RESEARCH ARTICLE

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2025-44
Cyprus J Med Sci 2025;10(4):272-278

Clinicopathological Profile and Outcomes of Appendiceal Neuroendocrine Tumors: A 10-Year Single-Center Study of 5,483 Appendectomy Specimens

Enver Yarıkkaya, Merve Cin

Clinic of Pathology, University of Health Sciences Türkiye, İstanbul Training and Research Hospital, İstanbul, Türkiye

Abstract

BACKGROUND/AIMS: This study aims to assess the demographic, histopathological, and immunohistochemical (IHC) features of appendiceal neuroendocrine tumors (aNETs) and investigate their associations with tumor location, grade, size, and pathological stage. The follow-up data on survival and surgical outcomes is utilized to improve risk stratification and management strategies.

MATERIALS AND METHODS: A retrospective analysis was conducted on 5,483 appendectomy specimens evaluated between 2010 and 2020 in a single tertiary center. Among 115 neoplastic lesions, 45 cases were confirmed as aNETs. Demographic data, histopathological parameters, and IHC markers were reviewed. Survival data were collected from national records.

RESULTS: The median patient age was 35, with a female-to-male ratio of 1.37. Most tumors were located in the distal appendix (70.5%) and graded as G1 (82.2%). Mean tumor diameter was 0.91 cm, and the median Ki-67 proliferation index was 1%. Tumor grade and size were significantly associated with both tumor location and pathological tumor stage. Diffuse and proximal tumors were more likely to be G2, larger in size, and in advanced stages (pT4). Lymphovascular invasion, perineural invasion, and surgical margin positivity were more frequent in higher pT stages. Chromogranin A negativity was observed exclusively in pT1 cases.

CONCLUSION: aNETs are typically small, well-differentiated tumors with indolent behavior. However, tumor location, size, grade, and invasion features are associated with pathological stage and may serve as prognostic indicators. These parameters should be considered collectively to optimize clinical decision-making and surgical planning.

Keywords: Appendiceal neuroendocrine tumors, appendectomy, histopathological classification, immunohistochemistry

INTRODUCTION

Appendiceal neuroendocrine tumors (aNETs) are the most commonly encountered neoplasms of the appendix, often diagnosed incidentally during histopathological evaluation following appendectomy for suspected acute appendicitis (AA).[1-3] Despite their relative rarity, aNETs account for 30-80% of all appendiceal neoplasms and typically exhibit indolent biological behavior.[4-6] Most are well-differentiated, measure less than 2 cm, and are located at the distal tip of the appendix.[7-10] As such, simple appendectomy is considered curative in the majority of low-risk cases.[7,11]

Current clinical guidelines by the European Neuroendocrine Tumor Society (ENETS) and the North American ETS (NANETS) recommend right hemicolectomy (RH) for tumors larger than 2 cm or in the presence of high-risk histopathological features such as mesoappendiceal invasion (MAI), lymphovascular invasion (LVI), high Ki-67 index, or positive surgical margins.[11,12] However, the appropriateness of RH remains a

To cite this article: Yarıkkaya E, Cin M. Clinicopathological profile and outcomes of appendiceal neuroendocrine tumors: a 10-year single-center study of 5,483 appendectomy specimens. Cyprus J Med Sci. 2025;10(4):272-278

ORCID IDs of the authors: E.Y. 0000-0002-4608-1016; M.C. 0000-0002-0656-497X.

Corresponding author: Enver Yarıkkaya
E-mail: enver.yarikkaya@sbu.edu.tr
ORCID ID: orcid.org/0000-0002-4608-1016

Received: 08.05.2025
Accepted: 11.06.2025
Publication Date: 15.08.2025

subject of ongoing debate, particularly for intermediate-sized tumors (1-2 cm) without additional risk factors.[13,14]

Although tumor size (TS), grade, and invasion characteristics have been associated with recurrence risk and survival in prior studies, real-world data evaluating these variables regarding long-term outcomes remains limited, particularly in patients managed conservatively.[2,5] Furthermore, the prognostic relevance of tumor localization within the appendix (a parameter not consistently addressed in major series) warrants further investigation.

