

Incidental histopathological findings in appendectomy specimens: A retrospective cohort study at a tertiary Center

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Abstract

Background

Incidental histopathological findings in appendectomy specimens are uncommon but may have important clinical implications, including the need for further investigation, surveillance, referral, or additional treatment. The frequency and spectrum of these findings vary across different populations and clinical settings. This study aimed to evaluate the prevalence and clinicopathological characteristics of incidental histopathological findings in appendectomy specimens and to examine their associations with age, sex, and surgical procedure.

Methods

A retrospective cohort study was performed on appendectomy specimens at King Khalid University Hospital, Riyadh, Saudi Arabia, between 1 February 2020 to 30 December 2025. The histopathological findings were classified into three groups: acute appendicitis, histologically normal appendix, and incidental histopathological findings. Multivariable logistic regression was used to assess the associations of age and sex with incidental histopathological findings. A separate exploratory model was used to assess the association between surgical procedure and incidental findings. Firth penalized logistic regression was used when the small number of cases made standard logistic regression unstable. All analyses were performed using Python 3.12.13 with pandas 3.0.1 and NumPy 2.3.5.

Results

A total of 1,502 records were included: 1,318 were classified as acute appendicitis, 153 as histologically normal appendix, and 31 as incidental histopathological findings. The mean age was 27.6 ± 15.5 years, and 814 patients (54.2%) were male. Incidental histopathological findings accounted for 2.1% of the cohort (95% CI, 1.5%–2.9%). LAMN was the most frequent diagnosis (23/31, 74.2%), followed by WD-NET, endometriosis, and mucocele (two cases each, 6.5%), and serrated lesion/polyp and adenocarcinoma (one case each, 3.2%). Appendiceal neoplasms accounted for 26/31 incidental findings (83.9%); positive resection margins were identified in 4/26 cases (15.4%), and two patients required additional surgery. Age per 10-year increase (aOR, 2.41; 95% CI, 1.95–2.99; $P < 0.001$) and age ≥ 40 years (aOR, 16.28; 95% CI, 6.86–38.61; $P < 0.001$) were associated with incidental histopathological findings, whereas female sex was not (aOR, 0.81; 95% CI, 0.39–1.70; $P = 0.579$). Appendectomy performed during another operation was also associated with incidental histopathological findings (aOR, 2.62; 95% CI, 1.12–6.12; $P = 0.026$).

Conclusion

Incidental histopathological findings were identified in 31 of 1,502 appendectomy records (2.1%), with LAMN accounting for most cases. Older age, particularly age ≥ 40 years, was independently associated with these findings, whereas sex was not. Clinically relevant pathological features included positive resection margins, extra-appendiceal involvement in LAMN, and perineural and lymphovascular invasion in WD-NET. Two patients required additional surgery, including one patient with LAMN and one with adenocarcinoma; the

adenocarcinoma case underwent right hemicolectomy because of a positive resection margin. These findings highlight the importance of careful histopathological assessment of appendectomy specimens and their potential impact on subsequent management.

1. Introduction

Routine histopathological examination of appendectomy specimens can reveal incidental histopathological findings other than acute appendicitis or a histologically normal appendix. These histopathological findings include neoplasms, endometriosis, serrated lesions, mucocèles, and fibrous obliteration, among others. Their reported frequency varies according to population, case definition, and sampling practice, with published series generally reporting uncommon findings in approximately 1%-4% of appendectomy specimens [1, 2, 3, 4, 5, 6].

These diagnoses are important because some require specific pathological reporting and further clinical follow-up. Low-grade appendiceal mucinous neoplasms require assessment of margin status, perforation, extra-appendiceal mucin, and whether the peritoneum is involved because these features influence surveillance and the risk of pseudomyxoma peritonei [7, 8]. Appendiceal neuroendocrine tumors require documentation of size, grade, margin status, mesoappendiceal invasion, and other risk features that guide staging and additional management [8, 9].

A previous study from our institution described the prevalence and clinicopathological profile of appendiceal neoplasms. The present study extends this institutional experience by evaluating the broader spectrum of appendiceal histopathological findings, including acute appendicitis, histologically normal appendices, and incidental histopathological findings, while also examining demographic and surgical associations [7].

The aim of this study is to determine the prevalence and spectrum of incidental histopathological findings in appendectomy specimens, compare the demographic and surgical characteristics of patients with incidental histopathological findings to those with normal appendix or acute appendicitis, and compare the surgical approaches chosen across the different histopathological groups.

Study objectives

1. To estimate the prevalence and spectrum of incidental histopathological findings, defined as diagnoses other than acute appendicitis or normal appendix, among appendectomy specimens.
2. To compare available demographic characteristics and operative approach across acute appendicitis, histologically normal appendix, and incidental histopathological findings.
3. To examine the exploratory associations of age and sex with incidental histopathological findings and the appendiceal neoplasm subset using adjusted logistic-regression models, and to compare surgical approach and surgical context across histopathological groups.

2. Materials and Methods

2.1 Study design and setting

A retrospective cohort study was conducted at King Khalid University Hospital, King Saud University Medical City, Riyadh, Saudi Arabia. The study included appendectomy specimens submitted for histopathological

examination from 1 February 2020 to 30 December 2025. This study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations.

2.2 Study population eligibility criteria

All appendectomy specimen records submitted for histopathological examination during the study period were screened for eligibility.

Inclusion criteria

Patients were included if an appendectomy specimen had a final histopathological diagnosis that applies to every group. Cases were classified as acute appendicitis, histologically normal appendix, or other histopathological findings.

Exclusion criteria

Patients were excluded if the final histopathological diagnosis could not be classified into one of the three study groups in the inclusion criteria, such as fibrous obliteration only and *Enterobius vermicularis*. Duplicated records representing the same patient and the same specimen were removed, with only one record retained for analysis.

2.3 Data sources and variables

Data were obtained from the histopathology department in King Khalid University Hospital database and available surgical records. Variables included age at surgery, sex, final histopathological diagnosis, and documented surgical procedure or operative approach. Indication for surgery was recorded for cases with incidental histopathological findings, and it represents the initial intraoperative diagnosis. For this group, additional histopathological variables were collected when available, including tumor size, differentiation, depth of invasion, resection margin status, perineural invasion, lymphovascular invasion, metastasis, and the need for additional surgery.

