

Clinical and Pathological Characteristics of Mucinous Adenocarcinoma in Colon Cancer: Comparison with Classic Adenocarcinoma

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Abstract

Background

Mucinous adenocarcinoma of the colon ($\geq 50\%$ extracellular mucin) is often regarded as biologically distinct from classic (non-mucinous) adenocarcinoma. We compared their clinicopathological profiles in a contemporary surgical series.

Methods

We retrospectively reviewed patients undergoing oncological resection for colon adenocarcinoma between October 2021 and March 2026. Rectal tumours, neoadjuvant-treated cases and signet ring cell carcinoma were excluded. Groups were compared with Mann–Whitney U and chi-square or Fisher's exact tests. Multivariable logistic regression assessed whether mucinous histology independently predicted advanced invasion (pT3–T4) and nodal metastasis (pN+), adjusting for age, sex and tumour laterality (and pT stage in the nodal model).

Results

The cohort included 155 colon cancers: 29 mucinous (18.7%) and 126 classic. Median age was 76 versus 70 years, and sex distribution was similar. Mucinous tumours were more often right-sided (75.9% vs 44.4%; OR 3.93, 95% CI 1.57–9.86; $p = 0.002$). Advanced pT stage was common and comparable (86.2% vs 82.5%; $p = 0.786$). Nodal metastasis was less frequent in mucinous cancers, although this difference did not reach statistical significance (31.0% vs 50.8%; OR 0.44, 95% CI 0.18–1.03; $p = 0.055$). TNM stage distribution differed overall ($p = 0.014$), with stage II more frequent in mucinous disease. Poor differentiation was markedly more common in mucinous tumours (24.1% vs 4.8%; OR 6.36; $p = 0.003$), whereas lymphovascular invasion was less frequent (10.3% vs 32.5%; OR 0.24; $p = 0.017$). In adjusted analyses, mucinous histology was not independently associated with pT3–T4 (aOR 1.40; $p = 0.578$) or pN+ (aOR 0.50; $p = 0.132$); pT3–T4 predicted nodal metastasis (aOR 3.84; $p = 0.009$).

Conclusions

In this colon-only cohort, mucinous cancers clustered on the right and were more often poorly differentiated, yet were not independently associated with deeper invasion or nodal spread after adjustment. Treating mucinous histology as a distinct subtype may add nuance to pathological risk assessment.

Introduction

Colorectal cancer remains a major global health problem. According to the most recent GLOBOCAN estimates, it is still among the most commonly diagnosed malignancies worldwide and one of the leading causes of cancer-related death. More recent burden analyses tell much the same story from another angle: even where age-standardised mortality has fallen, the absolute number of cases, deaths and disability-adjusted life years continues to rise, driven largely by population ageing and growth. Against that background, even less common histological subtypes deserve closer attention, because they still represent a substantial group of patients in everyday colorectal practice [1, 2].

Within this broader disease spectrum, mucinous adenocarcinoma warrants separate consideration. It is defined by extracellular mucin occupying at least 50% of the tumour and accounts for roughly 10–15% of colorectal adenocarcinomas in contemporary series [3, 4]. Over the past few years, the argument for treating mucinous adenocarcinoma as more than a purely descriptive microscopic variant has become stronger. Compared with classic adenocarcinoma, these tumours are more often proximal, more frequently poorly differentiated, and enriched for molecular features associated with mismatch repair deficiency, microsatellite instability, and BRAF-related biology. Multi-omic and immunopathology studies have gone further still, suggesting that the mucinous phenotype is associated with a distinct tumour microenvironment, with altered stromal and immune cell interactions and characteristic mucin-associated expression patterns, particularly involving MUC2 and MUC5AC [4–6].

What remains less clear is how these biological differences translate into clinicopathological behaviour. Recent retrospective cohorts have linked mucinous histology with larger tumours, more advanced T stage and, in some settings, a greater burden of metastatic disease [3, 4, 7]. Yet the prognostic signal has not been uniform. A 2024 systematic review and meta-analysis including 56 studies and more than 800,000 patients confirmed that mucinous adenocarcinoma differs from conventional adenocarcinoma across several clinicopathological variables and is associated with poorer overall survival, but not with a clear difference in disease-free survival; notably, lymphatic and perineural invasion were not consistently different between groups [7]. Contemporary cohort data have added nuance rather than resolving the issue. Some series suggest that adverse outcomes are driven mainly by left-sided or rectal disease, whereas others indicate that mucinous differentiation is strongly associated with proximal location, high grade, MMR deficiency, and BRAF mutation, but does not retain independent prognostic value after multivariable adjustment [4, 6, 7].

