

«The effect of cachexia on quality of life of patients with pancreatic cancer»

Η επίδραση της καχεξίας στην ποιότητα ζωής ασθενών με καρκίνο παγκρέατος

Abstract at the end of the article

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Introduction: 80% of patients with advanced gastrointestinal cancer present to have cachexia with a significant impact on survival. Rapid weight loss is an often underestimated symptom, in patients with pancreatic cancer.

Aim: The present research investigated the effects of cachexia (fat and muscle tissue loss) in patients with pancreatic cancer and how it is affected the patients' quality of life.

Materials and Methods: The study sample was patients with pancreatic cancer after random screening. Their demographics and anthropometrics data were recorded. At the same time, their quality of life was assessed using the EORTC QLQ-C30 questionnaire.

Results: The changes in the average weight of patients with pancreatic cancer steadily decreased, with the weight differences being statistically significant ($F=42.569$, $p<0.001$). Statistically significant was also the fat ($F=10.081$, $p<0.001$) and the muscle tissue ($F=3.294$, $p=0.018$) decrease. The quality of life (EORTC QLQ-C30) did not showed statistical significant changes.

Conclusions: Cancer cachexia is a serious multifaceted problem for patients with pancreatic cancer. Its management requires early detection, proper nutritional advisory, continuous evaluation. All this can be achieved through the interdisciplinary collaboration of health professionals.

Key words: pancreatic cancer, cachexia, eating disorders, quality of life

Introduction

The pancreas is a mixed gland,¹ which has both endocrine and digestive exocrine function. Its function focuses on regulating blood sugar levels, as well as with the pancreatic fluid it secretes neutralizes the acid that enters the duodenum from the stomach and with digestive enzymes it breaks down carbohydrates, proteins and fats of food.¹ It is located mainly behind the stomach and extends along the posterior abdominal wall from the duodenum to the right, to the spleen to the left. It is about 15 cm long and has the shape of a flattened pear. It consists of the head, hooked appendix, neck, body and tail.¹ Diseases of the pancreas are pancreatitis, carcinoma of the pancreas, as well as cysts and cystic neoplasms of the pancreas. Pancreatic cancer is the 4th leading cause of death in both sexes worldwide. It usually does not have recognizable symptoms in its early stages and is not diagnosed until it spreads beyond the pancreas.² This is why it has been called by many a silent disease with low survival rates.³ It rarely occurs before the age of 40 and more than half of cases of pancreatic adenocarcinoma occur in people over 70 years of age.⁷

Common symptoms of pancreatic adenocarcinoma that appear before diagnosis include: Pain in the upper abdomen or back, jaundice, unexplained weight, loss of appetite, loss of exocrine function resulting in poor digestion. Over 50% of people with pancreatic adenocarcinoma have diabetes at the time of diagnosis.⁵

Very often, and especially in cancer patients, we have the presence of cachexia, which is characterized as a "multifactorial and systemic syndrome" involving many organs, including skeletal muscle and adipose tissue as well as digestive, immune and central nervous system.⁹ Among them, altered skeletal muscle metabolism may play the most important role in worsening clinical outcomes. The presence of the tumor and its microenvironment causes chronic systemic inflammation. Physical inactivity in cancer patients additionally increases systemic inflammation due to reduced anti-inflammatory activity of chronic exercise.¹⁰ Minimal skeletal muscle contractions due to physical inactivity reduce anabolic stimuli for muscle protein synthesis in myocytes.

The relative lack of amino acids in skeletal muscle is caused by limited protein synthesis because amino acids are mainly consumed to produce acute phase protein in the liver. In addition, hypogonadism in male cancer patients¹¹ and tissue resistance to ghrelin ("hunger hormone")¹¹ and growth factors,¹² further inhibit muscle

protein synthesis. Cytokines, including tumor necrosis factor (TNF- α), interleukin (IL)-6 and IL-1 β , cause insulin resistance in the liver, skeletal muscle and adipose tissue, which, in turn, produce anabolic resistance.¹³

Overall, physical dysfunction in stunted patients can be caused by both quantitative¹⁴ and qualitative¹⁵ reduction in skeletal muscle, which, combined, further inhibits the patient's physical activity,¹⁶ resulting in a vicious cycle. Over time, this means that patients with cancer cachexia are more prone to chemotherapy toxicity¹⁷ and they often cannot complete all of their scheduled chemotherapy cycles. The presence of cancerous cachexia is associated with poor prognosis and low quality of life (QOL) from the time of diagnosis,¹⁸ during the treatment¹⁹ and at the end of their life.