2.4 Classification of pathological findings

Final histopathological diagnoses of appendectomy specimens were grouped into three principal categories:

1. **Acute appendicitis:** specimens showing histopathological evidence of acute appendiceal inflammation.
2. **Histologically normal appendix:** specimens without histopathological evidence of acute appendicitis or another specific pathological diagnosis, regardless of the original surgical indication.
3. **Incidental histopathological findings:** Incidental histopathological findings were operationally defined as any histopathological diagnosis other than acute appendicitis or a histologically normal appendix, regardless of the original surgical indication. Therefore, the term “incidental” reflects the study classification and does not necessarily indicate absence of preoperative or intraoperative suspicion.

Within the incidental histopathological findings group, the findings included lesions/neoplasms such as Low-grade appendiceal mucinous neoplasm (LAMN), well differentiated neuroendocrine tumor (WD-NET), serrated lesion or polyp, mucocoele, endometriosis and adenocarcinoma.

2.5 Surgical approach

The recorded surgical procedures were categorized as laparoscopic appendectomy, open appendectomy or laparotomy, laparoscopic surgery converted to open surgery, appendectomy with an unspecified approach, and other procedures involving appendectomy. For comparative analyses, surgical approach was further classified as laparoscopic versus all other documented approaches. Surgical context was separately classified as primary appendectomy versus appendectomy performed during another abdominal or pelvic operation.

2.6 Study outcomes

1. The prevalence and distribution of diagnoses within the predefined incidental histopathological findings
2. The prevalence and distribution of the primary lesions/neoplasms.
3. Comparisons of available demographic characteristics, surgical approach, and surgical context across appendix specimen groups.
4. Exploratory associations of age ≥ 40 years and sex with acute appendicitis, normal appendix and incidental histopathological findings.

2.7 Statistical analysis

Continuous variables were summarized using mean and standard deviation or median and interquartile range, as appropriate. Categorical variables were summarized using frequencies and percentages.

Age was compared among the three histopathological groups using the Kruskal–Wallis test. Sex, age groups, surgical approach, and surgical context were compared using Monte Carlo exact chi-square tests because some groups had small numbers.

Multivariable logistic regression was used to assess the associations of age and sex with histopathological outcomes. A separate model assessed the association between surgical context and incidental histopathological findings after adjustment for age and sex. Firth penalized logistic regression was used when the small number of cases made standard logistic regression unstable.

All tests were two-sided, and $P < 0.05$ was considered statistically significant. All analyses were performed using Python 3.12.13. Data management and numerical processing were conducted using pandas 3.0.1 and NumPy 2.3.5.

2.8 Ethical considerations

The study was approved by the Institutional Review Board of King Saud University Medical City, Riyadh, Saudi Arabia **E-25-10303**. Because the study involved retrospective analysis of routinely collected, de-identified data, the requirement for individual informed consent was waived.

3. Results

3.1 Cohort selection

Of 1,576 records screened, 74 exact duplicates were excluded, leaving 1,502 records for analysis. These comprised 1,318 records classified as acute appendicitis, 153 as histologically normal appendix, and 31 as incidental histopathological findings.

3.2 Patient characteristics

The mean age of the cohort was 27.6 ± 15.5 years, with a median of 24.0 years (IQR, 17.0–36.0) and a range of 0.0–82.0 years. One age value was unavailable. Overall, 814 records (54.2%) were male and 688 (45.8%) were female (Table 1).

Table 1
Demographic and surgical characteristics by histopathological group

Characteristic	Overall	Acute appendicitis	Histologically normal appendix	Incidental histopathological findings	Max SMD	P value
N	1502	1318	153	31		
Age, mean $\pm$ SD	27.6 $\pm$ 15.5	25.9 $\pm$ 13.9	36.5 $\pm$ 19.8	55.1 $\pm$ 17.6	1.84	P < 0.001
Age, median (IQR)	24.0 (17.0–36.0)	23.0 (16.0–34.0)	35.0 (21.0–54.0)	62.0 (42.5–65.5)		
Age category, n (%)						P < 0.001
0–17 years	399 (26.6%)	374 (28.4%)	25 (16.3%)	0 (0.0%)	0.89	
18–39 years	814 (54.2%)	749 (56.8%)	58 (37.9%)	7 (22.6%)	0.75	
40–64 years	245 (16.3%)	173 (13.1%)	59 (38.6%)	13 (41.9%)	0.68	
65 years or older	43 (2.9%)	22 (1.7%)	10 (6.5%)	11 (35.5%)	0.97	
Missing age	1 (0.1%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0.11	
Sex, n (%)						P < 0.001
Male	814 (54.2%)	754 (57.2%)	45 (29.4%)	15 (48.4%)	0.58	
Female	688 (45.8%)	564 (42.8%)	108 (70.6%)	16 (51.6%)	0.58	
Surgical approach, n (%)						P < 0.001
Laparoscopic	1311 (87.3%)	1243 (94.3%)	53 (34.6%)	15 (48.4%)	1.59	
Open/laparotomy	74 (4.9%)	27 (2.0%)	37 (24.2%)	10 (32.3%)	0.80	
Converted/mixed	26 (1.7%)	12 (0.9%)	13 (8.5%)	1 (3.2%)	0.36	
Approach not specified	31 (2.1%)	20 (1.5%)	7 (4.6%)	4 (12.9%)	0.45	
Other documented operation	30 (2.0%)	4 (0.3%)	25 (16.3%)	1 (3.2%)	0.61	
Not applicable approach	30 (2.0%)	12 (0.9%)	18 (11.8%)		0.46	

Table 2
Clinicopathologic features of patients with incidental histopathological findings

Patients' characteristics	Results
Patients (n)	31
Age [mean (SD), range], y	55.1 (17.6) [20.0–82.0]
Age median (IQR), y	62.0 (42.5–65.5)
Sex [n (%)]	
Male	15 (48.4%)
Female	16 (51.6%)
Age group [n (%)]	
18–39 years	7 (22.6%)
40–64 years	13 (41.9%)
65 years or older	11 (35.5%)
Indication of surgery [n (%)]	
Suspected acute appendicitis	5 (16.1%)
Incidental during other surgery	12 (38.7%)
Elective or recurrent	4 (12.9%)
Other or suspected appendiceal lesion	10 (32.3%)
Histopathologic diagnoses [n (%; 95% CI)]	
Low-grade appendiceal mucinous neoplasm (LAMN)	23 (74.2%; 95% CI, 56.8–86.3)
Well-differentiated neuroendocrine tumor (WD-NET)	2 (6.5%; 95% CI, 1.8–20.7)
Endometriosis	2 (6.5%; 95% CI, 1.8–20.7)
Mucocele or unspecified mucinous dilatation	2 (6.5%; 95% CI, 1.8–20.7)
Serrated lesion/polyp	1 (3.2%; 95% CI, 0.6–16.2)
Adenocarcinoma	1 (3.2%; 95% CI, 0.6–16.2)
appendiceal neoplasm cases (LAMN, WD-NET, and adenocarcinoma; n = 26)	n = 26 (83.9%; 95% CI, 67.4–92.9)
Surgical approach [n (%)]	
Laparoscopic surgery	15 (48.4%)
Open surgery/laparotomy	10 (32.3%)
Converted or mixed laparoscopic-to-open surgery	1 (3.2%)
Appendectomy with approach not specified	4 (12.9%)