This study aims to evaluate the demographic, histopathological, and immunohistochemical (IHC) characteristics of aNETs diagnosed over ten years at a single tertiary care institution. In addition to characterizing tumor features, the study seeks to explore potential associations between tumor location, grade, size, and pathological tumor (pT) and to examine clinical follow-up data focusing on survival and the need for further surgical intervention. Through these objectives, the study intends to contribute meaningful data toward refining risk stratification and management strategies in patients with aNETs.

MATERIALS AND METHODS

This study is a single-center, observational cohort study based on the retrospective analysis of appendectomy specimens collected between 2010 and 2020. The study was approved by the University of Health Sciences Türkiye, Non-Interventional Clinical Research Ethics Committee of İstanbul Training and Research Hospital (approval number: 99, date: 02.05.2025) and all data were obtained in accordance with the principles of the Declaration of Helsinki.

Case Selection and Data Collection

We included 5,483 appendectomy specimens evaluated in our institution's pathology laboratory between April 1, 2010, and April 1, 2020. Pathology reports and the hospital information system were reviewed to identify 115 neoplastic lesions, of which 45 were confirmed as aNETs. Diagnoses were verified by reevaluating hematoxylin-eosin stained slides and IHC analyses.

Data were collected from the hospital's electronic archive system, including detailed reviews of pathology reports, radiological imaging results, surgical, and oncological treatment records.

Tumor characteristics, including tumor diameter, location, histological grade (HG), pT, resection margin status, presence of mesoappendiceal, lymphovascular, perineural invasion (PNI), and concurrent histopathological findings (CHF) such as AA and diverticulitis, were recorded. Tumor grading was based on mitotic count (per 10 HPF/2 mm^2) and Ki-67 proliferation index (PI). The evaluation criteria were guided by the current American Joint Committee on Cancer, Cancer Staging Manual.[15]

IHC staining results for synaptophysin (Syn), chromogranin A (CgA), and Ki-67 antibodies were recorded following re-evaluation. A staining threshold of >10% was considered positive for Syn and CgA. The Ki-67 PI was determined manually by counting at least 500-2,000 cells in hotspot areas.

Clinical Data and Follow-up

Demographic data and overall survival (OS) status were also recorded. OS was defined as the time from diagnosis to death from any cause or last follow-up. The presence of distant metastasis was evaluated at diagnosis and five-year follow-up. Additionally, whether patients underwent further surgical treatment after diagnosis (such as RH) was also recorded. Survival information was obtained through the Ministry of Health's Death Notification System.

Statistical Analysis

Data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and Microsoft Office Excel 365 (Microsoft, Redmond, WA, USA). Continuous variables were tested for normality using the Shapiro-Wilk test. Normally distributed variables are expressed as mean and standard deviation (SD) and compared using the Independent Samples t-test, whereas non-normally distributed variables are presented as medians and analyzed using the Independent Samples Kruskal-Wallis test. Categorical variables are reported as frequencies and percentages and compared using the chi-square test, with Bonferroni correction applied for multiple comparisons. Survival analyses were conducted using the Kaplan-Meier method. Deaths that occurred between the date of diagnosis and April 2025 (the end date of the study) were recorded. Patients lost to follow-up or alive at the study endpoint were censored. The differences between survival curves were evaluated using the log-rank test, with a p-value of <0.05 considered statistically significant.

RESULTS

This study included 45 patients with aNETs. The mean age was 36 years (SD = 15), ranging from 14 to 70 years, with a median of 35 years. Of these, 26 patients (57.8%) were women, and 19 (42.2%) were men, resulting in a women-to-men ratio of 1.37:1 (Table 1).

Tumors were most frequently located in the distal appendix (70.5%), followed by diffuse (15.9%) and proximal (13.6%) locations. The mean TS was 0.91 cm (SD = 0.89), ranging from 0.1 to 5 cm. Histologically, 82.2% of tumors were classified as grade 1 and 17.8% as grade 2. No grade 3 tumors were observed.