Purpose and Objectives

The present study aims to record the effect of cachexia on the quality of life of patients with pancreatic cancer. More specifically, the study aims to investigate the degree of reduction or not of the quality of life of patients with pancreatic cancer, but also to record the evolution of the appearance of cachexia elements as a result of the disease.

Materials and methods

The sample of the research concerned patients with pancreatic cancer, who were monitored at the "Theageo" Hospital of Thessaloniki. The total number of patients under study reached 74 people and data were obtained through on-site measurements in the healthcare area with simple random sampling.

The survey data were recorded in a form of medical-demographic and anthropometric data. The collected demographic characteristics included the sex of patients, age, educational level, type of employment and marital status. At the same time it was recorded, the percentage of patients who were smokers, who had undergone surgery, who had experienced weight change, the level of physical activity and the way of feeding. Regarding the anthropometric data related to the development of cachexia syndrome on the part of patients, the following were recorded in 12 consecutive measurement phases:

Height in centimeters, Weight in kilograms, Ideal weight in kilograms, Body Mass Index (BMI), Body fat through the sum of four skin folds (triceps, biceps, scapula and iliac), Muscle mass circumference through formula: Arm circumference-(3,14×Triceps skin fold).

The EORTC QLQ-C30 scale of the European Agency for

Table 1. Descriptive statistics of the elements of the functionality scales	Mean	SD
Do you feel discomfort when doing strenuous tasks, such as carrying a heavy shopping bag or suitcase?	2,05	1,05
Do you feel discomfort when taking a long walk?	1,92	1,02
Do you feel discomfort when taking a short walk outside the house?	1,47	0,76
Do you need to stay in bed or in a chair during the day?	1,54	0,95
Need help when eating, dressing, washing or going to the toilet?	1,18	0,48
Have you limited yourself to your work or other daily activities?	1,80	0,95
Have you limited yourself to your amateur hobbies or other leisure activities?	1,73	1,02
Did you feel tense?	1,22	0,60
Did you feel sad?	1,76	0,84
Did you feel irritable?	1,28	0,59
Were you feeling depressed?	1,28	0,71
Did you have difficulty concentrating on things, such as reading the newspaper or watching TV?	1,15	0,43
Did you have difficulty remembering things?	1,23	0,59
Did your physical condition or the medication you were taking to treat you get in the way of your family life?	1,92	0,77
Did your physical condition or the medications you were taking for your treatment hinder your social events (social life)?	2,14	0,83

Table 2. Descriptive statistics of symptomatology scale data	Mean	SD
Did you need rest?	1,62	0,89
Did you feel weak?	1,65	0,93
Feeling tired?	1,54	0,91
Did you have a tendency to vomit?	1,18	0,58
Did you vomit?	1,09	0,44
Did it hurt?	1,36	0,85
Did the pain interfere with your daily activities?	1,26	0,66
Gasping?	1,24	0,59
Have you had trouble sleeping?	1,65	0,80
Did you had anorexia?	1,46	0,85
Did you have constipation?	1,11	0,36
Did you have diarrhea?	1,09	0,29
Did your physical condition or the medication you were taking for your treatment cause you financial difficulties?	2,11	0,90

Research and Treatment of Cancer was used to assess the quality of life level of patients with pancreatic cancer. Recurrence variance analysis to calculate the level of quality of life as determined by the QLQ-30 scales, the net score of each scale is first calculated divided by the average of the scores of its elements. The total score of each scale in a range of 0 to 100 is then calculated based on the formula: Total Score= $[1 - \text{score}/\text{range}] \times 100$, for

the functional scales and Total Score= $[\text{score}/\text{range}] \times 100$, for the symptomatology and general health/quality of life scales. The higher the relative scores, the greater the functionality, the symptomatology of the disease and the level of quality of life of patients.