Patients' characteristics	Results
Other documented operation involving appendectomy	1 (3.2%)
Missing/unclear approach	0 (0.0%)
Pathological features among appendiceal neoplasm cases (LAMN, WD-NET, and adenocarcinoma; n = 26)	
Tumor size [median (IQR), range], cm	5.0 (1.7-6.0), [0.4–15.5]
Grade/differentiation documented	n = 26
Low-grade LAMN or grade 1/well-differentiated tumor	25/26 (96.2%)
Grade 2 WD-NET	1/26 (3.8%)
Depth of invasion documented	n = 25
Muscularis propria	13/25 (52.0%) LAMN n = 12; Adenocarcinoma n = 1
Subserosa/mesoappendix	5/25 (20.0%) LAMN n = 3; WD-NET n = 2
Serosal involvement	4/25 (16.0%) LAMN n = 4
Perforated/through-serosa disease	3/25 (12.0%) LAMN n = 3
Margin status documented	n = 26
Negative margin	22/26 (84.6%)
Positive margin	4/26 (15.4%): LAMN n = 2; WD-NET n = 1; adenocarcinoma n = 1
Perineural invasion documented	10/26 (38.5%)
Perineural invasion present	1/10 (10.0%) (WD-NET n = 1)
Lymphovascular invasion documented	n = 22
Lymphovascular invasion present	1/22 (4.5%) (WD-NET n = 1)
Extra-appendiceal/metastatic involvement documented	n = 12
Extra-appendiceal/metastatic involvement present	6/12 (50.0%) (LAMN n = 6)
Additional surgery performed	2/26 (7.7%) (LAMN n = 1, Adenocarcinoma n = 1)

Table 3
Multivariable associations with pathological outcomes

Model outcome	Predictor	Events/exposed	Events/reference	Crude OR (95% CI)	Adjusted OR (95% CI)	P value
Incidental histopathological findings	Age, per 10-year increase	31/1,501 (2.1%)	Continuous	2.40 (1.94–2.98)	2.41 (1.95–2.99)	P < 0.001
incidental histopathological findings	Age ≥ 40 years	24/288 (8.3%)	7/1213 (0.6%) aged < 40	15.66 (6.68–36.73)	16.28 (6.86–38.61)	P < 0.001
incidental histopathological findings	Appendectomy was performed during another operation	13/141 (9.2%)*	15/1302 (1.2%) primary	8.65 (4.03–18.57)	2.62 (1.12–6.12)	P = 0.026
Histologically normal appendix	Female sex association with histologically normal appendix	108/672 (16.1%)	45/798 (5.5%) male	3.21 (2.23–4.62)	2.77 (1.90–4.04)	P < 0.001
Histologically normal appendix	Age ≥ 40 years	69/264 (26.1%)	83/1206 (6.9%) aged < 40	4.79 (3.36–6.82)	4.13 (2.88–5.92)	P < 0.001
*For the surgical-context analysis, 13 of 141 patients whose appendectomy was performed as part of another operation had incidental histopathological findings, compared with 15 of 1,302 patients undergoing primary appendectomy. The analysis was restricted to complete cases (n = 1,443).						

Most patients were aged 18–39 years: 399 patients (26.6%) were aged 0–17 years, 814 (54.2%) were aged 18–39 years, 245 (16.3%) were aged 40–64 years, and 43 (2.9%) were aged 65 years or older.

Laparoscopic surgery was documented in 1,311 records (87.3%), open surgery or laparotomy in 74 (4.9%), and conversion from laparoscopic to open surgery in 26 (1.7%). The surgical approach was not specified in 31 records (2.1%). Appendectomy performed as part of another abdominal or pelvic operation was documented in 30 records (2.0%), while other surgical procedures that could not be classified into the predefined categories were documented in 30 records (2.0%).

3.3 Histopathological findings

Incidental histopathological findings were identified in 31 records, corresponding to 2.1% of all records (95% CI, 1.5%–2.9%). Within the incidental histopathological findings, LAMN was the most frequent diagnosis, occurring in 23 patients (74.2%; 95% CI, 56.8%–86.3%). WD-NET, endometriosis, and mucocoele occurred in two patients each (6.5%; 95% CI, 1.8%–20.7% each). Serrated lesion/polyp and adenocarcinoma occurred in one patient each (3.2%; 95% CI, 0.6%–16.2% each).

The surgical indication among patients with incidental histopathological findings was also an incidental finding that was found during surgery in 12 records (38.7%), a suspected appendiceal lesion in 10 (32.3%), suspected

acute appendicitis in five (16.1%), and elective appendicitis in four (12.9%).

The surgical approach in patients with incidental histopathological findings was laparoscopic in 15 patients (48.4%), open/laparotomy in 10 patients (32.3%), converted into open in one patient (3.2%), appendectomy with approach not specified in four patients (12.9%), and appendectomy during another abdominal/pelvic operation in one patient (3.2%).

The appendiceal neoplasm cases included 26 patients with LAMN, WD-NET, and adenocarcinoma. These cases represented 83.9% of the incidental histopathological findings (95% CI 67.4%–92.9%) and 1.7% of all records.

The distribution of pathological features by diagnosis is shown in Fig. 4. Depth of invasion was documented in 25/26 appendiceal neoplasm cases (96.2%), including 22 LAMNs, two WD-NETs, and one adenocarcinoma; the specific

depth categories are presented in Fig. 3. Margin status was documented in all 26 cases, with positive resection margins identified in 4/26 (15.4%), comprising two LAMNs, one WD-NET, and one adenocarcinoma. Perineural invasion was documented in 10 cases (nine LAMNs and one WD-NET) and was present in one case (1/10, 10.0%), which was a WD-NET. Lymphovascular invasion was documented in 22 cases (19 LAMNs, two WD-NETs) and was present in one case 1/22 (4.5%) [WD-NET]. Extra-appendiceal or metastatic involvement was documented in 12 cases, all of which were LAMNs, and was present in 6/12 documented cases (50.0%).

