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Serum Biomarkers and CT-Derived Muscle Indices in Sarcopenia Associated with Pancreatic Neoplasm: A Comparative Clinical Study

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Rezumat

Biomarkeri serici și indici musculari derivați din CT în sarcopenia asociată cu neoplasmul pancreatic: un studiu clinic comparativ

Introducere: Sarcopenia este o afecțiune frecventă şi clinic relevantă la pacienții cu neoplasm pancreatic, contribuind la un prognostic nefavorabil, toleranță redusă la tratament şi mortalitate crescută. Identificarea unor biomarkeri circulanți de încredere, alături de evaluarea masei musculare prin metode imagistice, poate îmbunătăți detecția precoce şi stratificarea riscului.
Metode: Acest studiu prospectiv randomizat a inclus 61 de pacienți, dintre care 36 prezentau neoplasm pancreatic asociat cu sarcopenie, iar 25 au constituit grupul de control. Nivelurile serice de osteonectină (SPARC), fragment C-terminal al agrinei (CAF), propeptid N-terminal al procolagenului de tip III (P3NP), miostatină (MSTN) şi factor de creştere asemănător insulinei-1 (IGF-1) au fost determinate prin metoda ELISA. Indicele masei musculare scheletice (SMI) şi indicele muşchiului psoas (PMI) au fost evaluate prin tomografie computerizată la nivelul vertebrei L3.
Rezultate: Pacienții cu neoplasm pancreatic şi sarcopenie au prezentat profile ale biomarkerilor semnificativ modificate comparativ cu grupul de control. Osteonectina (mediană 936,4 vs. 539,9, $p < 0,001$), CAF (2135,9 vs. 1165,5, $p < 0,001$), P3NP (8,01 vs. 5,34, $p < 0,001$), miostatina (47,71 vs. 7,85, $p < 0,001$) şi IGF-1 (142 vs. 106,7, $p < 0,001$) au fost toate crescute. Cele mai ridicate niveluri ale biomarkerilor au fost observate constant în grupul cu neoplasm pancreatic. În plus, 100% dintre pacienți au prezentat valori reduse ale SMI, confirmând prevalența ridicată a sarcopeniei. Nivelurile biomarkerilor nu au fost influențate semnificativ de localizarea tumorii.
Concluzii: Utilizarea combinată a biomarkerilor circulanți şi a indicilor musculari derivați din CT reprezintă o abordare clinic relevantă pentru identificarea sarcopeniei în cancerul pancreatic.

Cuvinte cheie: sarcopenie, neoplasm pancreatic, biomarkeri, osteonectină, CAF, P3NP, miostatină, IGF-1, tomografie computerizată, indicele masei musculare scheletice

Abstract

Background: Sarcopenia is a frequent and clinically relevant condition in patients with pancreatic neoplasm, contributing to poor prognosis, reduced therapeutic tolerance, and increased mortality. The identification of reliable circulating biomarkers, alongside imaging-based muscle assessment, may improve early detection and risk stratification.

Methods: This randomized prospective study included 61 patients, of whom 36 had pancreatic neoplasm associated with sarcopenia and 25 served as controls. Serum levels of osteonectin (SPARC), C-terminal agrin fragment (CAF), procollagen type III N-terminal peptide (P3NP), myostatin (MSTN), and insulin-like growth factor-1 (IGF-1) were measured using ELISA. Skeletal muscle index (SMI) and psoas muscle index (PMI) were assessed using CT at the L3 level.

Results: Patients with pancreatic neoplasm and sarcopenia showed significantly altered biomarker profiles compared to controls. Osteonectin (median 936.4 vs. 539.9, $p < 0.001$), CAF (2135.9 vs. 1165.5, $p < 0.001$), P3NP (8.01 vs. 5.34, $p < 0.001$), myostatin (47.71 vs. 7.85, $p < 0.001$), and IGF-1 (142 vs. 106.7, $p < 0.001$) were all elevated. The highest biomarker levels were consistently observed in the pancreatic neoplasm group compared to other disease groups. Additionally, 100% of patients with pancreatic neoplasm exhibited reduced SMI, confirming the high prevalence of sarcopenia. Biomarker levels were not significantly influenced by tumor location.

Conclusions: The combined use of circulating biomarkers and CT-derived muscle indices provides a clinically relevant approach for identifying sarcopenia in pancreatic cancer.

Keywords: sarcopenia, pancreatic neoplasm, biomarkers, osteonectin, CAF, P3NP, myostatin, IGF-1, computed tomography, skeletal muscle index

Introduction

Pancreatic cancer represents the fourth leading cause of cancer-related mortality worldwide in both men and women (1). Despite therapeutic advances, the 5-year survival rate remains poor, with fewer than 20% of patients eligible for surgical treatment and approximately 80% presenting with advanced-stage disease at the time of diagnosis (2). The therapeutic response in patients with pancreatic neoplasm depends not only on tumor morphology but is also influenced by nutritional status. Before or during treatment, patients frequently experience metabolic alterations and significant weight loss. Therefore, the assessment of nutritional status is essential for determining the optimal therapeutic strategy, aiming to achieve prolonged survival with an acceptable quality of life (3).