Pathological staging revealed that 40% of tumors were pT1, 46.7% were pT3, and 13.3% were pT4. Surgical margins were negative in 90.5% of cases and positive in 9.5%. LVI was present in 17.8% of patients, PNI in 15.6%, and MAI in 6.7%. CHF included AA in 68.9%, mucinous neoplasia in 6.7%, and diverticulosis, and fibrous obliteration in 4.4% of cases (Table 1).

All tumors were positive for Syn. CgA was positive in 86.7% and negative in 13.3% of cases. The mean Ki-67 PI was 2.0% (SD = 2.9), with a median of 1%.

During follow-up, 93.3% of patients were alive, while 6.7% (n=3) had died. Two patients died due to cardiovascular comorbidities, and one patient died of sepsis. OS analysis was performed using the Kaplan-Meier method. Although only three deaths occurred during follow-up, a survival curve was generated for illustration (Figure 1). No statistical comparison was made due to the limited number of events.

At the time of diagnosis and during follow-up, no patients (0%) exhibited evidence of distant metastasis. Additionally, no patients underwent RH as a planned post-diagnostic treatment. However, four patients (8.9%) were diagnosed incidentally during RH procedures that had been performed for other clinical indications. Descriptive characteristics of the patients are summarized in Table 1.

Table 1. Patient characteristics

Characteristics		n (%)
Age (years)*		35 (14-70)
Sex		
	Women	26 (57.8)
	Men	19 (42.2)
Tumor localization		
	Proksimal half	6 (13.6)
	Distal half	31 (70.5)
	Body/diffuse	7 (15.9)
Tumor size (cm)*		0.7 (0.1-5)
pT		
	pT1	18 (40.0)
	pT2	0
	pT3	21 (46.7)
	pT4	6 (13.3)
HG		
	G1	37 (82.2)
	G2	8 (17.8)
	G3	0 (0.0)
Resection margin (positive)		4 (9.5)
MAI (present)		3 (6.7)
LVI (present)		8 (17.8)
PNI (present)		7 (15.6)
Synaptophysin (positive)		45 (100.0)
Chromogranin A (positive)		39 (86.7)
Ki-67 PI (%)*		1 (0-18)
CHF		
	Acute appendicitis	31 (68.9)
	Diverticulitis	2 (4.4)
	Mucinous neoplasia	3 (6.7)
	Fibrous obliteration	2 (4.4)
Post-diagnostic RH		0 (0.0)
Distant metastasis (present)		0 (0.0)

*Values are expressed as median (minimum-maximum)
pT: Pathological tumor stage, HG: Histological grade, MAI: Mesoappendiceal invasion, LVI: Lymphovascular invasion, PNI: Perineural invasion, PI: Proliferation index, CHF: Concurrent histopathological findings, RH: Right hemicolectomy

Correlation Between Tumor Location and Clinicopathological Features

Tumor location was significantly associated with HG (p=0.007), pT (p=0.045), and TS (p=0.042). Distal tumors were predominantly grade 1 (93.5%), while proximal (50.0%) and diffuse tumors (42.9%) demonstrated grade 2 differentiation. Similarly, pT1 tumors were mostly localized distally (51.6%), whereas diffuse tumors were more frequently staged as pT4 (42.9%, Table 2).

The median TS varied significantly by location, being largest in diffusely located tumors (1.00 cm), followed by distal (0.70 cm) and proximal (0.35 cm) locations (p=0.007).

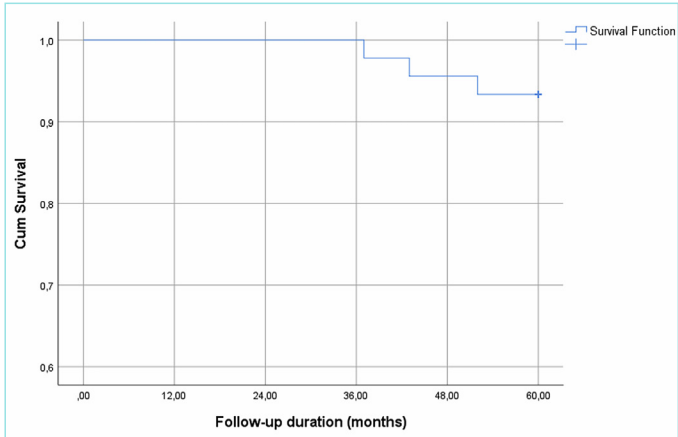

Figure 1. Kaplan-Meier curve illustrating overall survival of patients with appendiceal neuroendocrine tumors. A total of three deaths were observed during the follow-up period. No statistical comparisons were performed due to the limited number of events.