Results

63.5% of patients were male, 36.5% were female, with

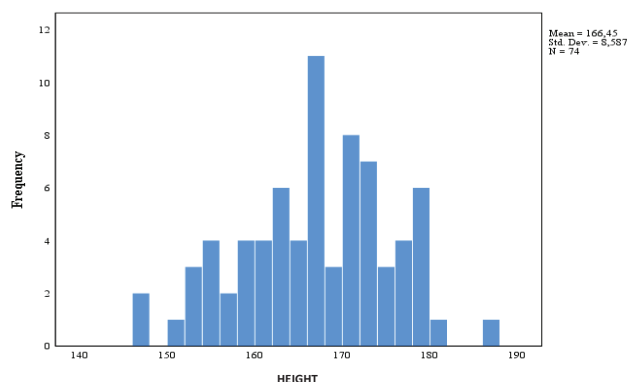


Figure 1: Descriptive height statistics

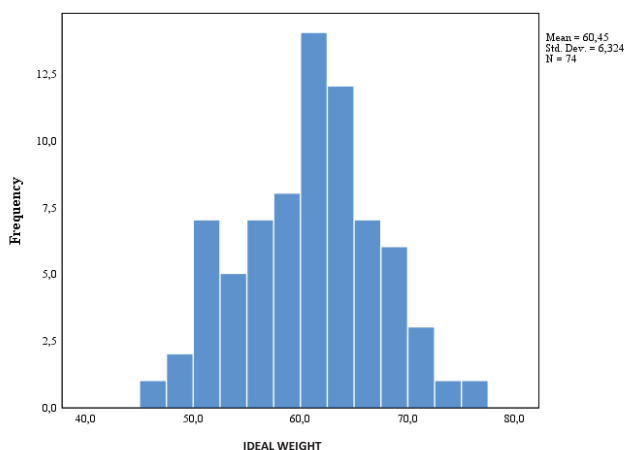


Figure 2: Descriptive ideal weight statistics

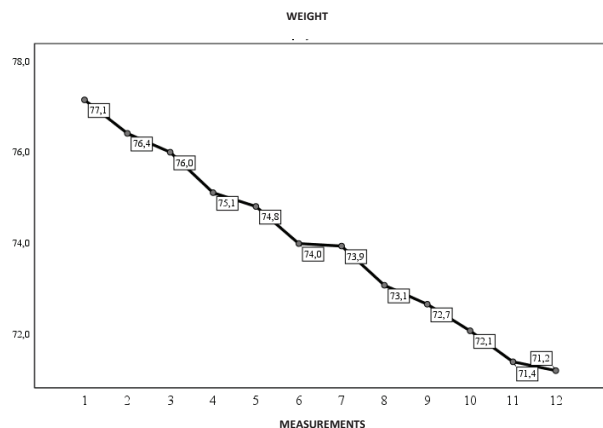


Figure 3: Average weight trend over time

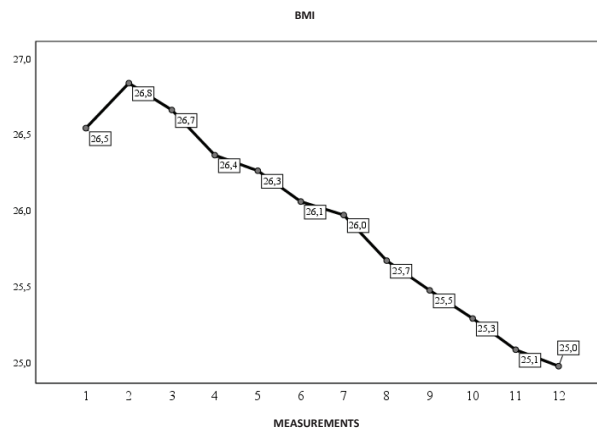


Figure 4: Average BMI trend over time

a mean age of 65.3 ± 9.2 years. 13.5% were employees, 16.2% unemployed, 17.6% self-employed, 52.7% pensioners, 4.1% single, 75.7% married, 8.1% divorced and 12.2% widowed. 43.2% were primary school graduates, 23.0% high school graduates, 25.7% high school graduates, 6.8% university or technological education graduates and 1.4% postgraduate or doctoral degrees. All patients had undergone some kind of surgery and showed a change in weight. 5.4% of patients performed low-intensity physical activity, 12.2% light, 23.0% moderate, 28.4% increased and 31.1% vigorous. 54.1% of patients were smokers, while all of them were fed themselves. The average height of patients was 168.5 ± 8.6 cm, while their average ideal weight was 60.5 ± 6.3 kg (Figure 1, 2).