Sarcopenia is defined as the progressive loss of muscle mass and strength associated with aging and has been shown to influence the prognosis of patients with various conditions, particularly malignancies. The incidence of sarcopenia in patients with pancreatic cancer is higher compared to other neoplastic diseases (4), possibly due to the activation of a pronounced inflammatory response characterized by catabolic mechanisms. Exocrine pancreatic insufficiency further contributes to malnutrition and weight loss, as pancreatic enzymes are essential for the digestion and absorption of fats and fat-soluble vitamins; their deficiency results in steatorrhea and severe maldigestion (5). *Fig. 1* presents the main risk factors associated with sarcopenia, including aging, genetics, hormonal changes, inflammation, chronic conditions, neurological disorders, mitochondrial dysfunction, abdominal obesity, physical

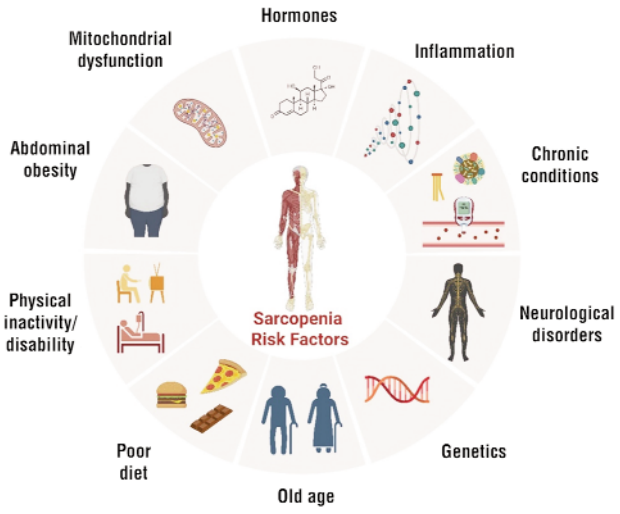

Figure 1. Risk factors for Sarcopenia. Created in https://BioRender.com (6)

inactivity or disability, and poor diet. These factors are illustrated as contributing elements surrounding the central concept of sarcopenia.

A system based on the evaluation of biomarkers related to cancer-associated cachexia could represent a valuable tool for monitoring and prognostic assessment. A variety of potential markers have been identified to date, including cachexia-inducing factors (5,6), pro-inflammatory cytokines (7,8), lipids (9), as well as proteins or lipid degradation products (10); however, none have met the required standards for widespread clinical use.

Regarding the utility of computed tomography in assessing muscle quality and mass, it is considered one of the most reliable techniques, given its extensive role in the screening, diagnosis, and monitoring of various acute and chronic conditions. One of the simplest methods for estimating skeletal muscle mass involves calculating the SMI and PMI at the level of the L3-L4 vertebrae, with muscle tissue attenuation values ranging between 29 and 150 Hounsfield Units (HU) (11). CT measurements can be performed by manually delineating regions of interest (ROI) on non-contrast scans, considering the increase in muscle attenuation values on post-contrast scans due to iodine uptake, which is why these are not taken into account (12). Common SMI cut-off values range from 52–55 cm^2/m^2 in males and 39–41 cm^2/m^2 in females (13), while PMI cut-off values are above 6.31 cm^2/m^2 in males and 3.91 cm^2/m^2 in females (14); however, there is currently no consensus regarding standardized threshold values.

Materials and Methods

Study Design

This randomized prospective study included a total of 61 patients admitted to the County Emergency Clinical Hospital between January 2022 and December 2023. The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Sf. Apostol Andrei County Emergency Hospital from Constanta, Romania, approval number 05/04.02.2022.

Inclusion and Exclusion Criteria

Patients were included if they had been admitted to the County Emergency Clinical Hospital between January 2022 and December 2023, aged between 45 and 84 years, and had complete clinical and paraclinical data available. Of the total cohort, 36 patients were clinically and paraclinically diagnosed with pancreatic neoplasm and sarcopenia according to the criteria of the European Working Group on Sarcopenia in Older People (EWGSOP) (15). The remaining 25 healthy individuals constituted the control group, with no known chronic diseases (10 males and 15 females). The diagnosis of pancreatic neoplasm was established based on clinical, imaging (contrast-enhanced CT), and endoscopic ultrasound (EUS) findings, with histopathological confirmation obtained through EUS-guided biopsy in the majority of cases where feasible.

Exclusion criteria comprised immobilized patients, those diagnosed with autoimmune diseases, and individuals with severe conditions affecting quality of life, including liver cirrhosis, heart failure, uremia, or septic shock.

Data Collection and Imaging Assessment

Blood samples were obtained by venipuncture, and biomarkers were quantified immediately. The remaining plasma was stored at −80°C for subsequent analyses. Levels of SPARC, CAF, procollagen P3NP, MSTN, and IGF-1 were determined using enzyme-linked immunosorbent assays (ELISA) (16), according to the manufacturer's protocol.

For imaging assessment of muscle quality and mass, computed tomography scans of the upper abdomen were performed. The SMI and PMI were measured on non-contrast scans at the level of the L3 vertebral body by delineating ROI. The cut-off values used were 52–55 cm^2/m^2 in males and 39–41 cm^2/m^2 in females for SMI, and a maximum of 6.31 cm^2/m^2 in males and 3.91 cm^2/m^2 in females for PMI (17).

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics 25 and Microsoft Office Excel/Word 2021 (18). Qualitative variables were expressed as absolute values or percentages, and differences between groups were assessed using Fisher's Exact Test. Z-tests with Bonferroni correction were applied to further analyze contingency table results (19).

