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## Evaluation of markers of oxidative and nitrosative stress in the blood of patients with neuroendocrine tumors

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*pharmaceuticals*



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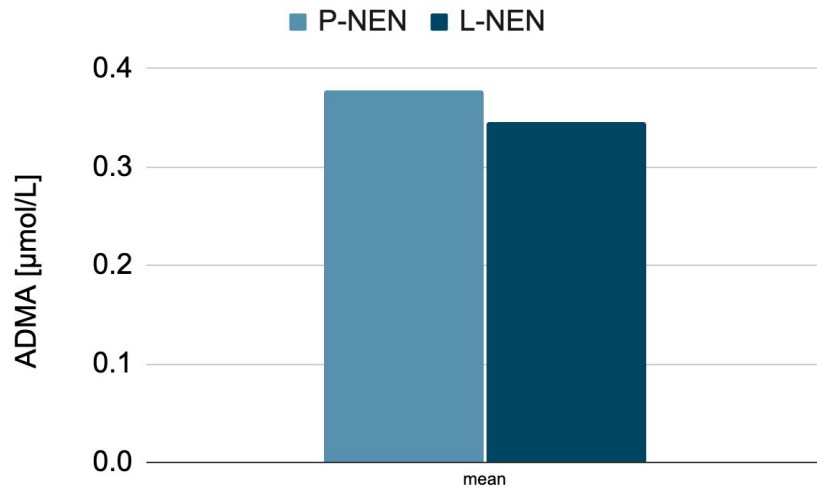
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## Evaluation of markers of oxidative and nitrosative stress in the blood of patients with neuroendocrine tumors

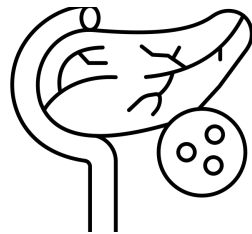
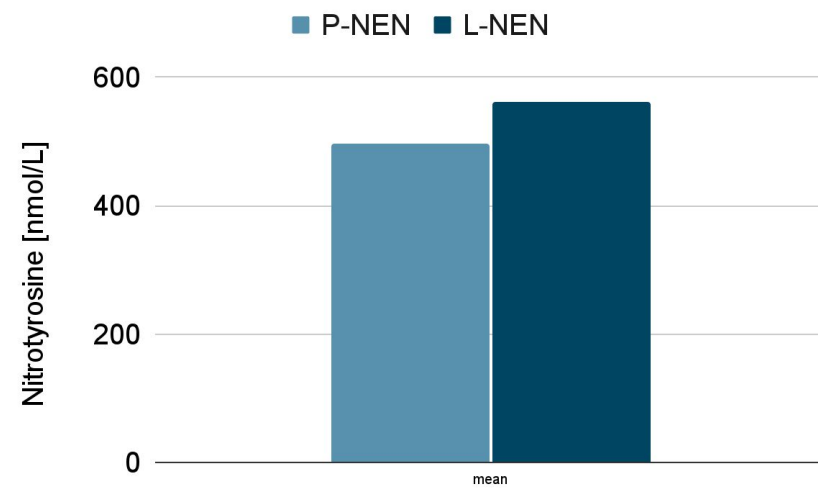
### Graphical Abstract



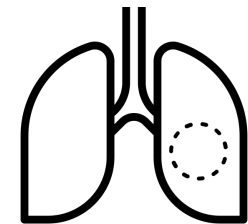
nitrosative  
stress



oxidative  
stress



PANCREATIC TUMOR



LUNG TUMOR



## **Abstract:**

Neuroendocrine neoplasms (NENs) are tumors arising from cells of the endocrine and nervous systems, found in various organs. Both nitrotyrosine and asymmetric dimethylarginine (ADMA) have significant effects on carcinogenesis, inducing oxidative and nitrosative stress and changes in proteins, lipids, and DNA. This study aimed to assess nitrotyrosine and ADMA levels in NEN patients based on tumor location, potentially improving diagnostic and therapeutic approaches.