Observing the changes in the average weight of patients with pancreatic cancer over time, it appears that it decreased steadily, with weight differences becoming

statistically significant ($F=42.569$, $p<0.001$). Through pairwise comparisons with Bonferroni's method, a consistent trend of statistically significant reduction in average patient weight was observed between measurements.

The Body Mass Index of patients increased slightly during the second measurement compared to the first, to follow a steady downward trend. The effect of time on the reduction of patients' BMI was also statistically significant ($F=10.081$, $p<0.001$), while based on the relevant Bonferroni tests, a slow differentiation of BMI values was observed, as their relative decrease was small in consecutive measurements.

Respectively, the results of fat measurement of patients were with the relative values steadily decreasing with small fluctuations and statistically significant differentiation between measurements ($F=10.081$, $p<0.001$).

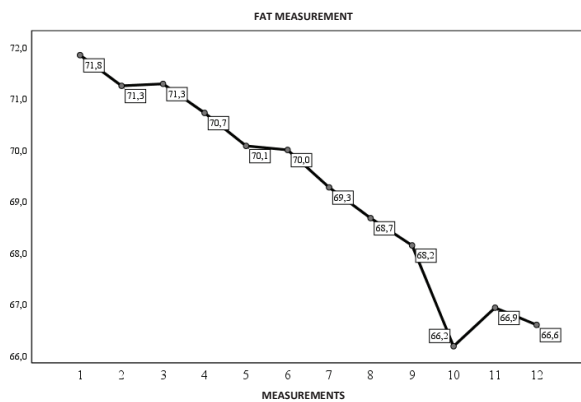


Figure 5: Average fat trend over time

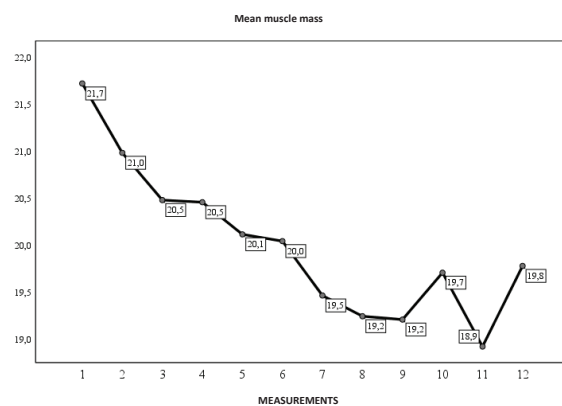


Figure 6: Trend in mean muscle mass over time

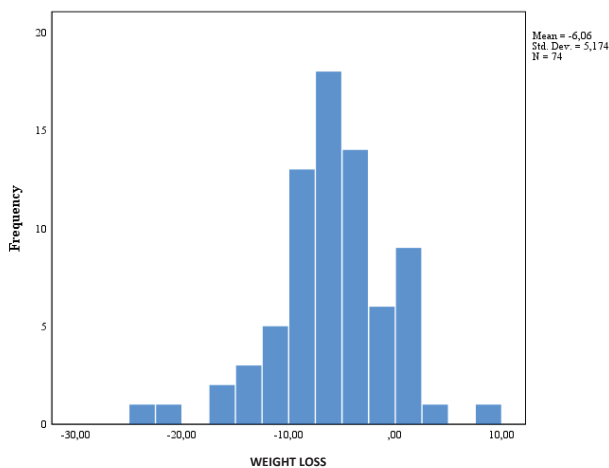


Figure 7: Percentage weight change

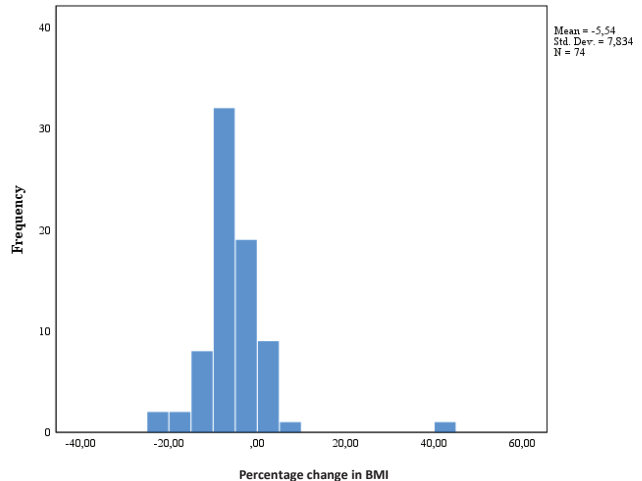


Figure 8: Percentage change in BMI

At the same time, as the intermediate period between measurements increased, the relative average values varied statistically significantly (Figure 5).