Quantitative variables were expressed as means with standard deviations or medians with inter-percentile ranges, and their distribution was assessed using the Shapiro-Wilk test (21). Quantitative variables with normal distribution were compared between groups using One-Way ANOVA or Welch ANOVA (depending on variance homogeneity assessed by Levene's test), followed by Games-Howell post hoc tests. Non-parametric quantitative variables were analyzed using the Kruskal-Wallis H test, followed by Dunn-Bonferroni post hoc tests (22).

Results

Distribution According to Population Characteristics

Of the total 61 patients included in the study, 36 (59.01%) were clinically and paraclinically diagnosed with pancreatic neoplasm and sarcopenia. The study cohort consisted of 27 males (75%) and 9 females (25%), aged between 45 and 85 years (mean age: 65.38 years).

The data presented in *Table 1* illustrate the comparison of patient age across the study groups. Age distribution was normal in all groups, as confirmed by the Shapiro–Wilk test ($p > 0.05$). Differences between groups were statistically significant according to the Welch ANOVA test ($p = 0.029$).

A predominance of male patients was observed in both groups, more pronounced in the pancreatic neoplasm group (72.2%) compared to the control group (55%). Conversely, females represented a higher proportion in the control group (44%) than in patients with pancreatic neoplasm (27.7%). However, these differences did not reach statistical significance, as indicated by the p-value ($p = 0.150$).

Distribution According to Biomarkers

Tumor staging was assessed according to the TNM classification. The majority of patients presented with advanced-stage disease, with most cases classified as stage III–IV, reflecting the late diagnosis typical of pancreatic malignancies.

Patients with pancreatic neoplasm exhibited markedly higher osteonectin values, with a median of 936.4 (IQR: 803.5–1168.1), compared to 539.9 (IQR: 482.7–635) in the control group. This difference was statistically significant, as indicated by the Kruskal-Wallis test ($p < 0.001$). Additionally, the mean rank was substantially higher in the pancreatic neoplasm group (84.93) compared to controls (22.70), further supporting the presence of elevated osteonectin levels in affected patients.

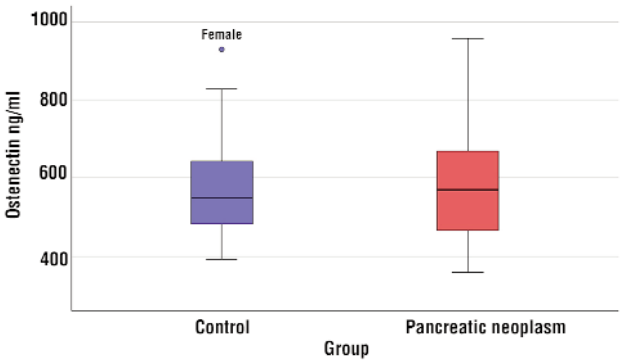

Figure 2. Comparison of osteonectin values across the study groups

Patients with pancreatic neoplasm exhibit higher osteonectin values compared to controls, as reflected by a higher median and an upward shift of the entire distribution (*Fig. 2*). The median osteonectin level is increased in the neoplasm group, consistent with the statistical findings reported in the table. Additionally, the interquartile range appears wider in the pancreatic neoplasm group, indicating greater variability in biomarker levels among affected patients. The control group shows lower and more tightly distributed values, suggesting a more homogeneous physiological range. An outlier is observed in the control group (labeled "Female"), indicating an isolated high value that does not reflect the general distribution.

Patients with pancreatic neoplasm showed markedly higher CAF values, with a median of 2135.9 (IQR: 1769.2 -2805.6), compared to 1165.5 (IQR: 1024.6-1369.4) in the control group (*Table 1*). This difference was statistically significant ($p < 0.001$), as indicated by the Kruskal-Wallis test. Furthermore, the mean rank was substantially higher in the pancreatic neoplasm group (62.12) compared to controls (25.78), confirming a consistent upward shift in CAF levels among affected patients. The non-normal distribution of the data, verified by

Table 1. Clinical and biomarker comparison between study groups

Parameter	Control group (n = 25) Median (IQR)	Pancreatic neoplasm group (n = 36) Median (IQR)	p-value
Age (years)	65 (56–69.25)	58.5 (48–70)	0.029
Male sex, n (%)	14 (55%)	26 (72.2%)	0.150
Osteonectin	539.9 (482.7–635)	936.4 (803.5–1168.1)	<0.001
CAF	1165.5 (1024.6–1369.4)	2135.9 (1769.2–2805.6)	<0.001
P3NP	5.34 (4.6–5.9)	8.01 (7.08–9.07)	<0.001
Myostatin	7.85 (6.02–15.78)	47.71 (34.33–76.9)	<0.001
IGF-1	106.7 (84–129)	142 (98.9–181.2)	<0.001
Reduced SMI, n (%)	–	36 (100%)	–