Additional surgery was performed in 2/26 (7.7%) of patients, and one of the two cases had a positive margin and perforated appendix (adenocarcinoma) (4.3%). Regarding the adenocarcinoma case, a well-differentiated adenocarcinoma arising from a tubulovillous adenoma was identified. The invasive component measured 1.3 cm, while the associated polyp involved the entire appendix and measured 7 cm in greatest dimension. The tumor invaded the muscularis propria and involved the appendiceal resection margin. No tumor deposits or lymphovascular invasion were identified. A completion right hemicolectomy was subsequently performed because of the positive resection margin.

Both WD-NETs had documented tumor size, with a median of 0.7 cm (IQR, 0.6–0.8). One case (1/2, 50%) showed positive margin, Perineural invasion and lymphovascular invasion were each present in only one case. No additional surgeries were performed.

3.4 Characteristics according to pathology group

Patients in the incidental histopathological findings group were older than those in the acute-appendicitis and histologically normal appendix groups. Mean age was 55.1 ± 17.6 years in the incidental histopathological findings group, compared with 25.9 ± 13.9 years in the acute-appendicitis and 36.5 ± 19.8 years in the histologically normal appendix ($P < 0.001$).

Incidental histopathological findings increased across age categories: zero of 399 patients aged 0–17 years (0.0%), seven of 814 aged 18–39 years (0.9%), 13 of 245 aged 40–64 years (5.3%), and 11 of 43 aged 65 years or older (25.6%) were in the incidental histopathological findings group ($P < 0.001$).

Female patients represented 16 of 31 records (51.6%) in the incidental histopathological findings group, compared with 564 of 1,318 (42.8%) in the acute-appendicitis group and 108 of 153 (70.6%) in the

histologically normal-appendix group ($P < 0.001$).

A laparoscopic approach was used in 94.3% of the acute-appendicitis group, 34.6% of the histologically normal appendix group, and 48.4% of the incidental histopathological findings group ($P < 0.001$). Primary appendectomy context was documented in 94.5%, 26.8%, and 48.4%, respectively (fixed-margin Monte Carlo exact $P < 0.001$).

3.5 Associations with available pathological outcomes

Age per 10-year increase was associated with incidental histopathological findings (aOR, 2.41; 95% CI, 1.95–2.99; $P < 0.001$). Age ≥ 40 years was also associated with incidental histopathological findings (aOR, 16.28; 95% CI, 6.86–38.61; $P < 0.001$).

Female sex was not independently associated with incidental histopathological findings after adjustment for age (aOR, 0.83; 95% CI, 0.39–1.77; $P = 0.627$) or age ≥ 40 years (aOR, 0.81; 95% CI, 0.39–1.70; $P = 0.579$). Appendectomy during another operation remained associated with incidental histopathological findings after adjustment for age per 10-year increase and sex (aOR, 2.62; 95% CI, 1.12–6.12; $P = 0.026$).

When the histologically normal appendix group was compared with the acute-appendicitis group, age ≥ 40 years (aOR, 4.13; 95% CI, 2.88–5.92; $P < 0.001$) and female sex (aOR, 2.77; 95% CI, 1.90–4.04; $P < 0.001$) were associated with histologically normal appendix.

Within the incidental histopathological findings group, an exploratory analysis compared the appendiceal neoplasm cases (LAMN, WD-NET, and adenocarcinoma) with the remaining findings (mucocoele, serrated lesion/polyp, and endometriosis). Because only five comparator cases were available and one sex category had no observations, standard logistic regression was unstable. A Firth penalized regression model was therefore used. Neither increasing age (aOR per 10 years, 1.81; 95% CI, 0.78–4.15; $P = 0.165$) nor female sex (aOR, 0.24; 95% CI, 0.01–5.58; $P = 0.372$) was significantly associated with the appendiceal neoplasm subset.

4. Discussion

In this cohort of 1,502 appendectomy records, incidental histopathological findings were identified in 31 records (2.1%), equivalent to approximately 1 in every 48 specimens. LAMN was the predominant diagnosis (23/31, 74.2%), followed by small numbers of WD-NET, endometriosis, mucocoele, serrated lesion/polyp, and adenocarcinoma.

The appendiceal neoplasm subset included 26 cases and accounted for 1.7% of the full cohort, indicating that most incidental histopathological findings in this study were appendiceal neoplasms.

Older age was the strongest demographic association; age ≥ 40 years remained strongly associated with incidental histopathological findings, whereas sex was not independently associated. Appendectomy performed during another operation was also associated with incidental histopathological findings.

The most notable feature of this cohort is the degree to which LAMN dominated the incidental histopathologic findings. LAMN accounted for 23 of 26 cases in the Appendiceal neoplasm cases (LAMN, WD-NET, and adenocarcinoma; $n = 26$) (88.5%). This pattern contrasts with several of the older series cited in this

manuscript. Akbulut et al. and Limaïem et al. reported parasitic infestation, particularly enterobiasis, as the dominant incidental finding [3, 4], while Dincel et al. identified fibrous obliteration and granulomatous appendicitis as leading categories in their series [5]. Several study-level explanations may account for this difference, and none should be interpreted as a proven mechanism.

King Khalid University Hospital is a tertiary referral center in King Saud University Medical City, and referral bias may plausibly augment the surgical caseload with atypical or incidentally discovered appendiceal lesions rather than uncomplicated acute appendicitis. The higher proportion of LAMN observed in such a center compared with community-hospital cohorts may partly reflect referral or management of patients with known or suspected mucinous neoplasia or those undergoing complex abdominal or gynecologic surgery for other indications.

The age distribution of the incidental-findings group itself is supportive of this interpretation. The mean age in this group was 55.1 ± 17.6 years compared to 25.9 ± 13.9 years in the acute-appendicitis group. The proportion of incidental findings increased from 0.0% in patients 0–17 years to 25.6% in patients 65 years or older. It is known that LAMN and other mucinous lesions accumulate with age; therefore, an older patient cohort would be expected to have a proportional increase in mucinous neoplasms and a corresponding decrease in parasitic or reactive findings that tend to occur in younger populations.

Twelve of thirty-one incidental findings (38.7%) were found incidentally during another operation and appendectomy during another operation was still independently associated with incidental findings (aOR, 2.62; 95% CI, 1.12–6.12; $P = 0.026$). If incidental appendectomy is performed at the time of gynecologic, colorectal, or other abdominal surgery, it is more likely to sample an appendix harboring an asymptomatic mucinous lesion than an appendix removed for acute inflammatory disease. This effect of the surgical context may be one of the reasons for the overrepresentation of LAMN relative to symptomatic diagnoses such as acute parasitic appendicitis, which is often asymptomatic or incidental on imaging or at laparotomy.