There was a borderline association between tumor location and positive surgical margins (p=0.060), with the highest rate observed in proximally located tumors (33.3%).

Other clinicopathological parameters, including sex, LVI, PNI, CHF, MAI, CgA expression and Ki-67 PI, were not significantly associated with tumor location (Table 2).

Correlation Between Pathological Tumor and Clinicopathological Parameters

pT was significantly associated with TS (p<0.001), Ki-67 PI (p=0.016), HG (p=0.003), LVI (p=0.038), and CgA expression (p=0.006) Table 3. TS and Ki-67 PI increased in higher pT stages, with median TSs of 0.30 cm, 0.80 cm, and 1.85 cm in pT1, pT3, and pT4 stages, respectively. Similarly, the median Ki-67 PI rose from 1.0% in pT1 and pT3 tumors to 5.5% in pT4 tumors. Grade 2 tumors were more frequently observed in advanced stages, accounting for 66.7% of pT4 tumors.

As shown in Table 3, LVI was absent in pT1 cases but present in 28.6% and 33.3% of pT3 and pT4 tumors, respectively. CgA negativity was exclusively observed in pT1 tumors (33.3%), whereas all pT3 and pT4 tumors were CgA positive.

There was a borderline association between pT and both PNI (p=0.054) and positive surgical margins (p=0.052), with rates of 33.3% in pT4 tumors for both parameters. No statistically significant associations were found between pT and age, sex, CHF, or MAI (Table 3).

DISCUSSION

This study evaluated the demographic, histopathological, and IHC characteristics of aNETs diagnosed over 10 years. Our main findings demonstrated that aNETs predominantly occur in middle-aged women, are most often localized at the distal tip of the appendix, and measure less than 1 cm. Most tumors were classified as WHO grade 1 with low Ki-67 PIs, and MAI was infrequent. Tumor location was significantly associated with HG, pT, and TS. OS outcomes were excellent, with a 93.3% survival rate during follow-up. These results are consistent

Table 2. Comparison of clinicopathological features according to tumor location

Clinicopathological features	Proximal (n=6)	Distal (n=31)	Diffuse (n=7)	p
Age (years)*	32 (20-70)	33 (14-64)	40 (24-65)	0.606
Sex				
Women	2 (33.3%)	17 (54.8%)	6 (85.7%)	0.151
Men	4 (66.6%)	14 (45.2%)	1 (14.3%)	
Tumor size (cm)*	0.35 (0.1-2.5)	0.7 (0.15-2.0)	1 (0.8-5.0)	0.007
Ki-67 PI (%)*	2.0 (1-6)	1.0 (0-5)	1.0 (1-18)	0.068
HG				
G1	3 (50.0%)	29 (93.5%)	4 (57.1%)	0.007
G2	3 (50.0%)	2 (6.5%)	3 (42.9%)	
pT				
pT1	2 (33.3%)	16 (51.6%)	0	0.045
pT3	3 (50%)	13 (41.9%)	4 (57.1%)	
pT4	1 (16.7%)	2 (6.5%)	3 (42.9%)	
LVI (present)	0	6 (19.4%)	2 (28.6%)	0.393
PNI (present)	1 (16.7%)	4 (12.9%)	1 (14.3%)	0.969
Resection margin (positive)	2 (33.3%)	1 (3.3%)	1 (16.7%)	0.060
MAI (present)	0	2 (6.5%)	0	0.644
Chromogranin A (positive)	5 (83.3%)	26 (83.9%)	7 (100%)	0.518
CHF (present)				
Acute appendicitis	5 (83.3%)	21 (67.7%)	5 (71.4%)	0.744
Diverticulitis	0	1 (3.2%)	1 (14.3%)	0.379
Mucinous neoplasia	0	2 (6.5%)	1 (14.3%)	0.589
Fibrous obliteration	1 (16.7%)	1 (3.2%)	0	0.288

