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Original Article

Appendiceal Mucinous Neoplasms and Peritoneal Spread: A Decade of Clinical Experience from Two Tertiary Hospitals in Yazd

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A B S T R A C T

Introduction: Appendiceal mucinous neoplasms (AMNs) are rare tumors. They range from benign cystadenomas to malignant mucinous adenocarcinomas, with potential for peritoneal spread and recurrence, particularly in high-grade or ruptured lesions.

Materials and Methods: This retrospective cross-sectional study aimed to determine the clinicopathologic features in patients with AMNs at Shahid Sadoughi and Shahid Rahnemon Hospitals (2014-2024). Inclusion required both appendiceal and peritoneal pathology specimens. Data were collected from medical records and follow-up interviews, and statistical analysis was performed using the Pearson Chi-square test.

Results: Fifty-seven patients (39 females, 18 males; mean age: 51.26 ± 16.09 years) were included, with the highest incidence in the 50–69 age group (63%). Abdominal pain was the most common symptom (78.9%), followed by a palpable mass (21.1%). Histologically, 68.4% had low-grade appendiceal mucinous neoplasms (LAMN), 21% mucinous adenocarcinoma. Peritoneal metastasis was seen in 47.4%, overall 75% of adenocarcinomas, 46.2% of LAMNs, and none in cystadenomas. Tumor recurrence occurred in six patients (10.5%), 7.7% of LAMN and 25% of mucinous adenocarcinoma of the appendix. No significant associations were found between tumor type or size and recurrence/metastasis. Three deaths (5.3%) were reported; overall survival was 94.7%.

Conclusions: LAMN was the most prevalent AMN subtype, typically with favorable outcomes despite frequent (46.2%) peritoneal involvement. The survival rate in LAMN was 92.3%, with one death reported in a patient with a tumor size of 5-10 cm, while no deaths were reported in mucinous adenocarcinoma of the appendices. Further studies with larger cohorts are needed to clarify prognostic factors and guide management.

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Introduction

Appendiceal mucinous neoplasms (AMNs) represent a rare and diverse group of epithelial tumors, ranging from benign mucinous cystadenoma to poorly differentiated mucinous adenocarcinomas. These lesions are characterized by abnormal mucin accumulation, often leading to cystic dilation of the appendix [1]. Although often discovered incidentally during imaging or surgery, they carry the potential for significant clinical consequences, particularly when associated with invasive components or peritoneal spread. Epidemiologically, AMNs are uncommon, with mucinous tumors reported to occur at an incidence rate of approximately 1.3 per 1,000,000 people annually. Despite their rarity, recent global data indicate a gradual increase in the prevalence of these neoplasms, though this trend has not been uniformly observed across all regions, such as the Persian Gulf States [2].

Histologically, these neoplasms are classified based on cellular atypia and invasive behavior into categories such as low-grade AMN grade I, High-grade AMN grade II, and signet ring cell carcinoma grade III. While LAMNs typically exhibit low-grade cytologic atypia and an invasive pushing growth pattern, mucinous adenocarcinomas demonstrate high-grade atypia with a pushing margin and/or an invasive infiltrating mucinous adenocarcinoma without a signet ring cell component. In contrast, Signet ring cell adenocarcinoma with numerous signet ring cells in mucin pools or infiltrating tissue is defined by destructive stromal invasion of numerous signet ring cells in tissue or mucin pools and carries a higher risk of metastasis and pseudomyxoma peritonei (PMP) [3].

Accurate histopathological evaluation is crucial, as prognosis and treatment strategies significantly depend on tumor type, grade, and extent of disease. Studies show that LAMNs are limited to the appendix and generally have excellent outcomes following surgical resection, with no recurrence or metastasis during long-term follow-up [4]. However, when these tumors extend beyond the appendix, especially in the presence of neoplastic epithelium within peritoneal mucin, the risk of recurrence and PMP increases [3].