That uncertainty is precisely why a focused colon-only analysis still has value. When colon and rectal cancers are examined together, and when the apparent effect of mucinous histology varies by site and stage, interpretation quickly becomes more difficult [4, 7, 8]. Because nodal status and invasion-related pathological features remain central to postoperative risk stratification, clarifying whether they truly differ in mucinous tumours is not just an academic question. In the present study, we compared mucinous adenocarcinoma with classic adenocarcinoma in patients undergoing resection for colon cancer, concentrating on the clinicopathological variables most likely to reflect biological aggressiveness in routine practice: tumour location, differentiation, pathological T and N stage, lymphovascular invasion, perineural invasion and tumour budding. We hypothesised that mucinous adenocarcinoma would be

associated with more advanced pathological local invasion and with a distinct pattern of nodal and invasion-related pathological findings [3, 4, 7, 8].

Materials and Methods

Study design and patient selection

This retrospective observational study was designed to compare the clinicopathological features of mucinous adenocarcinoma with those of classic adenocarcinoma in surgically treated colon cancer. Patients were identified from the study database covering the period from October 2021 to March 2026. The study was approved by the local ethics committee on 11 June 2026 with the approval number 11.06.2026/07. Eligibility was limited to patients with histopathologically confirmed colorectal adenocarcinoma who underwent oncological resection and had complete pathological staging data available for review. In keeping with the original study design, patients with neuroendocrine tumours, metastatic secondary involvement of the colon, recurrent tumours, concurrent malignancy, or incomplete pathological data were not considered eligible.

For the present colon-only analysis, three further exclusions were applied in advance: tumours recorded as rectal, patients who had received neoadjuvant chemotherapy, and patients with signet ring cell carcinoma. The cohort comprised 155 patients, including 126 with classic adenocarcinoma and 29 with mucinous adenocarcinoma.

Histological subtype was assigned from the final resection pathology report. Mucinous adenocarcinoma was defined as adenocarcinoma containing at least 50% extracellular mucin. Tumours recorded simply as adenocarcinoma and not meeting that threshold were classified as classic (non-mucinous) adenocarcinoma.

Data sources and variable definitions

Clinical records, operative notes and final pathology reports were reviewed retrospectively, and the relevant variables were entered into an electronic database for analysis. The demographic variables analysed were age and sex. The pathological and anatomical variables of interest were tumour location, histological subtype, differentiation grade, pT category, pN category, pM category, overall pathological stage, total lymph node count, number of metastatic lymph nodes, lymphovascular invasion, perineural invasion, and tumour budding.

The tumour site was available in the database in two forms: a broad anatomical location field and a detailed subsite field. The broad location field classified tumours as right colon, left colon, right flexure, or rectum. The detailed subsite field recorded the precise site as caecum, ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid colon, rectosigmoid colon, or rectum. Cohort selection for the present study was based on the broad location field. Accordingly, tumours classified overall as rectal were excluded, whereas cases recorded as rectosigmoid in the

detailed subsite field were retained if the primary location field categorised them as left colon. The same broad location variable was used for the laterality analysis; the broad anatomical location field was used as the primary classification variable. Tumours coded as right colon or right flexure were classified as right-sided, whereas tumours coded as left colon were classified as left-sided. Transverse colon and rectosigmoid cases were retained and analysed according to the corresponding broad location category recorded in the database.

Differentiation grade was recorded as well differentiated (grade 1), moderately differentiated (grade 2), or poorly differentiated (grade 3). Lymphovascular invasion and perineural invasion were recorded as present or absent. Tumour budding was documented in the pathology reports as low (Bd1), intermediate (Bd2), or high (Bd3).

Outcomes

The primary outcome of the study was advanced local tumour invasion, defined a priori as pT3–T4. The main secondary outcomes were nodal metastasis (pN positivity), distant metastasis (pM1), overall pathological stage, lymphovascular invasion, perineural invasion, tumour budding, differentiation grade, and lymph node yield.