*Values are expressed as median [minimum (min)-maximum (max)]. Continuous variables are presented as median (min-max), and categorical variables as counts (percentage). Statistical significance was assessed using the Kruskal-Wallis or Pearson chi-square tests, as appropriate.
PI: Proliferation index, HG: Histological grade, pT: Pathological tumor stage, LVI: Lymphovascular invasion, PNI: Perineural invasion, MAI: Mesoappendiceal invasion, CHF: Concurrent histopathological findings

with the existing literature and support current clinical management guidelines favoring simple appendectomy for small, well-differentiated tumors without adverse features.

In line with previous reports, the median age of our cohort was 35 years, with a slight female predominance (57.8%). These findings are consistent with several large series reporting median ages between 33 and 36.5 years and a female predominance ranging from approximately 54.5% to 64.5%.[2,3] These findings reinforce the understanding that aNETs typically affect young to middle-aged adults and exhibit a slight gender disparity. The demographic profile of our study thus mirrors the general epidemiological trends observed globally.

The predominant localization of tumors at the distal tip of the appendix (70.5%) and a mean TS of 0.91 cm were consistent with existing studies, which reported distal localization rates between 58.1% and 83.9% and TSs predominantly less than 1 cm in diameter.[2,10,16] This distribution is clinically relevant, as tumor location and TS significantly impact surgical decision-making and prognosis.

HG revealed that most tumors were grade 1 (82.2%), corroborating findings from prior studies where grade 1 tumors accounted for 60.7% to 90.9% of cases.[3,17] The observed low Ki-67 PI further reinforced the indolent nature of these neoplasms. Importantly, MAI was relatively infrequent (6.7%), supporting the generally favorable prognosis of small, well-differentiated aNETs.

Tumor location showed significant associations with HG, pT, and TS. Distally located tumors were more often grade 1 and staged as pT1, while diffuse tumors exhibited a tendency towards higher grades and stages. These results are in line with findings from Okut and Karahan[18] highlighting that proximally or diffusely located tumors warrant closer clinical scrutiny.

pT correlated strongly with TS, Ki-67 PI, HG, and invasion parameters, which echoesthe established understanding that deeper invasion, and larger TS are markers of more aggressive behavior.[9,19-21] LVI and PNIs, while relatively infrequent, were significantly associated with advanced pTs, aligning with international observations.[6,9]

All tumors showed positivity for Syn (100%), and 86.7%, were positive for CgA, comparable to prior reports where positivity rates for Syn and CgA exceeded 83%.10 The low Ki-67 PIs, with most cases under 3%, reflect the low proliferative activity that characterizes well-differentiated aNETs.

Notably, no patients in our cohort exhibited evidence of distant metastasis at the time of diagnosis or during the follow-up period.

Table 3. Comparison of clinicopathological features according to pathological tumor stage

Clinicopathological features	pT1 (n=18)	pT3 (n=21)	pT4 (n=6)	p
Age (years)*	36 (14-64)	35 (16-70)	34 (17-65)	0.896
Sex				
Women	10 (55.6%)	11 (52.4%)	5 (83.3%)	0.388
Men	8 (44.4%)	10 (47.6%)	1 (16.7%)	
Tumor size (cm)*	0.30 (0.1-1.0)	0.80 (0.1-2.5)	1.85 (0.8-5.0)	<0.001
Ki-67 PI (%)*	1.0 (0-3.8)	1.0 (0.4-5.0)	5.5 (1.0-18.0)	0.016
HG				
G1	16 (88.9%)	19 (90.5%)	2 (33.3%)	0.003
G2	2 (11.1%)	2 (9.5%)	4 (66.7%)	
LVI (present)	0	6 (28.6%)	2 (33.3%)	0.038
PNI (present)	0	5 (23.8%)	2 (33.3%)	0.054
Resection margin (positive)	0	2 (11.1%)	2 (33.3%)	0.052
MAI (present)	0	3 (14.3%)	0	0.159
Chromogranin A (positive)	12 (66.7%)	21 (100.0%)	6 (100.0%)	0.006
CHF (present)				
Acute appendicitis	12 (66.7%)	15 (71.4%)	4 (66.7%)	0.942
Diverticulitis	1 (5.6%)	1 (4.8%)	0	0.845
Mucinous neoplasia	0	2 (9.5%)	1 (16.7%)	0.283
Fibrous obliteration	1 (5.6%)	1 (4.8%)	0	0.845