Participants were divided into two subgroups, each with 10 patients. The first subgroup had pancreatic NENs (P-NENs), and the second had lung NENs (L-NENs). Venous blood samples were collected and processed to obtain blood serum. Nitrotyrosine and ADMA levels were measured using enzyme-linked immunosorbent assay (ELISA) tests. Results are presented as mean values with  $\pm$  standard error of the mean (SEM). A *p*-value less than 0.05 was considered statistically significant.

In the P-NEN group, nitrotyrosine averaged  $495.888 \pm 105.538$  nmol/L, while the L-NEN group had levels of  $561.587 \pm 158.929$  nmol/L. The ADMA concentration was  $0.378 \pm 0.027$   $\mu$ mol/L in the P-NEN patients and  $0.346 \pm 0.013$   $\mu$ mol/L in the L-NEN group. Statistical analysis revealed no significant differences between the two groups for both analytes. Based on current findings, tumor location does not significantly impact nitrotyrosine and ADMA levels in NEN patients. Further research with larger, diverse samples may offer valuable insights into their relationship, potentially enhancing NEN diagnostic and therapeutic approaches.

**Keywords:** biomarkers, neuroendocrine neoplasms, nitrosative stress, oxidative stress



## **Introduction**

Neuroendocrine neoplasms (NENs) are tumors originating from cells of both the endocrine and nervous systems and can develop in a variety of organs throughout the body. NENs account for about 0.5% of all cancers. Both nitrotyrosine and asymmetric dimethylarginine (ADMA) have significant effects on carcinogenesis. Studies show that reactive intermediates may undergo numerous chemical modifications, forming a number of chemical derivatives that induce oxidative and nitrosative stress and changes in proteins, lipids, and DNA.



## **Introduction - materials and methods**

This study involved 20 patients with NENs. The participants were divided into two subgroups, with 10 patients in each group. The first subgroup comprised patients with pancreatic NENs (P-NENs), while the second subgroup included patients with lung NENs (L-NENs). Venous blood samples were collected and processed in the laboratory to obtain blood serum. Nitrotyrosine and ADMA levels were measured using ready-to-use enzyme-linked immunosorbent assay (ELISA) tests. The results are presented as mean values with  $\pm$  standard error of the mean (SEM). A *p*-value of less than 0.05 was considered statistically significant.



## Introduction - characteristics of the study participants

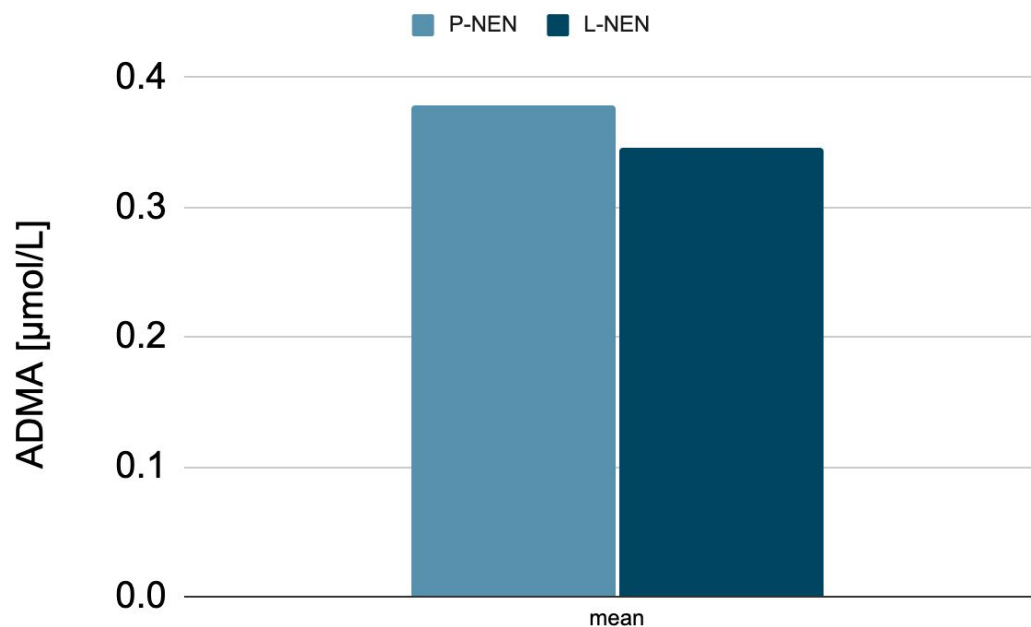
Anthropometric characteristic of the patients with pancreas and lung cancer divided according to the localization of the tumor. Each value is mean  $\pm$  SEM.

