticancer therapy has had a positive or stabilizing effect on QoL and pain management.[5,8,17] It has been suggested that QLQ-C30 score changes of $\geq$10 should be considered significant in clinical practice.[18] However, in a review[11] of 23 prospective studies, only four demonstrated a QoL benefit from anticancer therapy. The QLQ-C30 was the most used assessment in these studies. Five of the studies reported an improvement in QoL over time.[11]

The use of electronic patient-reported outcomes in supportive care has been shown to improve the QoL of patients with pancreatic cancer.[19] Some of these improvements are likely attributable, at least partly, to anticancer treatment.[20] In our study, no relevant changes in QoL were observed during the 4-month follow-up period. However, the study cohort varied throughout the study due to missing responses and patient dropout, which complicates the use of questionnaires during follow-up. We did not assess patients' experiences with completing the questionnaires. Instead, we gathered information on QoL measurement using different forms, with the aim of evaluating its possible contribution to symptom management and decision making. The information obtained from these questionnaires can support the evaluation and monitoring of symptoms and may inform decision making, but at least in our study, the time of impending death could not be predicted. Patients felt relatively well until they dropped out of the study due to clinical deterioration or death, with no indication of disease progression in their questionnaire responses before dropout. Nevertheless, the primary value of the questionnaires may lie in facilitating dialogue by highlighting the most important symptoms or main concerns expressed by the patient at the time of questionnaire completion. The usefulness of the questionnaires seems to be more on an individual level, offering a structured approach to understanding what matters most to each patient. In this study, QoL did not impact survival and could not be used to predict patient outcomes. Previous studies have shown that QoL data can provide prognostic information, and an association between QoL and survival has been reported.[21,22] A need-based electronic questionnaire could enhance symptom monitoring in patients at risk of rapid deterioration. Automated alerts to nursing staff may enable timely interventions, such as additional visits, supporting more responsive and individualized care.

Due to the aggressive disease trajectory and short life expectancy of pancreatic cancer patients, palliative care is recommended to be integrated concurrently with disease-modifying therapy.[10] These recommendations on early integrated palliative care in advanced cancer[23,24] were introduced at the time of this study. Integrating palliative care alongside conventional treatment in patients with advanced cancer has improved their QoL and, in some studies, also slightly extended their OS.[25,26] Given that early integrated palliative care may reduce aggressive treatments and hospitalizations at the end of life and facilitate earlier referral to specialized palliative care services,[26-28] it is increasingly being considered in the management of pancreatic cancer patients. At the beginning of this study, early integrated palliative care was not routinely implemented for pancreatic cancer patients at Turku University Hospital Department of Oncology. However, it became standard practice in late 2020 in line with recommendations.[28,29] During this study, 70% of patients contacted the Palliative Care Unit at least once during the follow-up period. A third of patients met a physician at the Palliative Care Unit at the initiation of anticancer therapy, which may indicate early palliative integration. Currently, all pancreatic cancer patients at the Department of Oncology meet a nurse at the Palliative Care Unit early in the disease trajectory. Previous studies have shown that a nurse-led palliative care intervention may improve the QoL of these patients.[30,31]

The study cohort was a representative sample of the population, and increasing the sample size would probably not have influenced the results. We believe that these results are generalizable to the care of pancreatic cancer patients in other countries.

One drawback of the study is that the surveys only captured symptoms over a single week, limiting their benefit. Additionally, this was a single-center study with a small study sample. A further limitation was the significant patient dropout, even during the short follow-up period, which complicates the drawing of conclusions and limits the validity of statistical analyses.

Conclusion

The shorter QLQ-C15-PAL questionnaire provided an adequate picture of patient well-being. While the QLQ-PAN26 is not a stand-alone tool, it added valuable insights into pancreatic cancer-related symptoms. The information provided by the QoL questionnaires can be used to evaluate symptoms, facilitate better dialogue between patients and clinicians, and support decision making, especially at single time points rather than across the follow-up period.

Author contributions

All authors participated in the design of the study and interpretation of the data. All authors read and approved the final manuscript. The data were collected by SM. EL performed the statistical analyses. SM drafted the manuscript and tables, which were revised by all authors.

Acknowledgements

Adelaide Lönnberg (MapleMountain Editing) revised the language of the text.

Funding Declaration

This work was supported by grants awarded to SM from the Cancer Society of Southwest Finland (Turku, Finland), the Finnish Society of Oncology, the Turku University Hospital Education and Research Foundation, and the Turunmaa Duodecim Society.

Ethics declaration

The study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the Wellbeing Services County of Southwest Finland, Turku University Hospital (ETMK 43/2019). Informed consent was obtained from all patients participating in the study.

Availability of data and materials

Due to the nature of this research, participants did not provide consent for their data to be shared publicly. Therefore, the supporting data are not publicly available but can be obtained from the corresponding author upon reasonable request.

This prospective study was conducted with the permission of the authorities of Turku University Hospital and the approval of the relevant ethics committee. As this was a purely observational study, trial registration was not required, in accordance with Finnish legislation governing research.

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Figure Legends

Table 1. Patient characteristics

Table 2. Time intervals

Figure 1. Overall QoL at three time points

Table 3. Most common moderate or severe symptoms reported by patients (%=percentage of patients experiencing moderate or severe symptoms/concerns at different time points, n= number of patients answering the question at different time points)

Supplement 1. EORTC-QLQ-C30 and EORTC-QLQ PAN26 score percentages at baseline and follow-up