*Values are expressed as median [minimum (min)-maximum (max)]. Continuous variables are presented as median (min-max), and categorical variables as counts (percentage). Statistical significance was assessed using the Kruskal-Wallis or Pearson chi-square tests, as appropriate.
PI: Proliferation index, HG: Histological grade, LVI: Lymphovascular invasion, PNI: Perineural invasion, MAI: Mesoappendiceal invasion, CHF: Concurrent histopathological findings

This finding aligns with most published series, which consistently report very low rates of metastatic spread in small, well-differentiated aNETs (typically <1%). Distant metastases are reported in a small subset of patients, often associated with high-grade or deeply invasive tumors.[4,22,23] These results underscore the indolent behavior of aNETs and reinforce the appropriateness of conservative surgical management in low-risk cases.

The majority of patients in this cohort underwent only appendectomy, aligning with ENETS and NANETS guidelines, which recommend simple appendectomy for tumors smaller than 1 cm without high-risk features.[11,12] The necessity of RH remains debated for tumors between 1 and 2 cm, particularly in the absence of adverse features.[17] In our cohort, the observation of negative surgical margins in most cases (90.5%) and a low frequency of adverse histopathological features may support the safety of conservative management in selected patients, which aligns with current guideline recommendations.

Survival outcomes were favorable, with a 93.3% OS rate at last follow-up and no evidence of disease recurrence, comparable to other series reporting 5-year disease-free survival rates exceeding 90%.[3,11,13,19]

Study Limitations

This study has several limitations, primarily its retrospective single-center design, which may limit generalizability. The relatively small sample size and limited number of adverse events also precluded advanced multivariate analysis. Furthermore, although the follow-up duration was substantial, long-term outcomes (>5 years) remain unexplored.

Future Directions

Further prospective multicenter studies are needed to validate prognostic markers and improve surgical decision-making, especially for tumors measuring between 1 and 2 cm. Recent proposals suggest that INSM1 and other novel IHC markers could assist in more precise risk stratification.[24]

Molecular profiling studies also offer a promising frontier for understanding tumor behavior and tailoring therapy, especially considering the biological heterogeneity observed among EC-cell and L-cell tumors.[25,26]

Moreover, with the rising trend toward non-operative management of AA, the potential risk of missing incidental aNETs merits close surveillance and possibly the development of preoperative predictive algorithms.[16,17,27]

CONCLUSION

Our findings reinforce the generally indolent behavior of aNETs, characterized by small TS, distal location, low-grade histology, and favorable prognosis. These results support the current guidelines advocating for appendectomy as the definitive treatment in the majority of cases and highlight the need for vigilance in assessing histopathological features indicative of higher-risk disease. Continued research into the biological diversity of aNETs and longer-term follow-up studies are essential to optimize patient outcomes.

MAIN POINTS

- The majority of appendiceal neuroendocrine tumors (aNETs) in our cohort were small (mean size 0.91 cm), well-differentiated (82.2% grade 1), and located distally (70.5%), reflecting indolent tumor biology.
- Tumor location was significantly associated with grade, size, and pathological stage; distal tumors were more likely to be low-grade and early-stage, while diffuse or proximal tumors showed more aggressive features.
- No distant metastasis was observed during diagnosis or long-term follow-up, even in patients with intermediate-sized tumors (1-2 cm) who did not undergo completion right hemicolectomy.
- Positive resection margins and mesoappendiceal invasion were relatively uncommon (9.5% and 6.7%, respectively), which questions the necessity of radical surgery in most aNET cases.
- Our findings support a conservative surgical approach in selected patients and may contribute to refining risk stratification algorithms in current aNET management guidelines.