The referral pattern, the older age structure of the incidental-findings group, and the high proportion of incidental appendectomies all contribute plausible non-exclusive explanations for the LAMN-heavy spectrum observed here. The single-center retrospective design does not allow us to distinguish between these explanations, which would require multicenter data with consistent ascertainment of cases across time periods.

Older age showed a strong association with incidental histopathological findings. The proportion increased from 0.0% among patients aged 0–17 years to 25.6% among patients aged 65 years or older. After adjustment for sex, age ≥ 40 years remained strongly associated with incidental histopathological findings.

Previous research has similarly identified older age as an important marker of underlying appendiceal neoplasia. A multicenter analysis found that patients older than 40 years, particularly those with an enlarged appendix on computed tomography, had an increased probability of appendiceal malignancy [10]. The current study supports careful pathological and clinical review in older patients while preserving routine histopathological examination across all ages.

The findings underscore the potential clinical value of routine histopathological examination of appendectomy specimens. Macroscopic inspection alone may not reliably identify small neuroendocrine tumors, serrated

lesions, early mucinous neoplasms, endometriosis, or fibrous obliteration [1, 6]. The high proportion of LAMN among the primary lesion/neoplasm subset is clinically important. Pathology reports for LAMN should document appendix integrity, perforation, proximal resection-margin status, extension of mucin or neoplastic epithelium beyond the appendix, acellular or cellular extra-appendiceal mucin, peritoneal involvement, and pathological stage [8]. Similarly, appendiceal NET reports should include tumor size, grade, Ki-67 proliferative index, depth and extent of invasion, margin status, lymphovascular invasion, and mesoappendiceal involvement. These features guide whether appendectomy is sufficient or whether staging, surveillance, or additional surgical assessment should be considered [9, 11].

This study has several notable strengths. It adds to the contemporary institutional datasets from Saudi Arabia describing the full spectrum of incidental histopathological findings in appendectomy specimens, contributing locally relevant data to a topic in which data from the gulf region remains limited. In addition, this study benefits from examining three comparator groups simultaneously (acute appendicitis, histologically normal appendix, and incidental histopathological findings) rather than the two-group case-versus-control structure, which allows the demographic and surgical approach profile of incidental findings to be interpreted against two distinct reference populations rather than one. The inclusion of appendectomies performed both as primary procedures and incidentally during other operations provides a broader view of the institutional appendiceal pathology caseload than studies restricted to emergency appendectomy alone.

This study has several limitations. First, its retrospective, single-center design may limit generalizability and is susceptible to selection bias and incomplete or inconsistent documentation. Second, the relatively small number of incidental histopathological findings (31 cases) limited the statistical power for diagnosis-specific and subgroup analyses and increased uncertainty around the corresponding estimates.

Third, the available data were limited primarily to age, sex, final histopathological diagnosis, surgical indication and operative text, and selected tumor-related variables. Several clinically relevant variables, including symptoms, imaging findings, laboratory results, operative appearance, and comorbidities, were unavailable. Documentation of tumor-related variables was also incomplete in some cases.

Fourth, longitudinal postoperative data, including recurrence, additional treatment, complications, readmissions, and survival, were unavailable, precluding assessment of long-term clinical outcomes. Finally, the inclusion of appendectomies performed as part of other surgical procedures may have introduced referral or selection effects and may limit the generalizability of the observed histopathological distribution.

Fifth, in comparison with the three prior series, tumor size in the present cohort was markedly larger overall (median 5.0 cm, IQR 1.7–6.0, range 0.4–15.5 cm), driven by LAMN, whereas Akbulut et al. reported a mean tumor diameter of 6.8 mm (range, 4–10 mm) [3], Limaïem et al. reported neuroendocrine tumor sizes of 1–23 mm [4], and Dincel et al. reported carcinoid tumors of 0.3–0.8 cm [5]; the present cohort's WD-NET subset (median 0.7 cm, IQR 0.6–0.8) closely matched these sub-centimeter figures. Depth of invasion was similarly limited across studies, with most lesions confined to the muscularis propria or subserosa in the present series (13/25, 52.0%) and in Akbulut et al. and Limaïem et al., where spread ranged from submucosal to subserosal [3, 4]. None of the three comparator studies reported margin status, perineural invasion, lymphovascular invasion, or extra-appendiceal mucin, so the present findings of a 15.4% positive-margin rate (4/26) and 50.0% extra-appendiceal involvement (6/12 documented LAMN cases) cannot be directly compared. Additional surgery

was required in 7.7% of neoplasm cases (2/26) here, lower than the 100% hemicolectomy rate among Limaïem et al.'s two adenocarcinoma patients [4], but consistent with the appendectomy-alone approach reported by Akbulut et al. and Dincel et al., in whom no tumor patient required hemicolectomy [3, 5].

5. Conclusion

Incidental histopathological findings were identified in 31 of 1,502 appendectomy records (2.1%), with LAMN accounting for most cases. Older age, particularly age ≥ 40 years, was independently associated with these findings, whereas sex was not. Clinically relevant pathological features included positive resection margins, extra-appendiceal involvement in LAMN, and perineural and lymphovascular invasion in WD-NET. Two patients required additional surgery, including one patient with LAMN and one with adenocarcinoma; the adenocarcinoma case underwent completion right hemicolectomy because of a positive resection margin. These findings highlight the importance of careful histopathological assessment of appendectomy specimens and its potential impact on subsequent management.

Abbreviations

aOR

adjusted odds ratio

CI

confidence interval

IQR

interquartile range

IRB

Institutional Review Board

LAMN

low-grade appendiceal mucinous neoplasm

NET

neuroendocrine tumor

OR

odds ratio

SD

standard deviation

STROBE

Strengthening the Reporting of Observational Studies in Epidemiology

WD-NET

well-differentiated neuroendocrine tumor.

Declarations

Ethical approval

Ethical approval was obtained from the Institutional Review Board of King Saud University Medical City, Riyadh, Saudi Arabia **E-25-10303** ,20/9/2025.

Consent to participate

The requirement for informed consent was waived because this was a retrospective study using de-identified routinely collected data.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Author Contribution

TA provided supervision and guidance, contributed to manuscript development, and critically revised the manuscript. AA contributed to data collection, data cleaning, interpretation of the results, manuscript drafting, coordination of manuscript development, and figures design. MA, SA, FA, SJ, MH, MA, RH, and FA contributed to data collection and review of the study data and editing the manuscript. Ahmed Alhumidi contributed to study supervision, interpretation of the findings, and critical revision of the manuscript. Abdullah Alkhudiar contributed to manuscript review and revision. All authors reviewed and approved the final manuscript and agreed to be accountable for the work.