Finally, a steady decrease in the muscle mass perimeter of patients was observed, until the 9th measurement, when its mean value increased showing significant fluctuations thereafter ($F=3.294$, $p=0.018$). However, there were no statistically significant differences in patients' muscle mass circumference between measurements based on the Bonferroni tests.

The mean change in patients' body weight from the 1st to the last measurement was equal to -6.06% ($SD=5.17\%$), while the mean change in their Body Mass Index corresponded to -5.54% ($SD=7.83\%$). Of similar magnitude and equal to -5.43% ($SD=10.23\%$) and -6.27% ($SD=28.17\%$) were the mean changes in fat measurement and muscle mass circumference values of patients from

the 1st to the last measurement (Figure 7, 8, 9, 10).

The decrease in functional capacity of patients with pancreatic cancer, as well as the related dysphoric symptomatology due to the disease, presented fairly low levels, with the degree of assessment of the level of general health status and quality of life being at a moderate level.

The mean EORTC QLQ-C30 symptomatology scales scored low, as patients experienced low levels of nausea and vomiting (average = 4.50, T.A. = 15.43), constipation (mean = 3.65, $t=11.87$) and diarrhea (average = 3.15, $t=9.82$). Low were the levels of pain (mean = 10.36, $SD=24.00$), dyspnea (mean = 8.11, $SD=19.75$) and loss of appetite (mean = 15.32, $SD=28.24$), while slightly higher were the symptoms of fatigue (mean = 20.12, $SD=27.44$) and insomnia (mean = 21.62, $SD=26.71$). It is worth noting that the disease caused an increased de-

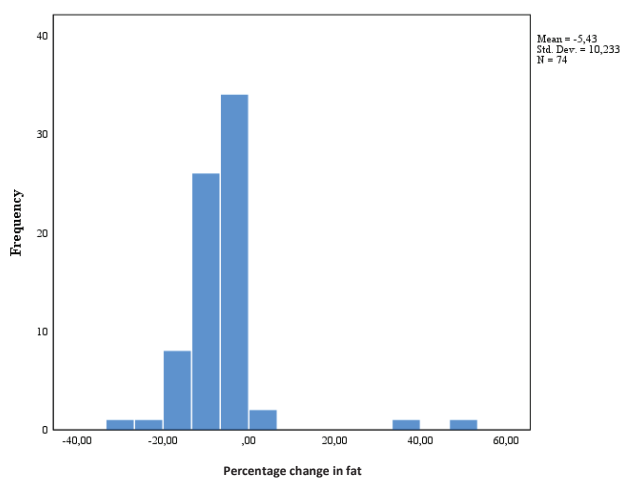


Figure 9: Percentage change in fat

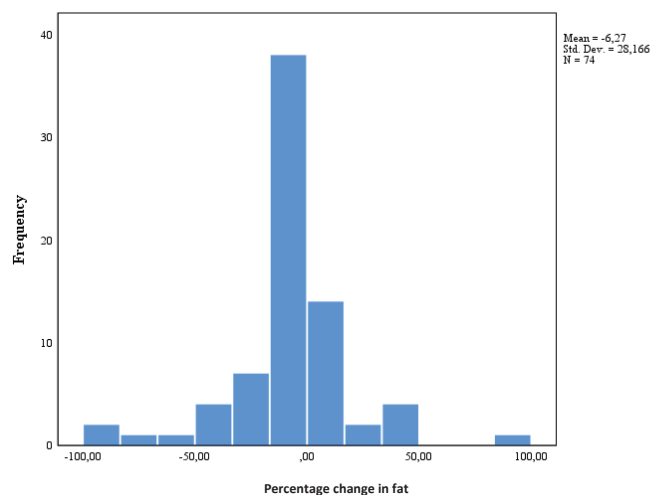


Figure 10: Percentage change in muscle mass

gree of financial problems (mean = 36.94, SD= 30.00).