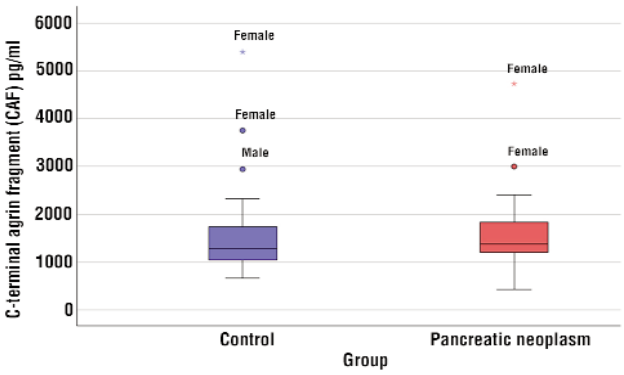

Figure 3. Comparison of CAF values across the study groups

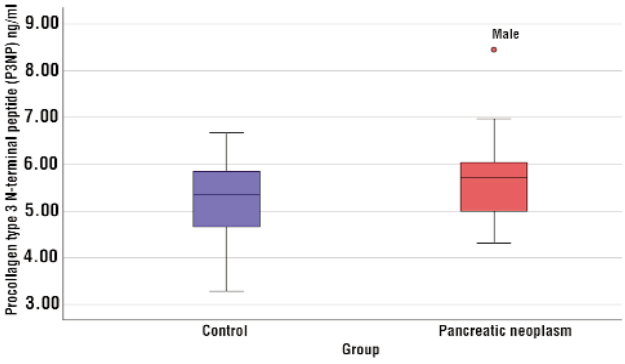

Figure 4. Comparison of P3NP values across the study groups

the Shapiro-Wilk test, supports the use of non-parametric statistical analysis.

Patients with pancreatic neoplasm demonstrate higher CAF values compared to controls, as indicated by a higher median and an overall upward shift in the distribution. The median CAF level is clearly increased in the neoplasm group, consistent with the statistically significant difference reported in the table ($p < 0.001$). Additionally, the interquartile range appears slightly wider in the pancreatic neoplasm group, suggesting increased variability in biomarker levels among affected patients (*Fig. 3*). The control group shows lower median values with a more compact distribution, although several high-value outliers are present. Notably, both groups include extreme outliers (labeled by sex), particularly among female patients, indicating that some individuals exhibit markedly elevated CAF levels beyond the typical range.

The data in *Fig. 4* illustrate the comparison of P3NP values across the analyzed study groups. There is a statistically significant difference in P3NP levels between the control group and patients with pancreatic neoplasm. Patients with pancreatic neoplasm exhibited markedly higher P3NP values, with a median of 8.01 (IQR: 7.08-9.07), compared to 5.34 (IQR: 4.6-5.9) in the control group. This difference was highly significant ($p < 0.001$), as indicated by the Kruskal-Wallis test. The mean rank was substantially higher in the pancreatic neoplasm group (84.73) compared to controls (20.28), indicating a consistent elevation of P3NP levels in affected patients. The non-normal distribution of the data, confirmed by the Shapiro-Wilk test, justified the use of non-parametric statistical methods.

The data presented in *Fig 5* illustrate the compari-son of myostatin values across the analyzed study groups.

Patients with pancreatic neoplasm exhibited markedly higher myostatin values, with a median of

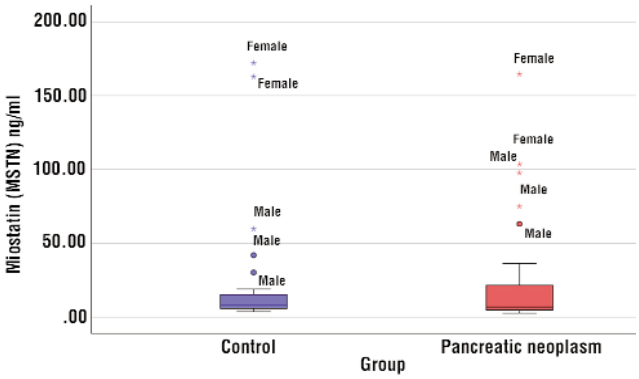

Figure 5. Comparison of myostatin values across the study groups

47.71 (IQR: 34.33-76.9), compared to 7.85 (IQR: 6.02-15.78) in the control group. This difference was highly significant ($p<0.001$), according to the Kruskal-Wallis test. The mean rank was substantially higher in the pancreatic neoplasm group (87.33) compared to controls (30.27), indicating a consistent elevation of myostatin levels in affected patients. The Shapiro-Wilk test confirmed a non-normal distribution of the data, supporting the use of non-parametric statistical methods.

Patients with pancreatic neoplasm show higher and more widely distributed myostatin values compared to the control group. Although the median values appear relatively close, the upper range and variability are clearly greater in the neoplasm group, indicating a broader dispersion of elevated values. This is consistent with the statistical findings, where significantly higher overall levels were observed in patients with pancreatic neoplasm. The control group demonstrates lower and more tightly clustered values, suggesting a more homogeneous physiological distribution. In contrast, the pancreatic neoplasm

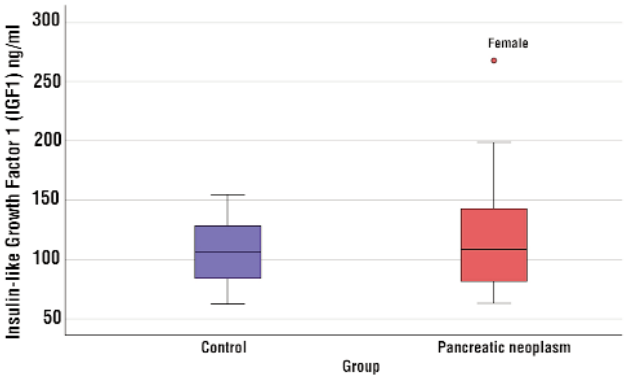

Figure 6. Comparison of IGF-1 values across the study groups

group exhibits multiple high-value outliers, affecting both males and females, with some extreme elevations exceeding 150 ng/mL.