For selected analyses, some pathological variables were examined in dichotomised form to improve clinical interpretability. Differentiation was analysed both as a three-level categorical variable and as poor differentiation (grade 3) versus grades 1–2. Tumour budding was analysed both across the original Bd1/Bd2/Bd3 categories and as intermediate/high budding (Bd2–3) versus low budding (Bd1). Overall stage was considered both in its original I–IV form and, where relevant, as stage I–II versus stage III–IV. All pathological variables were taken from the final resection specimen report rather than from preoperative biopsy material.

Statistical analysis

Because this was a retrospective study based on a fixed study period, no a priori sample size calculation was performed. Continuous variables were assessed for distributional normality using the Shapiro–Wilk test. As the continuous variables included in the analysis were not normally distributed in at least one comparison group, they were summarised as medians and interquartile ranges (IQRs) and compared using the Mann–Whitney U test.

Categorical variables were presented as numbers (n) and percentages (%). Between-group comparisons were performed using Pearson's chi-square test or Fisher's exact test, as appropriate according to expected cell counts. All tests were two-sided, and p-values <0.05 were considered statistically significant.

To quantify the association between histological subtype and selected clinicopathological features, univariable odds ratios (ORs) with 95% confidence intervals (CIs) were calculated from 2 × 2 contingency tables. In addition, two multivariable binary logistic regression models were constructed.

The first model examined whether mucinous histology was independently associated with advanced pT stage (pT3–T4) and included histological subtype, age, sex, and tumour laterality as covariates. The second model examined predictors of nodal metastasis (pN positivity) and included histological subtype, age, sex, tumour laterality, and advanced pT stage. Results from the regression analyses were reported as adjusted ORs with 95% CIs.

The final analytic dataset was complete for all variables included in the reported analyses; therefore, no missing-data imputation was required, and all analyses were performed on a complete-case basis.

All statistical analyses were carried out in Python 3.11 (Python Software Foundation, Wilmington, DE, USA). Data management was performed using pandas 2.2.3 and NumPy 2.3.5. Statistical testing was undertaken with SciPy 1.17.0 and statsmodels 0.14.6. Figures were prepared using Matplotlib 3.10.8.

Results

The cohort comprised 126 classic adenocarcinomas and 29 mucinous adenocarcinomas; the mucinous subtype accounted for 18.7% of eligible colon cancers. The subsequent analyses were organised to address, in sequence, the clinicodemographic profile of the cohort, the anatomical distribution of tumours, pathological stage and nodal status, histological aggressiveness markers, and finally the univariable and multivariable effect estimates associated with mucinous histology. No missing values were present in the variables entered into the analysis.

Table 1 summarises the basic demographic and anatomical features of the cohort. Age was somewhat higher in the mucinous group, with a median of 76 years (IQR 64–84) compared with 70 years (IQR 64–77) in the classic group, although the difference did not reach statistical significance ($p = 0.113$). Sex distribution was similar between groups (male 55.2% vs 61.9%; $p = 0.503$). The clearest anatomical difference lay in tumour laterality. Mucinous adenocarcinomas were much more often right-sided than classic adenocarcinomas (75.9% vs 44.4%; $p = 0.002$). When detailed colonic subsites were examined, the distribution also differed significantly between histological subtypes ($p = 0.015$). Mucinous tumours were proportionally more frequent in the caecum, ascending colon and hepatic flexure, whereas classic adenocarcinomas were concentrated mainly in the sigmoid and rectosigmoid colon (Table 2, Fig. 1).

Table 1
Clinicodemographic characteristics and tumour laterality

Characteristic	Classic adenocarcinoma (n = 126)	Mucinous adenocarcinoma (n = 29)	p value
Patients, n	126	29	—
Age, years, median (IQR) ^m	70 (64–77)	76 (64–84)	0.113
Male sex, n (%) ^t	78 (61.9%)	16 (55.2%)	0.503
Tumour laterality, n (%)^t			0.002
Left-sided	70 (55.6%)	7 (24.1%)	
Right-sided	56 (44.4%)	22 (75.9%)	

Data are presented as n (%) unless otherwise indicated. Continuous variables are shown as median (IQR). P values were derived from the Mann–Whitney U test (^m), Pearson's chi-square test (^t), or Fisher's exact test, as appropriate.