Regarding the General Health/Quality of Life scale, the conclusion of its moderate relative assessed level was confirmed.

The comparison of the results showed that the only cases where a statistically significant association of Pearson was observed were between the percentage change in BMI and the level of cognitive function of patients ($r=-0.229$, $p=0.049$) and the percentage change in fat and pain symptoms ($r=0.267$, $p=0.021$).

The increase in the change in the weight of the patients led to a decrease in the level of their cognitive function, while at the same time, the increase in the change of their adipose tissue to increased levels of pain and vice versa.

Finally, no statistically significant effect of the change in patients' anthropometric measurements on EORTC QLQ-C30 scale scores was observed (table 1,2), except in the case of percentage change in fat at the level of pain symptoms ($F=5.033$, $p=0.028$).

Discussion

This is the first study in Greece that tried to investigate the effect of cachexia on the quality of life of patients with pancreatic cancer. Through periodic measurements, the occurrence of cachexia and its effect on the quality of life of 74 pancreatic cancer patients were recorded. Medical demographic and anthropometric

data were used, while the Greek version of the EORTC QLQ-C30 scale was used to measure the patients' quality of life.

According to international data,^{21,22} the incidence of pancreatic cancer is higher in men than in women, which was also observed in our study (63.5% men compared to 36.5% women). All study participants underwent some type of surgery. Overall, patients experienced an average weight loss of 6.08%. This change was expected postoperatively, mainly due to the catabolic process following such surgeries, which has been documented in numerous randomized studies.²³⁻²⁷ However, the continued steady weight loss recorded throughout our follow-up does not align with some other studies showing an increasing trend in patient weight six months post-surgery.^{28,29} The factors contributing to this discrepancy should be investigated further in the future.

More specifically, examining each parameter of the anthropometric data separately, we observe that while patients' Body Mass Index (BMI) initially appears to increase, it subsequently shows a steady downward trend, averaging a total reduction of 5.54%. Cachexia often leads to a decrease in BMI due to significant weight loss, loss of muscle mass, and alterations in fat distribution. This result agrees with similar studies concerning pancreatic cancer patients.³⁰⁻³²

Additionally, patients' fat measurement values decrease steadily, and the longer the period between

measurements, the more statistically significant the recorded reduction becomes. The final average reduction in fat tissue corresponds to 5.43%, reinforcing the results of other similar studies.^{27,32-34} Finally, a reduction is also observed in the circumference of patients' muscle mass, with an average recorded decrease of 6.27%, indicating the presence of sarcopenia, as documented in other related studies of pancreatic cancer patients.^{32,34-35}

Patients with advanced pancreatic cancer often experience substantial and rapid weight loss, which affects their physical well-being and quality of life.³⁶ A systematic review found a negative correlation between quality of life and weight loss in 23 out of 27 studies involving patients with cancer cachexia.³⁷ Another study highlights that pancreatectomies, even when performed without post-operative complications, significantly impact the quality of life of cancer patients.³⁸

The results of this study regarding quality of life in relation to cachexia and weight loss indicate that the reduction in functional ability of pancreatic cancer patients and the associated distressing symptoms due to the disease present fairly low levels. In contrast, the overall health status and quality of life are evaluated at a moderate level. Only the percentage change in fat was significantly statistically related to the level of pain experienced by patients ($F=5.033$, $p=0.028$), and the percentage change in BMI to the level of cognitive function ($r=-0.229$, $p=0.049$).

Regarding functionality scales, it is deemed that the disease has not significantly impacted the physical and emotional state of patients, a finding supported by other related studies.^{37,39-40} An additional systematic review indicated that weight loss negatively affects quality of life, as the loss of muscle mass is a major cause of fatigue, and weight loss is linked to decreased functional ability.⁴⁰

Overall, the results of our study regarding the impact

of cachexia on the quality of life of pancreatic cancer patients seem to align with some data from other research in the field, although not sufficiently supported.^{36,37,39,40}

A methodological limitation of this study is the limited sample size, resulting in reduced generalizability. Another limitation is the monocentric study design. Additionally, the study did not include data on patient diet and physical activity due to a lack of available data, which may have affected the results. Finally, the fact that the final assessment of the participants' quality of life was not conducted due to the COVID-19 pandemic limits its scientific contribution to the field.