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Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request and subject to institutional and ethical restrictions.

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Figures

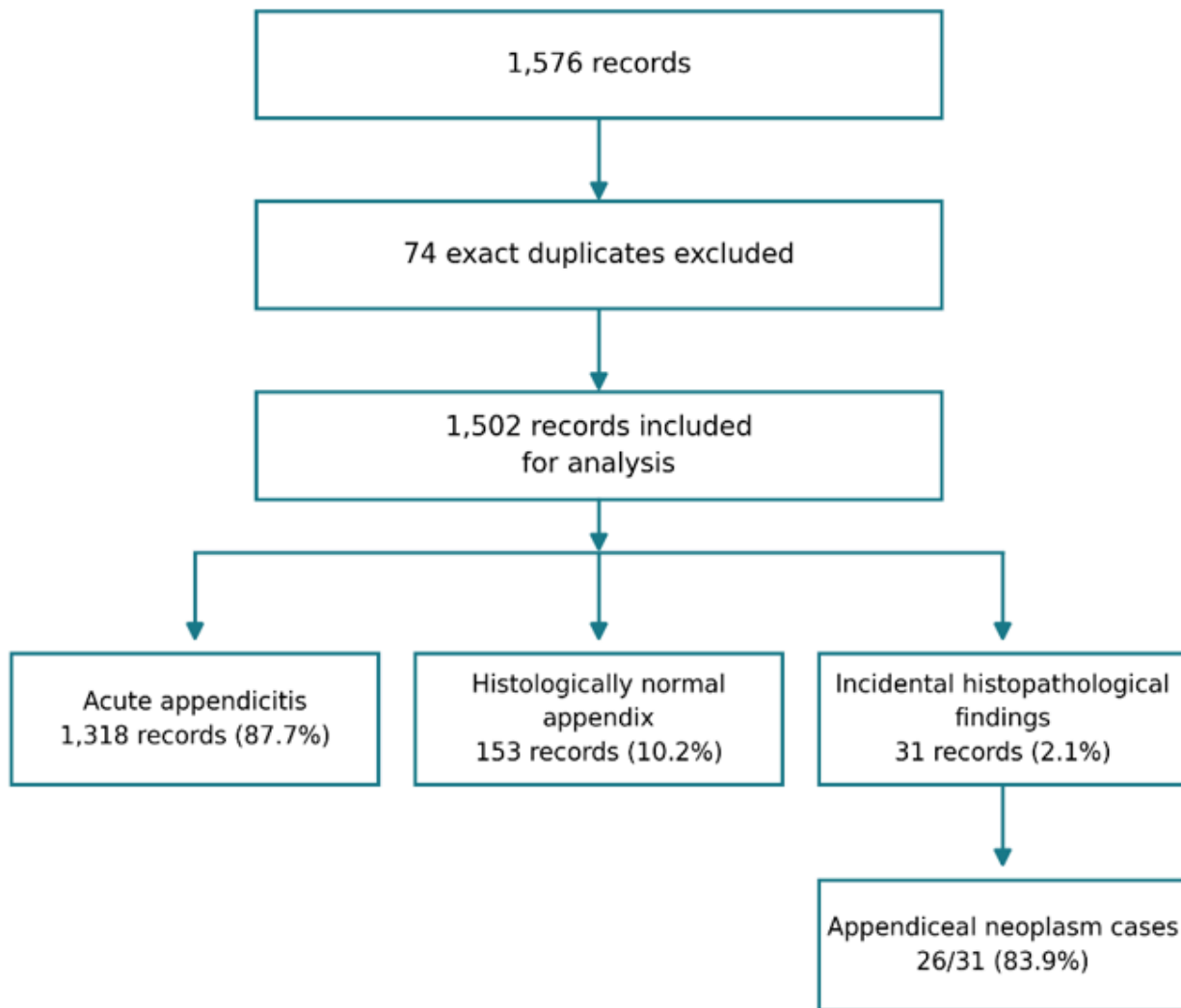


Figure 1

Study flow and distribution of histopathological findings.