Table 2
Detailed colonic subsite distribution by histological subtype

Characteristic	Classic adenocarcinoma (n = 126)	Mucinous adenocarcinoma (n = 29)	p value
Detailed colonic subsite, n (%)^t			0.015
Caecum	21 (16.7%)	8 (27.6%)	
Ascending colon	18 (14.3%)	6 (20.7%)	
Hepatic flexure	10 (7.9%)	6 (20.7%)	
Transverse colon	8 (6.3%)	3 (10.3%)	
Splenic flexure	4 (3.2%)	1 (3.4%)	
Descending colon	6 (4.8%)	3 (10.3%)	
Sigmoid colon	44 (34.9%)	1 (3.4%)	
Rectosigmoid colon	15 (11.9%)	1 (3.4%)	

Percentages are calculated within each histology group. The p-value refers to the overall comparison across subsites and was derived from Pearson's chi-square test (^t). Rectosigmoid cases were retained because the primary location field classified these tumours as left-sided colon rather than rectal lesions.

Bars show the percentage distribution within each histology group; the overall comparison across subsites was significant ($p = 0.015$).

Pathological stage and nodal findings are detailed in Table 3, with the stage profile illustrated in Fig. 2. Local tumour depth was similar in the two groups. Advanced pT stage (T3–T4) was common in both mucinous and classic tumours (86.2% vs 82.5%; $p = 0.786$), and the full pT distribution did not differ significantly (overall $p = 0.670$). Nodal disease, however, showed a somewhat different pattern. Patients with mucinous adenocarcinoma had a lower rate of pN positivity than those with classic adenocarcinoma (31.0% vs 50.8%); however, this difference did not reach statistical significance ($p = 0.055$).

Distant metastasis at pathological staging was numerically more frequent in the mucinous group (17.2% vs 7.1%), although again the difference was not statistically significant ($p = 0.141$). The overall TNM stage profile did differ between groups ($p = 0.014$). Stage II disease was more common in mucinous adenocarcinoma (55.2% vs 32.5%), whereas stage III disease predominated in the classic group (20.7% vs 46.0%). Once the stage was collapsed into stages I–II versus III–IV, the between-group difference was no longer significant (37.9% vs 53.2%; $p = 0.139$). Median lymph node yield was similar in the two groups (20 [IQR 14–27] vs 18 [IQR 13–25.8]; $p = 0.341$), as was the median number of positive nodes, although the latter was lower in mucinous tumours and approached significance (0 [IQR 0–1] vs 0.5 [IQR 0–2]; $p = 0.088$).

Table 3
Pathological stage and lymph node findings

Characteristic	Classic adenocarcinoma (n = 126)	Mucinous adenocarcinoma (n = 29)	p value
pT category, n (%)^t			0.670
T1	6 (4.8%)	0 (0.0%)	
T2	16 (12.7%)	4 (13.8%)	
T3	90 (71.4%)	21 (72.4%)	
T4	14 (11.1%)	4 (13.8%)	
Advanced pT stage (T3–T4), n (%) ^f	104 (82.5%)	25 (86.2%)	0.786
pN category, n (%)^t			0.157
N0	62 (49.2%)	20 (69.0%)	
N1	44 (34.9%)	6 (20.7%)	
N2	20 (15.9%)	3 (10.3%)	
Nodal metastasis (pN+), n (%) ^t	64 (50.8%)	9 (31.0%)	0.055
Distant metastasis (pM1), n (%) ^f	9 (7.1%)	5 (17.2%)	0.141
TNM stage, n (%)^t			0.014
Stage I	18 (14.3%)	2 (6.9%)	
Stage II	41 (32.5%)	16 (55.2%)	
Stage III	58 (46.0%)	6 (20.7%)	
Stage IV	9 (7.1%)	5 (17.2%)	
Stage III–IV disease, n (%) ^t	67 (53.2%)	11 (37.9%)	0.139
Total lymph nodes examined, median (IQR) ^m	18 (13–25.8)	20 (14–27)	0.341
Positive lymph nodes, median (IQR) ^m	0.5 (0–2)	0 (0–1)	0.088

Data are presented as n (%) unless otherwise indicated. Continuous variables are shown as median (IQR). Two-sided p values were derived from the Mann–Whitney U test (^m), Pearson's chi-square test (^t), or Fisher's exact test (^f), as appropriate.

Each bar sums to 100% within the relevant histology group. Values printed inside the bars show the count and within-group percentage for each stage.