Despite these limitations, the results of this study can contribute to the development of strategies for preventing and managing cachexia and sarcopenia in pancreatic cancer patients, leading to the adoption of practices that will reduce its negative impact on patients' quality of life.

Conclusions

It seems that cachexia is a complex disease which is a significant problem in patients with pancreatic cancer. It seems to worsen during their hospitalization, therefore, it is imperative to recognize and treat unintentional weight loss. Each component of its pathogenesis is a potential target for interventions to improve outcomes. In pancreatic cancer it is a multifactorial syndrome, and this makes the cooperation of many specialties from the health sector necessary. A beneficial proposal to address the problem is the implementation of ERAs protocols. These are rapid recovery protocols, as well as a set of guidelines for all stages of patient care. Their effectiveness is achieved through the harmonious cooperation of many specialties (such as surgery, anesthesiology team, cardiologists, pathologists, dieticians, endocrinologists, psychologists, nurses, etc.).

ΠΕΡΙΛΗΨΗ

Η επίδραση της καχεξίας στην ποιότητα ζωής ασθενών με καρκίνο παγκρέατος

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Εισαγωγή: Το 80% των ασθενών με προχωρημένο καρκίνο του γαστρεντερικού συστήματος παρουσιάζει καχεξία η οποία έχει σημαντική επίδραση στην επιβίωση και στην ποιότητα ζωής. Η μαζική απώλεια βάρους σε ασθενείς με καρκίνο του παγκρέατος είναι ένα σύμπτωμα που συχνά υπο- αξιολογείται.

Σκοπός: Στην παρούσα μελέτη διερευνήθηκαν οι επιπτώσεις της καχεξίας (με έμφαση στη μείωση του λιπώδους και του μυϊκού ιστού) στην ποιότητα ζωής ασθενών με καρκίνο παγκρέατος

Μέθοδος: Το δείγμα της έρευνας αφορούσε 74 ασθενείς με καρκίνο του παγκρέατος, οι οποίοι παρακολουθούνταν στο Α.Ν.Θ. «Θεαγένειο». Οι μετρήσεις πραγματοποιήθηκαν στον χώρο του νοσοκομείου. Η επιλογή των ασθενών ήταν τυχαία. Τα δεδομένα (ιατροδημογραφικά, ανθρωπομετρικά) καταγράφηκαν σε ειδική φόρμα και για την μέτρηση της ποιότητας ζωής χρησιμοποιήθηκε το ερωτηματολόγιο EORTC QLQ-C30.

Αποτελέσματα: Τα αποτελέσματα της έρευνας έδειξαν ότι οι μεταβολές του μέσου βάρους των ασθενών με καρκίνο του παγκρέατος μειώνονταν σταθερά, με τις διαφορές του βάρους να καθίστανται στατιστικά σημαντικές ($F=42,569$, $p<0,001$). Αντίστοιχα είναι τα αποτελέσματα της λιπομέτρησης ($F=10,081$, $p<0,001$) και της περιμέτρου της μυϊκής μάζας των ασθενών ($F=3,294$, $p=0,018$). Τα αποτελέσματα που αφορούσαν την ποιότητα της ζωής (EORTC QLQ-C30) δεν παρουσίασαν στατιστικά σημαντικές αλλαγές κατά τη διάρκεια των μετρήσεων.

Συμπεράσματα: Η καρκινική καχεξία αποτελεί ένα σοβαρό πολύπλευρο πρόβλημα των ασθενών με καρκίνο του παγκρέατος. Η διαχείρισή του απαιτεί έγκαιρη ανίχνευση, σωστές διατροφικές και μη συμβουλευτικές, συνεχή αξιολόγηση. Όλα αυτά μπορούν να επιτευχθούν μέσα από τη διεπιστημονική συνεργασία των επαγγελματιών υγείας.

Λέξεις Ευρητηρίου: καρκίνος παγκρέατος, καχεξία, διατροφικές διαταραχές, ποιότητα ζωής

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