The data presented *Fig. 6* illustrate the comparison of IGF-1 values across the analyzed study groups.

Patients with pancreatic neoplasm exhibited higher IGF-1 values, with a median of 142 (IQR: 98.9–181.2), compared to 106.7 (IQR: 84–129) in the control group. The mean rank was also higher in the pancreatic neoplasm group (69.45) compared to controls (40.22), suggesting an overall increase in IGF-1 levels among affected patients. The Shapiro-Wilk test indicated a non-normal distribution of the data, supporting the use of non-parametric statistical analysis.

Patients with pancreatic neoplasm show slightly higher IGF-1 values compared to the control group, as reflected by a modest increase in the median. However, the difference between groups appears less pronounced than for other biomarkers. The interquartile range is wider in the pancreatic neoplasm group, indicating greater variability in IGF-1 levels among affected patients. The control group demonstrates a more compact distribution, suggesting more homo-geneous values within the physiological range. In contrast, the pancreatic neoplasm group presents a broader spread and includes a high-value outlier (noted in a female patient), which contributes to the increased variability observed in this group.

Of the total number of sarcopenic patients included in the study, 30 exhibited decreased SMI and PMI values below the reference limits (*Figs. 7* and *8*), a finding more frequently observed in males (24 males and 6 females).

Distribution According to Tumor Location

Fig. 9 illustrates the distribution of age and sex across different anatomical locations of pancreatic neoplasm (cephalic, corporal, and caudal) in the study group.

Patients across all tumor locations fall predominantly within the middle-aged to elderly range, with most values clustering between approximately 45 and 75 years. No clear age gradient is observed between tumor locations, suggesting that tumor localization does not appear to be strongly associated with patient age in this cohort. Regarding sex distribution, both males and females are represented across all anatomical subgroups, although a slight predominance of males can be observed, particularly in cephalic and corporal localizations. Female patients are present in all groups but appear less frequent overall. Importantly, there is no evident pattern indicating that a specific tumor location is associated with a particular sex.

The data presented in *Table 2* and *Fig. 10* shows the comparison of osteonectin values in patients with pancreatic neoplasm according to tumor location.

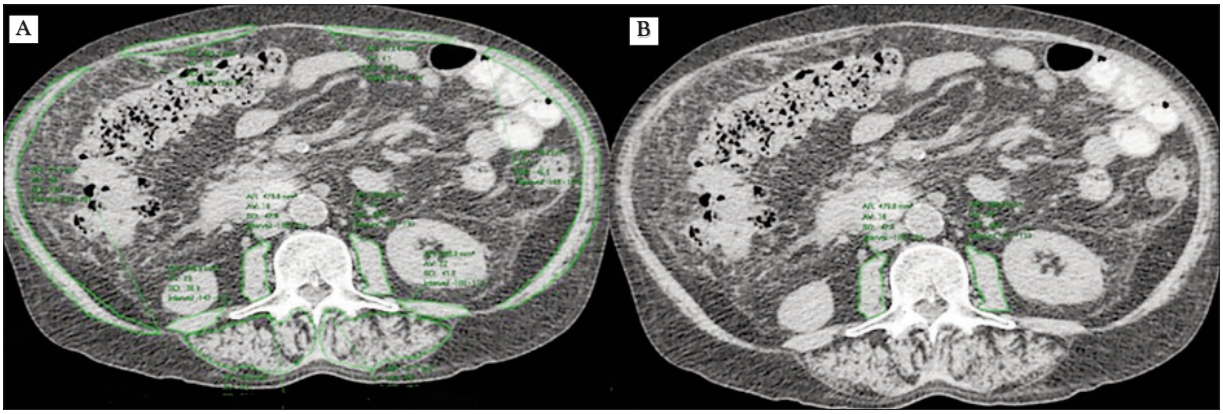

Figure 7. Native axial CT images showing SMI = 35.28 cm²/m² **(A)** and PMI = 3.01 cm²/m² **(B)**.

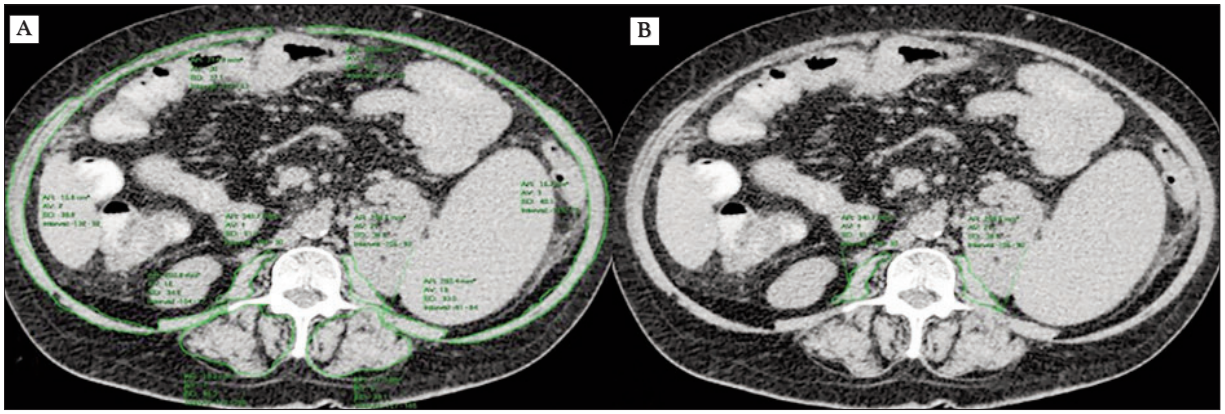

Figure 8. Native axial CT images showing SMI = 30 cm²/m² **(A)** and PMI = 2.35 cm²/m² **(B)**.