Several studies have explored the behavior and management of these tumors. For instance, research by Alexandros et al. and Li et al. found that LAMNs limited to the appendix rarely recur and are associated with excellent long-term survival [5]. In contrast, data from Sugarbaker and colleagues, and others, demonstrate significantly lower survival rates in patients with high-grade tumors and incomplete cytoreduction [6-9].

Given the complexity and rarity of AMNs and the significant variation in their biological behavior, accurate diagnosis, staging, and individualized treatment planning are essential. This article aims to describe clinicopathologic features and prognostic factors of these tumors, with a focus on their surgical management and outcomes.

Materials and Methods

This retrospective cross-sectional study evaluated patients diagnosed with AMNs at the pathology departments of Shahid Sadoughi and Shahid Rahnemon hospitals in Yazd from 2014 to 2024. All adult patients with a confirmed diagnosis of appendiceal mucinous neoplasm, for whom their clinical records and appendiceal and peritoneal samples were available, were included. Patients with incomplete clinical or pathological information were excluded. We reviewed archived pathology records and extracted a pre-designed checklist that included demographic variables (age and sex), clinical presentation, histopathological diagnosis, and the presence of peritoneal metastasis. Follow-up data, including recurrence of appendiceal mucinous neoplasm and survival time after initial surgery, were collected through interviews with patients or their relatives using contact information available in their medical records.

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 23 (Armonk, New York, USA). Descriptive statistics were employed to summarize patient demographics, clinical presentations, histopathological subtypes, tumor sizes, recurrence, peritoneal metastasis, and survival outcomes. Categorical variables, including tumor type, tumor size, recurrence, and presence of peritoneal metastasis, were compared using the Pearson Chi-square test. Associations between tumor type and recurrence, tumor size and recurrence, tumor type and peritoneal metastasis, and tumor size and peritoneal metastasis were evaluated; p-values < 0.05 were considered statistically significant. Due to the limited number of events (only three reported deaths), survival analysis could not be conducted. Results were reported in terms of frequencies, percentages, and mean ± standard deviation for continuous variables.

Results

In this retrospective study, 57 patients diagnosed with mucinous appendiceal neoplasms were evaluated. The mean age of the patients was 51.26 ± 16.09 years, with the highest prevalence (63%) in the 50–69 years age group. Female patients comprised the majority, accounting for 68.4% (39 cases), while males made up 31.6% (18 cases). The most common presenting symptom was abdominal pain, seen in 78.9% of patients, followed by palpable abdominal mass in 21.1% (Table 1). Pathologically, LAMN was the most frequent diagnosis, observed in 68.4% of patients, and mucinous adenocarcinoma of the appendix was identified in 21% of cases. Overall, 21.05% of tumors were malignant, while the remaining (78.9%) had malignant potential. Peritoneal metastasis was confirmed in 47.4% of all patients (15.8% from mucinous adenocarcinoma and 31.6% from LAMN), with no metastasis observed in cystadenoma cases.

Tumor recurrence was reported in 6 patients (10.5%): 3 with LAMN and 3 with mucinous adenocarcinoma of the appendix. Three patients (5.3%) died with LAMN and peritoneal metastasis, while the remaining 94.7% were alive at the time of data collection. Among the

different histologic subtypes, all patients with cystadenoma and mucinous adenocarcinoma survived (100% survival), while the survival rate among LAMN patients was 92.3%.

Tumor size analysis showed that most LAMNs ranged between 5–10 cm (53.84%), with fewer cases <5 cm (30.76%) and >10 cm (15.4%). Peritoneal metastasis was observed in 80% of tumors <5 cm, 45.5% of tumors 5–10 cm, and none of the patients with tumors>10 cm. In patients with malignant tumors, the prevalence of peritoneal metastasis was 100% in the group with tumor size less than 5 cm, 66.6% in the group with tumor size 5–10 cm, and none in the group with tumor size greater than 10 cm. Tumor recurrence occurred exclusively in tumors sized 5–10 cm, with no recurrence seen in tumors <5 cm or >10 cm. Among patients with malignant tumors, recurrence was seen in three cases (25%) with a tumor size of 5-10 cm.