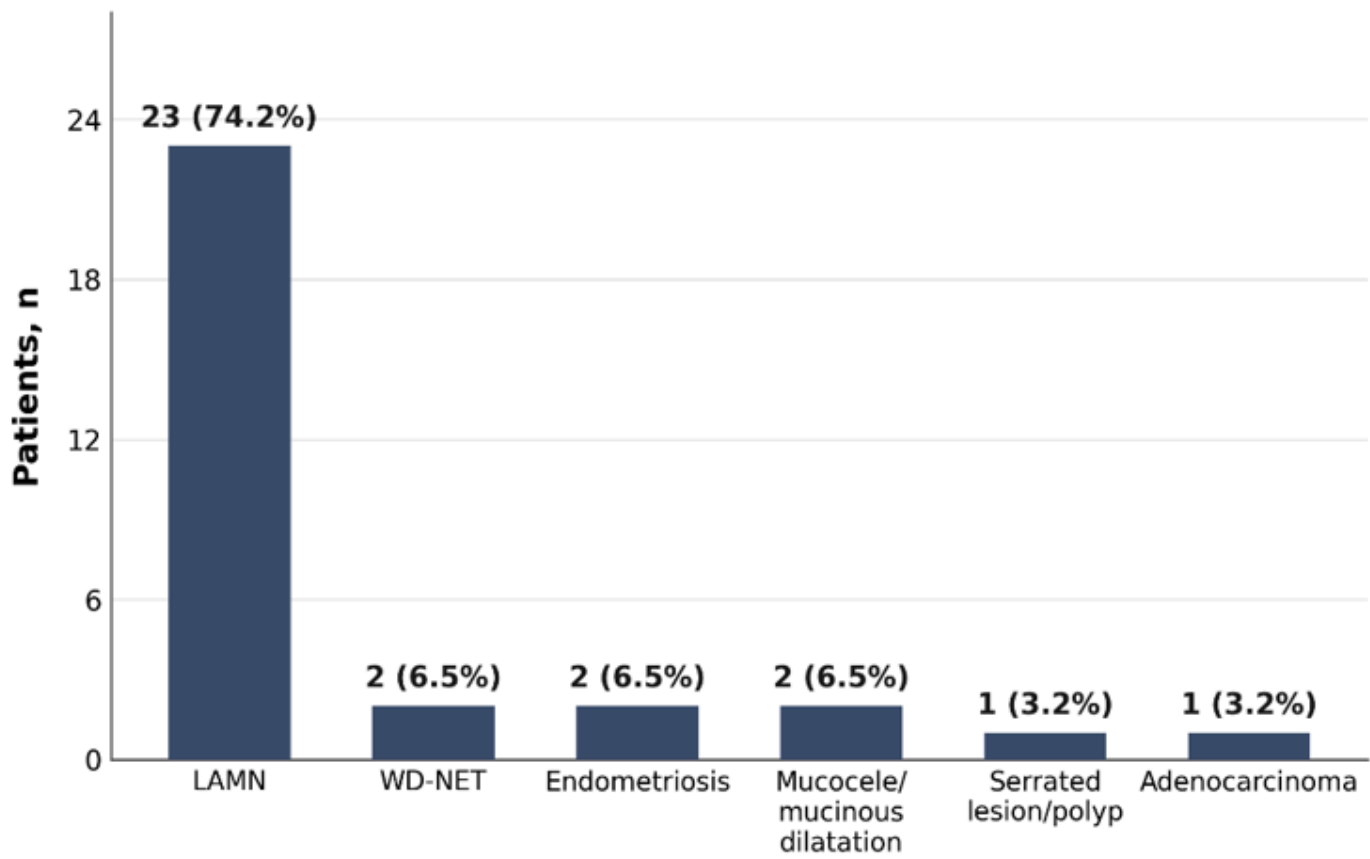


Figure 2

Distribution of incidental Histopathological Diagnoses.

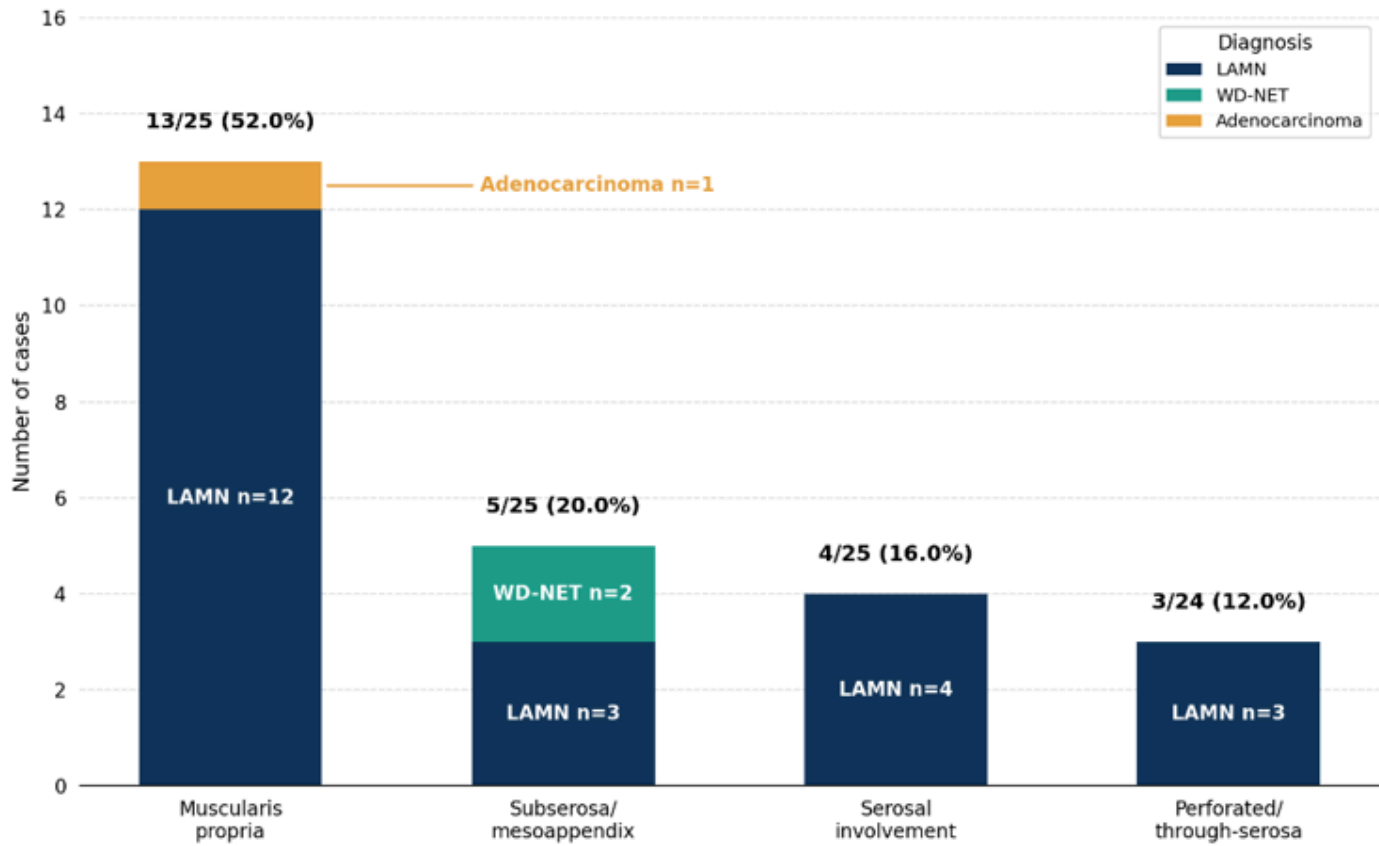


Figure 3

Depth of invasion among appendiceal neoplasm cases (LAMN, WD-NET, and adenocarcinoma; n = 26).