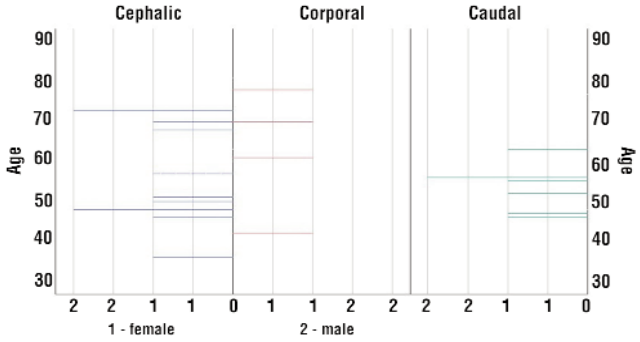

Figure 9. Age and sex distribution according to pancreatic tumor localization

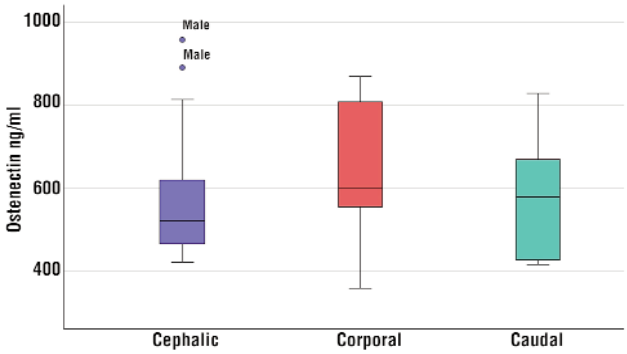

Figure 10. Comparison of osteonectin values in patients with pancreatic neoplasm according to tumor location

The distribution of osteonectin values was non-parametric in patients with cephalic localization, as indicated by the Shapiro-Wilk test (p=0.007).

Differences between groups were not statistically significant according to the Kruskal-Wallis H test (p=0.577), indicating that osteonectin values did not differ significantly based on tumor location.

The data presented in *Fig. 11* highlight the comparison of CAF values in patients with pancreatic neoplasm according to tumor location.

The distribution of CAF values was normal across all groups, as indicated by the Shapiro-Wilk test ($p > 0.05$).

Differences between groups were not statistically significant based on the Welch ANOVA test ($p = 0.213$), indicating that CAF values did not differ significantly according to tumor location.

The data presented in *Fig. 12* present the comparison of P3NP values in patients with pancreatic neoplasm according to tumor location.

Table 2. Biomarker distribution according to tumor localization

Parameter	Cephalic Median (IQR)	Corporal Median (IQR)	Caudal Median (IQR)	p-value
Osteonectin	844.4 (772.9–1097.5)	1013.6 (910.5–1235.8)	917.5 (821.6–1258.5)	0.577
CAF	2271.8 (1801.5–2868.5)	2489.1 (1374.8–3749.1)	1945.2 (1660.4–2341.9)	0.213
P3NP	8.65 (7.27–9.89)	7.68 (7.01–8.01)	8.51 (6.62–9.06)	0.422
Myostatin	50 (34.05–76.9)	55.8 (40.25–136.56)	45.4 (32.15–88)	0.691
IGF-1	142 (125–178.71)	136.26 (91–208.5)	123.17 (95.14–166)	0.452
Reduced SMI, n (%)	14 (100%)	6 (100%)	10 (100%)	–

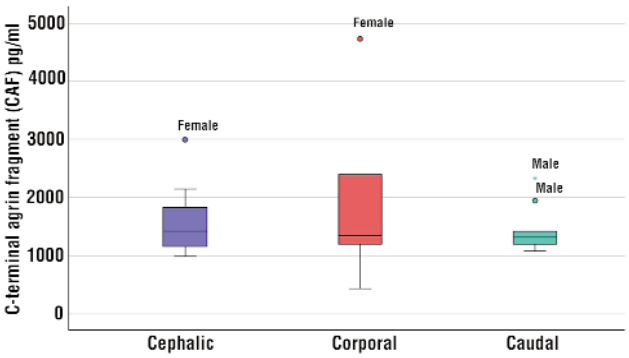

Figure 11. Comparison of CAF values in patients with pancreatic neoplasm according to tumor location

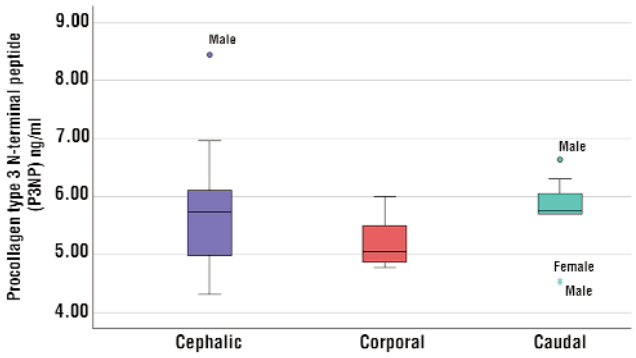

Figure 12. Comparison of P3NP values in patients with pancreatic neoplasm according to tumor location

The distribution of P3NP values was normal across all groups, as indicated by the Shapiro-Wilk test ($p > 0.05$).