Histopathological markers of aggressiveness are presented in Table 4. Differentiation grade differed materially between the two histological subtypes (overall $p = 0.003$). Poor differentiation was substantially more common in mucinous adenocarcinoma, affecting 24.1% of cases compared with 4.8% in the classic group ($p = 0.003$). By contrast, lymphovascular invasion was less frequent in mucinous tumours (10.3% vs 32.5%; $p = 0.017$). Perineural invasion did not differ significantly between groups (10.3% vs 21.4%; $p = 0.173$). Tumour budding showed a similar pattern: neither the full Bd1–Bd3 distribution ($p = 0.487$) nor the proportion with intermediate or high budding (13.8% vs 18.3%; $p = 0.568$) differed significantly.

Table 4
Histological aggressiveness markers

Characteristic	Classic adenocarcinoma (n = 126)	Mucinous adenocarcinoma (n = 29)	<i>p</i> value
Differentiation grade, n (%)^t			0.003
Well differentiated (Grade 1)	82 (65.1%)	15 (51.7%)	
Moderately differentiated (Grade 2)	38 (30.2%)	7 (24.1%)	
Poorly differentiated (Grade 3)	6 (4.8%)	7 (24.1%)	
Poor differentiation (Grade 3), n (%) ^f	6 (4.8%)	7 (24.1%)	0.003
Lymphovascular invasion, n (%) ^t	41 (32.5%)	3 (10.3%)	0.017
Perineural invasion, n (%) ^t	27 (21.4%)	3 (10.3%)	0.173
Tumour budding, n (%)^t			0.487
Low (Bd1)	103 (81.7%)	25 (86.2%)	
Intermediate (Bd2)	17 (13.5%)	4 (13.8%)	
High (Bd3)	6 (4.8%)	0 (0.0%)	
Intermediate/high tumour budding (Bd2–Bd3), n (%) ^t	23 (18.3%)	4 (13.8%)	0.568

Data are presented as n (%). *P* values were derived from Pearson's chi-square (^t) test or Fisher's exact test (^f), as appropriate.

Univariable effect estimates are shown in Table 5 and Fig. 3. Mucinous histology was strongly associated with right-sided location (OR 3.93, 95% CI 1.57–9.86) and with poor differentiation (OR 6.36, 95% CI 1.95–20.74). It was inversely associated with lymphovascular invasion (OR 0.24, 95% CI 0.07–0.84). By contrast, the confidence intervals for advanced pT stage, nodal metastasis, distant metastasis, stage III–IV disease, perineural invasion and tumour budding all crossed unity.

Table 5
Univariable odds ratios for selected clinicopathological features

Feature	Mucinous	Classic	Univariable OR (95% CI)	p value
Right-sided tumour location	22/29 (75.9%)	56/126 (44.4%)	3.93 (1.57–9.86)	0.002
Advanced pT stage (T3–T4)	25/29 (86.2%)	104/126 (82.5%)	1.32 (0.42–4.18)	0.786
Nodal metastasis (pN+)	9/29 (31.0%)	64/126 (50.8%)	0.44 (0.18–1.03)	0.055
Distant metastasis (pM1)	5/29 (17.2%)	9/126 (7.1%)	2.71 (0.83–8.80)	0.141
Stage III–IV disease	11/29 (37.9%)	67/126 (53.2%)	0.54 (0.24–1.23)	0.139
Poor differentiation (Grade 3)	7/29 (24.1%)	6/126 (4.8%)	6.36 (1.95–20.74)	0.003
Lymphovascular invasion	3/29 (10.3%)	41/126 (32.5%)	0.24 (0.07–0.84)	0.017
Perineural invasion	3/29 (10.3%)	27/126 (21.4%)	0.42 (0.12–1.50)	0.173
Intermediate/high tumour budding (Bd2–Bd3)	4/29 (13.8%)	23/126 (18.3%)	0.72 (0.23–2.26)	0.568

Odds ratios greater than 1 indicate that the feature was more common in mucinous adenocarcinoma than in classic adenocarcinoma. Odds ratios were calculated from 2 × 2 contingency tables.

Markers indicate the point estimate and horizontal lines the 95% confidence interval. Odds ratios above 1 favour a higher prevalence in mucinous adenocarcinoma.