Statistical analysis using the Pearson Chi-square test revealed no significant relationship between tumor type and recurrence ($p = 0.608$), tumor size and recurrence ($p = 0.67$), tumor type and peritoneal metastasis ($p = 0.156$), or tumor size and peritoneal metastasis ($p = 0.88$). Evaluation of survival in relation to tumor type, size, or metastasis was limited due to the small number of deaths (n = 3), precluding statistical analysis.

Discussion

In the present study, conducted in Yazd between 2014 and 2024 on 57 patients diagnosed with AMNs, the female predominance was notable, with 68.4% of cases occurring in females and 31.6% in males. This female predominance contrasts with several other studies. For example, in the study by El-Esawy et al. in Saudi Arabia, among 2,476 appendectomy patients, AMNs were more frequent in males (55.6%) than females (44.4%) [10]. Similar trends were observed in studies by Tajima et al. in Japan (59% male vs. 41% female) [11], Kwak et al. in Korea (60% male vs. 40% female) [12], and Shaib et al. in Ohio, USA (54.6% male vs. 45.4% female) [13].

However, our findings are more aligned with other studies, such as that of Guner et al. (2023) in Turkey, where 45% of patients were female and 55% male [14], Matias-García et al. (2021) in Australia (62.5% female vs. 37.5% male) [15], and Gündoğar et al. in Turkey (2018), where 78.9% were female and 21.05% male [16]. These variations could be attributed to geographical, ethnic, or other differences in our inclusion criteria or sample sizes across studies. The mean age of patients in our study was 51.26 ± 16.09 years, which is relatively lower than that reported in most other studies. For instance, the mean age was 57.2 ± 14.3 years in the study by El-Esawy et al. [10], 59.7 years in both the Matias-Garcia and Young studies [15, 17], 57.3 years in the Kwak study [12], 59.6 in Shaib's study [13], and 60 ± 15 years in the Gündoğar study [16]. The younger age in our study may be due to the smaller sample size or early exposure to potential risk factors in the local population.

Table 1. Summary of clinicopathologic features, metastasis, recurrence, and survival in patients with appendiceal mucinous neoplasms (n=57)

Parameter	Category	Count (n)	Percentage (%)
Age distribution	50–69 years	36	63
	Mean age ± SD	51.26 ± 16.09	51.26 ± 16.09
Gender distribution	Female	39	68.4
	Male	18	31.6
Initial presentation	Abdominal pain	45	78.9
	Palpable mass	12	21.1
Final pathologic diagnosis	LAMN	39	68.4
	Mucinous adenocarcinoma	12	21.0
Tumor malignancy potential	Mucinous cystadenoma	6	10.5
	Malignant (Adenocarcinoma)	12	21.05
	Premalignant (LAMN+Cystadenoma)	45	78.9
Peritoneal metastasis	Present	27	47.4
	LAMN	18	46.2
	Adenocarcinoma	9	75
	Cystadenoma	0	0
Tumor recurrence	Total	6	10.5
	LAMN	3	7.7
	Adenocarcinoma	3	25
	Cystadenoma	0	0
Survival outcome	Alive	54	94.7
	Deceased	3	5.3
Survival by tumor type	LAMN	36.39	92.3
	Adenocarcinoma	12.12	100
	Cystadenoma	6.6	100
Survival by peritoneal metastasis	With metastasis	24.27	88
	Without metastasis	30.30	100
Recurrence by tumor size	5–10 cm	6	18
	<5 cm or >10 cm	0	0