Differences between groups were not statistically significant based on the One-Way ANOVA test ($p = 0.422$), indicating that P3NP values did not differ significantly according to tumor location.

The data presented *Fig. 13* offer a comparison of myostatin values in patients with pancreatic neoplasm according to tumor location.

The distribution of myostatin values was non-parametric in patients with caudal localization, as indicated by the Shapiro–Wilk test ($p = 0.008$).

Differences between groups were not statistically significant based on the Kruskal-Wallis H test ($p = 0.691$), indicating that myostatin values did not differ significantly according to tumor location.

The data presented in *Fig. 14* show the comparison of IGF-1 values in patients with pancreatic neoplasm according to tumor location.

The distribution of IGF-1 values was normal across all groups, as indicated by the Shapiro-Wilk test ($p > 0.05$).

Differences between groups were not statistically significant ($p = 0.452$), indicating that IGF-1 values did not differ significantly according to tumor location.

All patients included in the pancreatic neoplasm group met the diagnostic criteria for sarcopenia, which explains the uniform presence of reduced SMI values across all tumor locations. Therefore, no comparative differences could be identified based on tumor localization.

Fig. 15 highlights the distribution of patients with pancreatic neoplasm according to SMI values and tumor location, showing a uniform pattern across all anatomical subgroups.

Table 3 shows that all patients, regardless of tumor localization (cephalic, corporeal, or caudal), presented

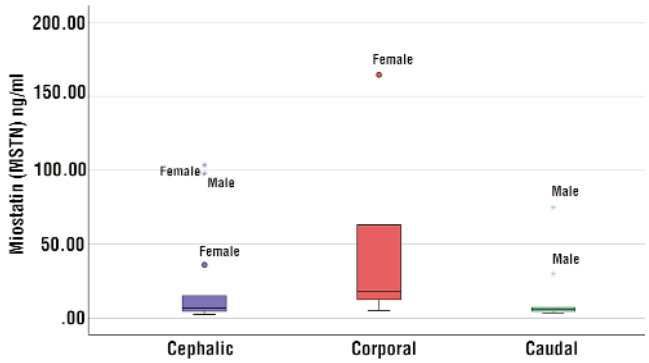

Figure 13. Comparison of myostatin values in patients with pancreatic neoplasm according to tumor location

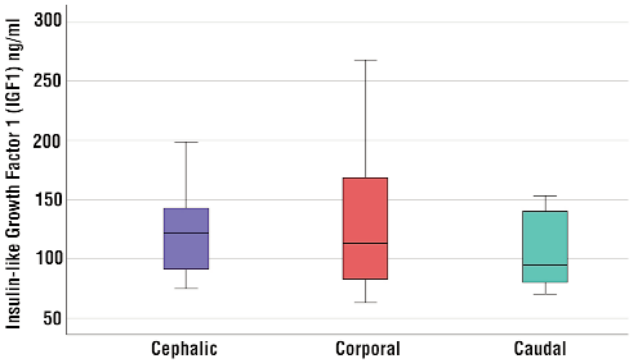

Figure 14. Comparison of IGF-1 values in patients with pancreatic neoplasm according to tumor location

Table 3. Distribution of patients with pancreatic neoplasm according to SMI values and tumor location

SMI value/Localisation (No., %)	Cephalic	Corporal	Caudal	p*
Normal	0 (0%)	0 (0%)	0 (0%)	-
Decreased	14 (100%)	6 (100%)	10 (100%)	

*Fisher's Exact Test

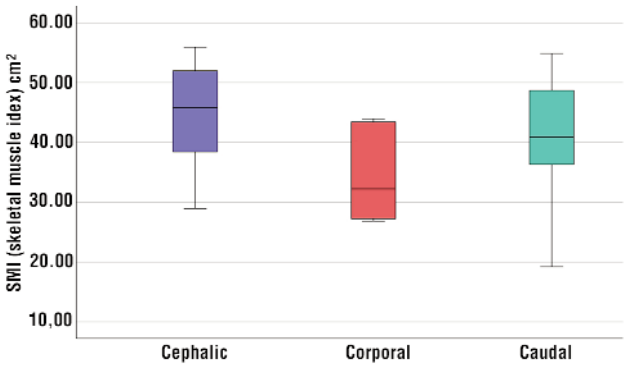

Figure 15. Distribution of patients with pancreatic neoplasm according to SMI values and tumor location

decreased SMI values (100%), with no cases of normal SMI identified. This homogeneous distribution indicates that reduced skeletal muscle mass is consistently present across all tumor locations, suggesting that sarcopenia is a generalized characteristic in this patient population rather than being influenced by the anatomical site of the pancreatic tumor.

Discussion

The present study characterizes the biomarker profile and imaging-derived muscle indices in patients with pancreatic neoplasm and sarcopenia, highlighting the potential utility of combining biochemical and imaging parameters in this specific clinical context. Our findings demonstrated markedly elevated levels of SPARC, CAF, P3NP, myostatin, and IGF-1 in patients with pancreatic neoplasm compared to controls, alongside a universal reduction in SMI, reinforcing the high prevalence of sarcopenia in this population. These results are consistent with recent literature, which accentuates sarcopenia as a frequent and prognostically unfavorable condition in pancreatic cancer.