ETHICS

Ethics Committee Approval: The study was approved by the University of Health Sciences Türkiye, Non-Interventional Clinical Research Ethics Committee of İstanbul Training and Research Hospital (approval number:99, date: 02.05.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.Y., M.C., Concept: E.Y., M.C., Design: E.Y., M.C., Data Collection and/or Processing: E.Y., Analysis and/or Interpretation: E.Y., Literature Search: M.C., Writing E.Y.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study had received no financial support.

REFERENCES

1. Bayhan Z, Yildiz YA, Akdeniz Y, Gonullu E, Altintoprak F, Mantoglu B, et al. Appendix neuroendocrine tumor: retrospective analysis of 4026 appendectomy patients in a single center Emerg Med Int. 2020; 2020: 4030527.
2. Başkent A, Alkan M, Memişoğlu E, Ok O. Neuroendocrine tumours detected after appendectomy: 5-year single center experience with 4888 acute appendicitis patients East J Med. 2023; 28(1): 179-84.
3. Süleyman M. Incidental presentation of appendix neuroendocrine tumor: Long-term results from a single institution. Ulus Travma Acil Cerrahi Derg. 2023; 29(9): 972-7.
4. Constantin M, Petrescu L, Mătanie C, Vrancianu CO, Niculescu AG, Andronic O, et al. The vermiform appendix and its pathologies. Cancers (Basel). 2023; 15(15): 3872.
5. Tokoçin M, Meriç S, Aktokmakyan TV, Güllü HF, Buğdaycı N, Özdoğan K, et al. Neuroendocrine tumor of the appendix: retrospective 7266 analysis of appendectomy patients in a single center: neuroendocrine tumor of the appendix. Med Sci Discov. 2023; 10(10): 907-10.
6. Rodriguez Franco S, Ghaffar SA, Jin Y, Weiss R, Hamermesh M, Khomiak A, et al. Pathological features associated with lymph node disease in patients with appendiceal neuroendocrine tumors. Cancers. 2024; 16(16): 2922.
7. Muñoz de Nova JL, Hernando J, Sampedro Núñez M, Vázquez Benítez GT, Triviño Ibáñez EM, Del Olmo García MI, et al. Management of incidentally discovered appendiceal neuroendocrine tumors after an appendicectomy. World J Gastroenterol. 2022; 28(13): 1304-14.
8. Anwar K, Desai M, Al-Bloushi N, Alam F, Cyprian FS. Prevalence and clinicopathological characteristics of appendiceal carcinoids in Sharjah (United Arab Emirates). World J Gastrointest Oncol. 2014; 6(7): 253-6.
9. Alexandraki KI, Kaltsas GA, Grozinsky-Glasberg S, Chatzellis E, Grossman AB. Appendiceal neuroendocrine neoplasms: diagnosis and management. Endocr Relat Cancer. 2016; 23(1): R27-41.
10. Nazir MW, Shah JR, Shah KM, Bashir N, Bilal S. Incidental neuroendocrine tumors of appendix: study from a tertiary care hospital. J Radiat Cancer Res. 2024; 15: 113-6.
11. Pape UF, Niederle B, Costa F, Gross D, Kelestimur F, Kianmanesh R, et al. ENETS Consensus Guidelines for neuroendocrine neoplasms of the appendix (excluding goblet cell carcinomas). Neuroendocrinology. 2016; 103(2): 144-52.
12. Boudreaux JP, Klimstra DS, Hassan MM, Woltering EA, Jensen RT, Goldsmith SJ, et al. The NANETS consensus guideline for the diagnosis and management of neuroendocrine tumors: well-differentiated neuroendocrine tumors of the Jejunum, Ileum, Appendix, and Cecum. Pancreas. 2010; 39(6): 753-66.
13. Moris D, Tsilimigras DI, Vagios S, Ntanasis-Stathopoulos I, Karachaliou GS, Papalampros A, et al. Neuroendocrine the appendix: a review of the literature Anticancer Res. 2018; 38(2): 601-11.
14. Ozcelik CK, Turanli S, Bozdogan N, Dibekoglu C. Clinical experience in appendiceal neuroendocrine neoplasms. Contemp Oncol (Pozn). 2015; 19(5): 410-3.
15. Woltering EA, Bergsland EK, Beyer DT, O'Dorisio TM, Rindi G, Klimstra DS, et al. Neuroendocrine tumors of the appendix. In: Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK et al. editors. AJCC cancer staging manual. 8th ed. New York: Springer; 2017.p.389-394.
16. Pogorelić Z, Ercegović V, Bašković M, Jukić M, Karaman I, Mrklić I. Incidence and management of appendiceal neuroendocrine tumors in pediatric population: a bicentric experience with 6285 appendectomies. Children (Basel). 2023; 10(12): 1899.
17. Kunduz E, Bektasoglu HK, Unver N, Aydogan C, Timocin G, Destek S. Analysis of appendiceal neoplasms on 3544 appendectomy specimens for acute appendicitis: retrospective cohort study of a single institution. Med Sci Monit. 2018; 24: 4421-6.
18. Okut G, Karahan M. Malignant tumors of the appendix: evaluation of 6748 appendectomy cases. Sanamed. 2021; 16(2): 143-8.
19. Pawa N, Clift AK, Osmani H, Drymousis P, Cichocki A, Flora R, et al. Surgical Management of Patients with Neuroendocrine Neoplasms of the Appendix: Appendectomy or More. Neuroendocrinology. 2018; 106(3): 242-51.
20. Chawrylak K, Leśniewska M, Mielniczek K, Sędłak K, Pelc Z, Kobiałka S, et al. Current status of treatment among patients with appendiceal tumors-old challenges and new solutions? Cancers (Basel). 2024; 16(5): 866.
21. Shibahara Y, Krzyzanowska M, Vajpeyi R. Appendiceal well-differentiated neuroendocrine tumors: a single-center experience and new insights into the effective use of immunohistochemistry. Int J Surg Pathol. 2023; 31(3): 252-9.