	P-NEN	L-NEN	<i>p</i> -value
<i>n</i>	10	10	---
Sex (f/m)	6/4	5/5	0.673320
Age [yrs]	63.5 $\pm$ 3.76	56.5 $\pm$ 2.86	0.966692
Body mass [kg]	84.50 $\pm$ 1.22	80.50 $\pm$ 3.67	0.351104
Height [cm]	171.4 $\pm$ 2.01	173.0 $\pm$ 2.71	0.503448
BMI [kg/m <sup>2</sup> ]	28.05 $\pm$ 0.73	26.35 $\pm$ 1.45	0.765857



## Results and discussion - ADMA

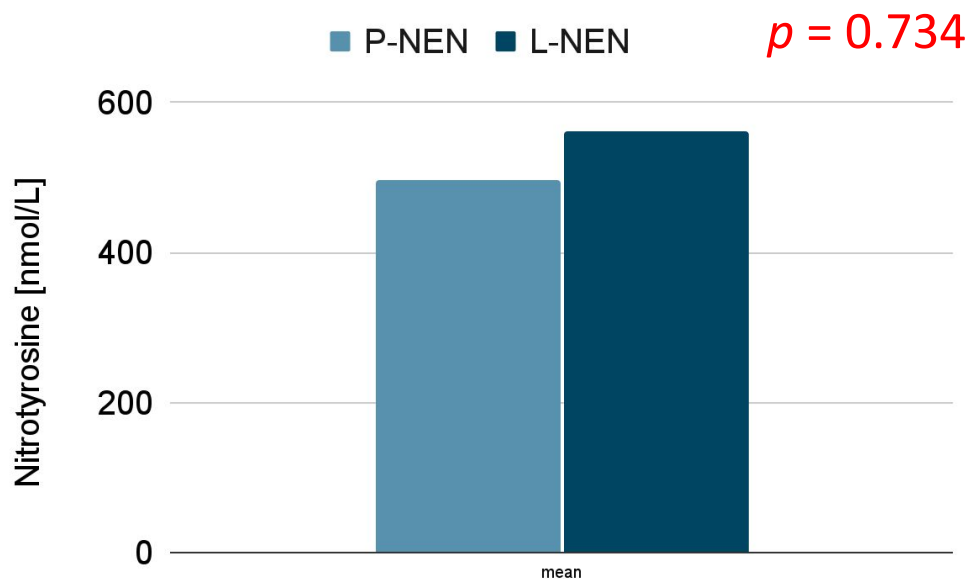
$p = 0.304$



ADMA [μmol/L]	P-NEN	L-NEN	<i>p</i> -value
Mean	0.378	0.346	0.304
SEM	0.027	0.013	



## Results and discussion - nitrotyrosine



Nitrotyrosine [nmol/L]	P-NEN	L-NEN	<i>p</i> -value
Mean	495.888	561.587	0.734
SEM	105.538	158.929	





## Conclusions

Based on the current findings, it can be concluded that the location of the tumor does not significantly influence the levels of nitrotyrosine and ADMA in patients with NENs. Despite the lack of significant differences observed in this study, further research with larger sample sizes and more diverse patient populations may provide valuable insights into the relationship between nitrotyrosine, ADMA, and NENs. These additional studies could potentially contribute to the development of improved diagnostic and therapeutic approaches for patients with suspected NENs.



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