Two multivariable logistic models were fitted and are summarised in Table 6. After adjustment for age, sex and tumour laterality, mucinous histology was not independently associated with advanced pT stage (adjusted OR 1.40, 95% CI 0.42–4.66; $p = 0.578$). In the nodal metastasis model, which additionally included advanced pT stage, mucinous histology again did not emerge as an independent predictor (adjusted OR 0.50, 95% CI 0.20–1.23; $p = 0.132$). Within that model, advanced pT stage was the only covariate that remained statistically significant (adjusted OR 3.84, 95% CI 1.41–10.46; $p = 0.009$). Both

models converged without fitting problems; the nodal model showed modestly better overall explanatory performance than the pT model (pseudo-R² 0.071 vs 0.030).

Table 6
Multivariable binary logistic regression models

Variable	Adjusted OR (95% CI)	p value	Model
Model 1: Advanced pT stage (T3–T4) as dependent variable			
Mucinous histology (vs classic)	1.40 (0.42–4.66)	0.578	Model 1
Age (per year)	1.02 (0.98–1.05)	0.342	Model 1
Male sex	2.04 (0.84–4.97)	0.116	Model 1
Right-sided location	0.76 (0.31–1.88)	0.552	Model 1
Model 2: Nodal metastasis (pN+) as dependent variable			
Mucinous histology (vs classic)	0.50 (0.20–1.23)	0.132	Model 2
Age (per year)	0.99 (0.96–1.02)	0.428	Model 2
Male sex	0.86 (0.42–1.75)	0.673	Model 2
Right-sided location	0.57 (0.28–1.16)	0.119	Model 2
Advanced pT stage (T3–T4)	3.84 (1.41–10.46)	0.009	Model 2

Model 1 used advanced pT stage (T3–T4) as the dependent variable and included histology, age, sex and tumour laterality. Model 2 used nodal metastasis (pN+) as the dependent variable and included histology, age, sex, tumour laterality and advanced pT stage. Model 1: N = 155, pseudo-R²=0.030, AIC = 145.99, likelihood-ratio p = 0.377. Model 2: N = 155, pseudo-R²=0.071, AIC = 211.18, likelihood-ratio p = 0.010.

Discussion

The present study provides a focused colon-only analysis of mucinous adenocarcinoma in surgically treated colon cancer. By excluding rectal tumours, neoadjuvant-treated cases and signet ring cell carcinoma, we aimed to examine mucinous histology in a more homogeneous surgical setting than many mixed colorectal series allow. Within this framework, mucinous tumours in our cohort showed a

recognisable phenotype: they were predominantly right-sided and more often poorly differentiated. At the same time, they were not independently associated with more advanced local invasion or nodal disease after adjustment, and lymphovascular invasion was less frequent. This combination suggests that mucinous histology may represent a distinct clinicopathological subtype rather than a uniform marker of aggressive disease.

Recent outcome studies have reported inconsistent findings regarding the prognostic significance of mucinous histology. Kim et al. reported that the adverse prognostic effect of mucinous histology in stage II and III colon cancer was driven largely by stage III disease, whereas Powers et al. found no overall survival disadvantage for mucinous stage III colon cancer in multivariable analysis. Bong et al., analysing non-metastatic disease, similarly observed no survival difference in stages I–II but reported worse outcomes in stage III mucinous cancers. By contrast, Zhang et al., in a 2022 meta-analysis of patients treated with postoperative first-line adjuvant chemotherapy, concluded that mucinous histology was associated with poorer prognosis. Taken together, these studies suggest that the prognostic significance of mucinous histology is real in some settings, but is strongly shaped by stage and treatment context rather than being uniform across all colon cancers [9–12].

In our own series, the clearest signal was anatomical. Mucinous tumours were much more likely to arise on the right side, and this finding is consistent with current biology-oriented literature. In a US national cohort, Gutierrez et al. showed that MSI-high/dMMR colorectal adenocarcinomas were most prevalent in stage I–II disease and carried the familiar clinicopathological profile of right-sided, mucinous or poorly differentiated tumours. Chen et al. similarly found dMMR in 16.8% of mucinous adenocarcinomas and showed that both dMMR and BRAF-mutant cancers were more likely to be right-sided and poorly differentiated. More recently, Dragomir et al. reported that a higher proportion of mucinous morphotype across tumour sections was associated with higher grade, right-sided location and microsatellite instability. Seen together, these data make our own results easier to interpret: the mucinous phenotype appears to cluster with a distinct right-sided biology, even when stage-related variables are not clearly worse [13–15].