22. Koçarslan S, Güldür ME, Ekinci T, Aparı R, Yücel Y, Ulaş T. Apendektomi materyallerinde rastlantısal olarak saptanan nöroendokrin tümörlerin sıklığı: on yıllık arşiv taraması. J Clin Exp Invest. 2014; 5(4): 563-6.

23. Nagesh VK, Aguilar IK, Elias D, Mansour C, Tran HH, Bhuju R, et al. Factors affecting survival outcomes in neuroendocrine tumor of the appendix over the past two decades. Diseases. 2024; 12(5): 96.

24. Koyuncuer A, Canbak T, Acar A, Şahin O. Evaluation of immunohistochemical expression of novel neuroendocrine marker INSM1 and histological tumor growth pattern in well-differentiated neuroendocrine tumors of the appendix: 15-year single tertiary center experience. Indian J Pathol Microbiol. 2024; 67(2): 282-8.

25. Mete O, Dodington DW, Shen DL, Asa SL. The Clinicopathological significance of tumor cell subtyping in appendiceal neuroendocrine tumors: a series of 135 tumors. Endocr Pathol. 2024; 35(2): 107-12.

26. Clementi M, Pietroletti R, Ciarrocchi A, d'Ascanio F, Rindi G, Carlei F. Appendiceal neuroendocrine tumors and anorectal melanoma. In: Lasfar A, Cohen-Solal K, Brzozowski T, editors. Tumor progression and metastasis [Internet]. IntechOpen, 2020.p.1-9. [Accessed 08.05.2025].

27. Rait JS, McGillicuddy J, Ajzajian J. Appendiceal neoplasms and histological involvement of the mesoappendix: a case series. Ann Med Surg (Lond). 2020; 56: 64-7.