LAMN= Low-grade appendiceal mucinous neoplasms

Histopathologically, LAMN was the most prevalent diagnosis in our study, accounting for 68.4% of cases, followed by mucinous adenocarcinoma (21%). This distribution is consistent with findings from several studies, including El-Esawy et al. [10] and Matias-García et al. [15], in which LAMN was also the most common pathology (66% and 83.3%, respectively). Similarly, Gündoğar et al. reported LAMN in 57.89% of cases and mucinous adenocarcinoma in 10.5% [16]. In contrast, Tajima et al. reported a more equal distribution between LAMN and mucinous adenocarcinoma (both 35.29%) [11], and in the study by Alter et al. in Qatar, LAMN accounted for 82%, mucinous adenocarcinoma 10%, and cystic mucinous adenoma 6% [18]. Recurrence was observed in 10.5% of our cases, specifically 3

cases each of LAMN (5.26% of the total; 7.7% of LAMN cases) and mucinous adenocarcinoma (5.26% of the total; 25% of adenocarcinoma cases). Gündoğar et al. reported no recurrence in their study [16], whereas El-Esawy et al. noted a combined recurrence and metastasis rate of 22.2%, although recurrence was not separately analyzed [10]. Given the small sample sizes in both our study and Gündoğar's, recurrence data may not be statistically robust for broad comparisons.

Regarding clinical presentation, abdominal pain was the most common symptom (78.9%), followed by palpable abdominal mass (21.1%). This is in agreement with other studies: El-Esawy et al. reported abdominal pain in 44.4%, palpable mass in 22.2%, and other symptoms in 33.6% of cases [10] Tajima et al. found pain in 64.7%, mass in 11.7%, and other symptoms in 23.48% [11] and Gündoğar et al. reported 61% with pain, 16% with mass, and 23% with other symptoms [16]. These findings highlight abdominal pain as the primary presenting feature in AMN patients across different populations. In our study, patient survival was 94.7%, with only three deaths reported in the LAMN group. This finding is consistent with survival rates in studies by Gündoğar (94.7%) [16] and Young et al. (94.9%) [17], reflecting the generally favorable prognosis of AMNs, particularly LAMNs.

Peritoneal metastasis PMP was found in 47.4% of our patients, with 46.2% of LAMNs and 75% of mucinous adenocarcinomas) being affected. In contrast, Gündoğar et al. reported an overall PMP rate of 15.78%, with all cases (100%) of mucinous adenocarcinoma and one case (9.09%) of LAMN showing metastasis [16]. The discrepancy in PMP rates may stem from sample size limitations or differences in diagnostic and staging protocols.

Conclusion

This study was conducted on 57 patients diagnosed with AMNs. Based on pathological diagnosis, the most common subtype was LAMN in 68.4% of patients, followed by mucinous adenocarcinoma (21%) and appendiceal cystadenoma (10.5%). Among these, 21.05% of the neoplasms were classified as malignant, while 78.94% were neoplasms with malignant potential, including LAMN.

The most frequent presenting symptom was abdominal pain, reported in 78.9% of patients, followed by the presence of a palpable abdominal mass in 21.1%. Peritoneal metastasis was observed in 47.4% of the total cohort, including 75% of patients with mucinous adenocarcinoma and 46.2% of those with LAMN. Tumor recurrence occurred in 10.5% of patients: Three cases in the LAMN group (7.7%) and three in the mucinous adenocarcinoma group (25%). The overall survival rate in this study was 94.7%, with only three reported deaths, which occurred in patients diagnosed with LAMN.

Given the limited sample size in this study, we recommend conducting future research with a larger patient population to allow for more precise estimation of key clinical parameters. Further studies should also investigate the correlation between tumor stage, histological subtype, and patient survival outcomes to enhance clinical understanding and treatment strategies for AMNs.

Ethical Considerations

Data collection commenced following the approval of the research proposal by the Department of Pathology Research Council and the Ethics Committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.MEDCINE.REC.1401.138).

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Conflict of Interest

The authors declared no conflict of interest.

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Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Authors' Contributions

M.A: Data curation, investigation, writing original draft. M.E: Investigation, review and editing. M.V: Data curation, investigation, project administration, review and editing.

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