Recent studies have reported sarcopenia prevalence rates ranging between 40% and 70% in pancreatic cancer patients, with strong associations with reduced survival and increased postoperative complications (23–25). In our cohort, the observation that 100% of patients exhibited decreased SMI suggests an even higher burden, likely reflecting advanced disease stages or metabolic derangements characteristic of pancreatic malignancies.

The elevated osteonectin levels identified in our study align with findings by Guweidhi et al. (2022), who demonstrated increased SPARC expression in pancreatic cancer patients with cachexia, correlating with extracellular matrix remodeling and tumor progression. Similarly, CAF has emerged as a reliable biomarker of neuromuscular junction degradation, with elevated levels reported in cancer-associated sarcopenia (27, 28). Our observation of significantly higher CAF levels in pancreatic neoplasm patients supports its role as an indicator of muscle degradation severity.

P3NP, a marker of collagen turnover, was also significantly increased in our cohort. This is consistent with recent reports indicating that elevated P3NP reflects increased muscle fibrosis and remodeling in sarcopenic patients with malignancies (29,30). The particularly high levels observed in pancreatic neoplasm cases further suggest a more aggressive catabolic state compared to other cancer types.

Myostatin, a well-known negative regulator of muscle growth, was markedly elevated in our study group. This finding corroborates previous evidence demonstrating that increased myostatin levels contribute to muscle wasting in cancer cachexia (31,32). Experimental studies conducted by Wagner et al. (33) and Wetzlich et al. [34] have also also shown that myostatin inhibition may attenuate muscle loss, highlighting its potential as a therapeutic target.

Interestingly, IGF-1 levels were also elevated in our pancreatic cancer cohort. While IGF-1 is generally considered anabolic, recent studies suggest a complex, context-dependent role in cancer, where increased levels may reflect compensatory mechanisms or tumor-related metabolic alterations (35). This dual role may explain the variability observed across studies.

From an imaging perspective, CT-derived SMI remains the gold standard for sarcopenia assessment. Our findings are consistent with recent meta-analyses demonstrating that reduced SMI is independently associated with poorer outcomes in pancreatic cancer patients (36,37). The lack of variation in biomarker levels according to tumor location further supports the concept that sarcopenia in pancreatic cancer is a systemic process rather than a localized phenomenon (38).

Compared to other malignancies, such as colorectal cancer, our results indicate a more pronounced alteration in both biomarkers and muscle indices in pancreatic neoplasm, which has also been reported in recent comparative studies (39,40). This may be explained by the unique metabolic and inflammatory profile of pancreatic cancer, including exocrine insufficiency and profound systemic inflammation (41).

The present study has several limitations that should be acknowledged. First, the relatively small sample size, particularly within subgroup analyses based on tumor localization, may limit statistical power and reduce the generalizability of the findings.

Second, differences between study groups may

introduce potential bias, as the control group consisted of healthy individuals, which may not fully reflect the complexity of clinical populations.

Third, due to the sample size and dataset structure, multivariate analyses adjusting for potential confounding factors could not be performed. Important variables such as tumor stage, body mass index, inflammatory status, and prior oncological treatments were not included in adjusted models. Future studies with larger cohorts should address these aspects to provide a more comprehensive evaluation.

Another limitation of the present study is the absence of additional comparison groups, such as patients with pancreatic neoplasm without sarcopenia or patients with sarcopenia in the absence of malignancy, which would have enhanced the generalizability and comparative strength of the findings.

Thus, our study reinforces the growing evidence that a multimodal approach combining circulating biomarkers with imaging parameters offers improved diagnostic and prognostic value in sarcopenia associated with pancreatic cancer. However, the lack of standardized cut-off values and biomarker specificity remains a limitation. Future research should focus on validating these biomarkers in larger cohorts and integrating them into clinical risk stratification models.

Conclusions

This study describes the biochemical and imaging characteristics of patients with pancreatic neoplasm and sarcopenia, demonstrating significantly altered biomarker profiles and reduced muscle indices within this predefined cohort. Patients with pancreatic cancer exhibited significantly elevated levels of osteonectin, CAF, P3NP, myostatin, and IGF-1 compared to controls, indicating a pronounced catabolic and inflammatory state contributing to muscle degradation. Among these biomarkers, CAF, P3NP, and myostatin showed the most marked increases, suggesting their potential utility as indicators of muscle wasting severity in this patient population.

From an imaging perspective, the consistent reduction of SMI across all included patients reflects the predefined inclusion criteria and underscores the importance of systematic muscle assessment in this population. Additionally, decreased PMI values were observed in the majority of cases, further supporting the presence of significant muscle loss. Importantly, biomarker levels and imaging indices were not influenced by tumor location, indicating that sarcopenia represents a systemic manifestation of pancreatic malignancy rather than a localized effect.

Clinically, these findings highlight the importance of early detection and comprehensive assessment of sarcopenia in patients with pancreatic cancer. The combined use of circulating biomarkers and CT-derived muscle indices may improve risk stratification, guide therapeutic decisions, and ultimately contribute to better patient management and outcomes.

Conflicts of Interest

The authors declare that they have no conflicts of interest regarding the publication of this article. The authors confirm that there are no financial, personal, or institutional relationships that could inappropriately influence or bias the work reported in this manuscript.

Ethical Statement

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of "Sf. Apostol Andrei" County Emergency Hospital, Constanța, Romania (approval number 05/04.02.2022). All participants were informed about the study protocol, and written informed consent was obtained prior to inclusion. Patient confidentiality and data protection were strictly maintained throughout the study. No identifying personal information is disclosed in this manuscript.

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