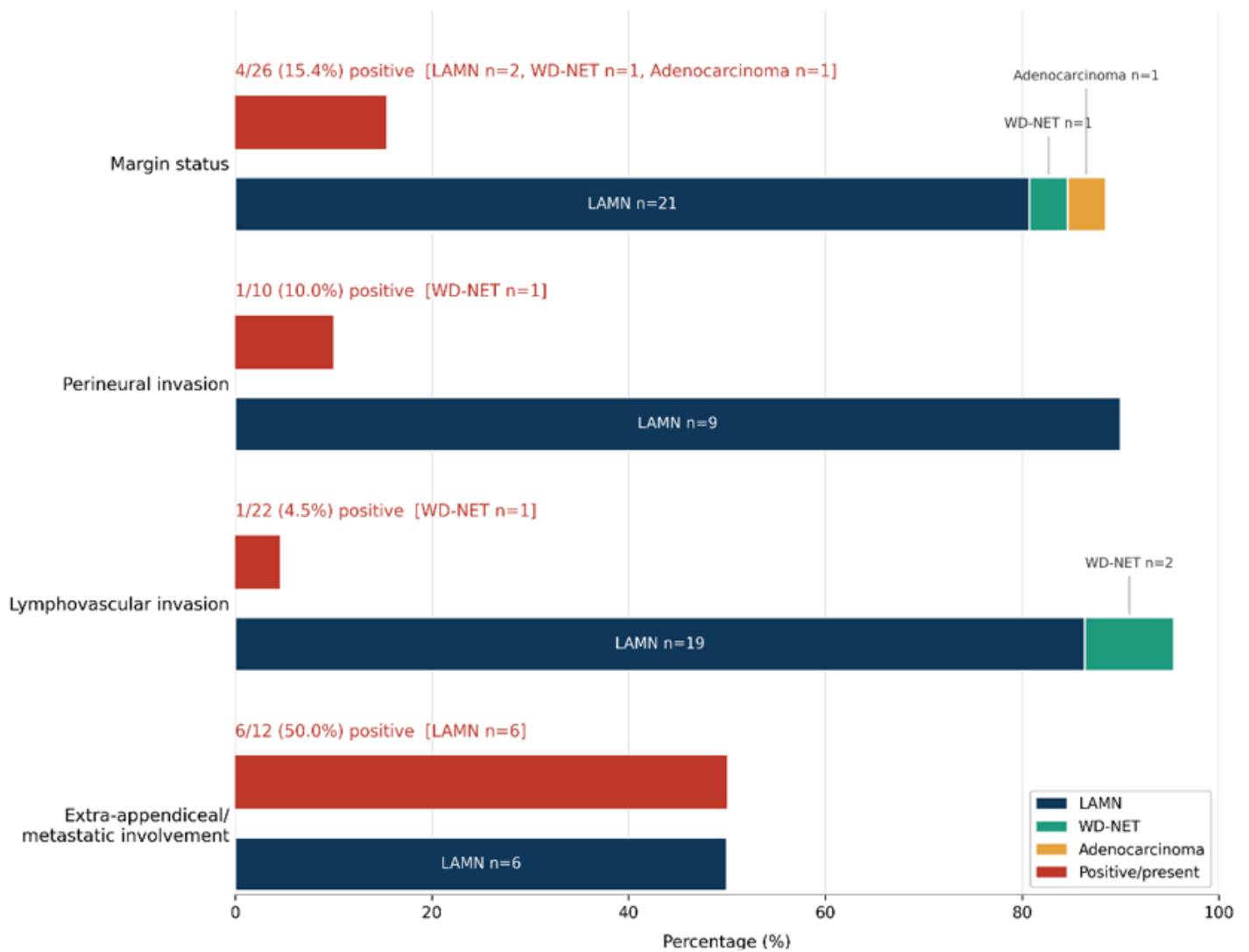


Figure 4

Pathological features among appendiceal neoplasm cases (LAMN, WD-NET, and adenocarcinoma; n = 26).

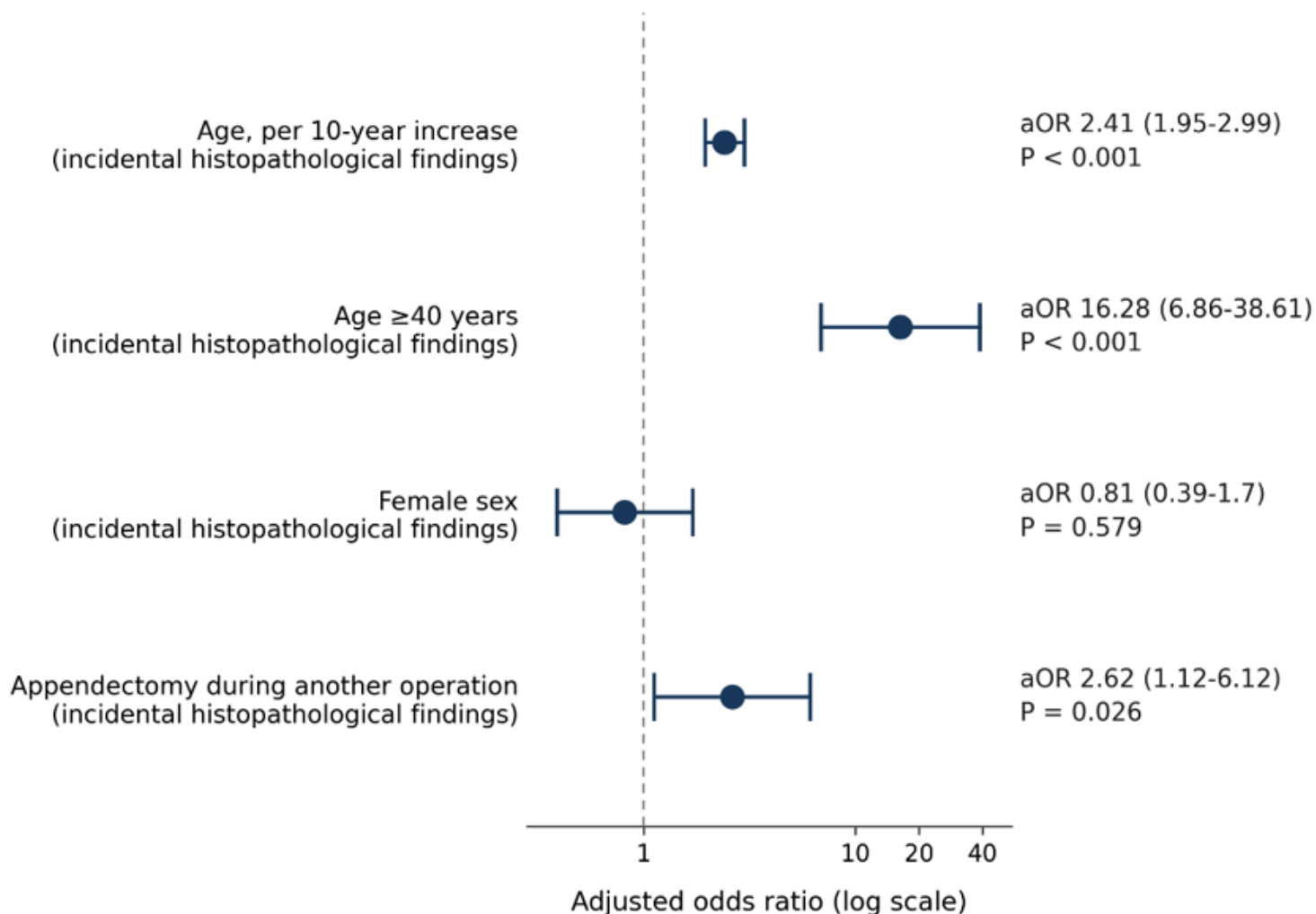


Figure 5

Multivariable adjusted associations with incidental histopathological findings.

Supplementary Files

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