That may also help explain why poor differentiation in our cohort did not translate into a more advanced pT category or more nodal disease after adjustment. In colon cancer, particularly within the MSI/dMMR spectrum, poor differentiation does not necessarily carry the same meaning that it does in chromosomal-instability-driven disease. Gutierrez et al. showed that MSI-high/dMMR tumours were most common in stage I–II disease, and Chen et al. found dMMR to be associated with earlier stage and absence of perineural invasion. Dragomir et al. likewise linked mucinous morphology to MSI rather than simply to a more advanced stage. In a related pathology-focused study, van Zwam et al. argued that prognosis in mucinous colon cancer is determined more by histological biomarkers than by microsatellite instability alone. Although our results cannot resolve this issue, they are consistent with a more nuanced interpretation: mucinous cancers may show distinct morphological characteristics without necessarily presenting with deeper invasion or a higher rate of nodal metastasis at the time of resection [13–16].

One of the more interesting findings in the present study was the lower rate of lymphovascular invasion in mucinous tumours. This finding contrasts with the common assumption that mucinous histology is consistently associated with more prominent invasion-related pathological features. Yet the recent literature suggests that this area is more heterogeneous than is often acknowledged. In a large nationwide Chinese study, Yuan et al. showed that mucinous adenocarcinomas containing additional pathological components, particularly signet ring cell or neuroendocrine differentiation, had markedly higher rates of lymphovascular invasion, perineural invasion, T4 disease and N2 disease than classic mucinous adenocarcinoma. That point matters here because our design intentionally excluded signet ring carcinoma and therefore removed one source of histological admixture that may exaggerate adverse pathological features in other series. At the other end of the spectrum, a small 2025 pilot colon study from Bangladesh reported an inverse association between mucinous histology and lymphovascular invasion, with no significant difference in perineural invasion. Those data are limited, certainly, but they at least suggest that our findings are biologically plausible rather than wholly aberrant [17, 18].

We also did not observe a significant difference in tumour budding. This finding should be interpreted cautiously. Tumour budding remains an established adverse feature in colorectal cancer, but its assessment in mucin-rich tumours is not entirely straightforward. Äijälä et al. recently showed that tumour bud-like structures suspended within extracellular mucin do not add prognostic information beyond conventional budding assessment and should not be incorporated into routine scoring. In practical terms, this means the architecture of mucinous tumours can complicate the observation and counting of budding, which may partly explain why this variable does not consistently separate mucinous from non-mucinous cancers, as might be expected [19].

Study Limitations

This study has several limitations. First, its retrospective single-centre design and the modest number of mucinous cases may limit generalisability and increase the possibility of type II error, especially for nodal status. We also did not have comprehensive molecular profiling for the entire cohort, so any mechanistic link with MSI, MMR status or BRAF mutation remains interpretive rather than demonstrated. Finally, because the study was designed around pathological comparison at resection, it does not resolve the survival question, which remains one of the most unsettled parts of the literature.

Conclusion

In conclusion, in this carefully selected colon-only surgical cohort, mucinous adenocarcinoma showed a distinct clinicopathological profile, characterised by right-sided predominance and a higher frequency of poor differentiation. However, mucinous histology was not independently associated with advanced local invasion or nodal metastasis after adjustment. These findings suggest that mucinous adenocarcinoma should be considered a distinct histological subtype in pathological risk assessment,

but not necessarily as a uniform marker of aggressive disease. Larger colon-only studies incorporating molecular data are needed to better define the subgroup of mucinous tumours with genuinely adverse biological behaviour.

Declarations

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Author contributions: All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Data availability: The datasets generated and analysed during the current study are not publicly available due to participant confidentiality, but anonymised data may be obtained from the corresponding author upon reasonable request.

Ethics approval and consent to participate: This retrospective observational study was approved by the Ethics Committee of Giresun University Faculty of Medicine (Approval No: 11.06.2026/07). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki, as revised in 2013. As the study was based on retrospective review of existing clinical and pathological records and all data were analysed anonymously, the requirement for written informed consent was waived by the Ethics Committee.

Clinical trial number: Not applicable.

Conflict of Interest: The authors have no conflicts of interest to declare that are relevant to the content of this article.

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Figures

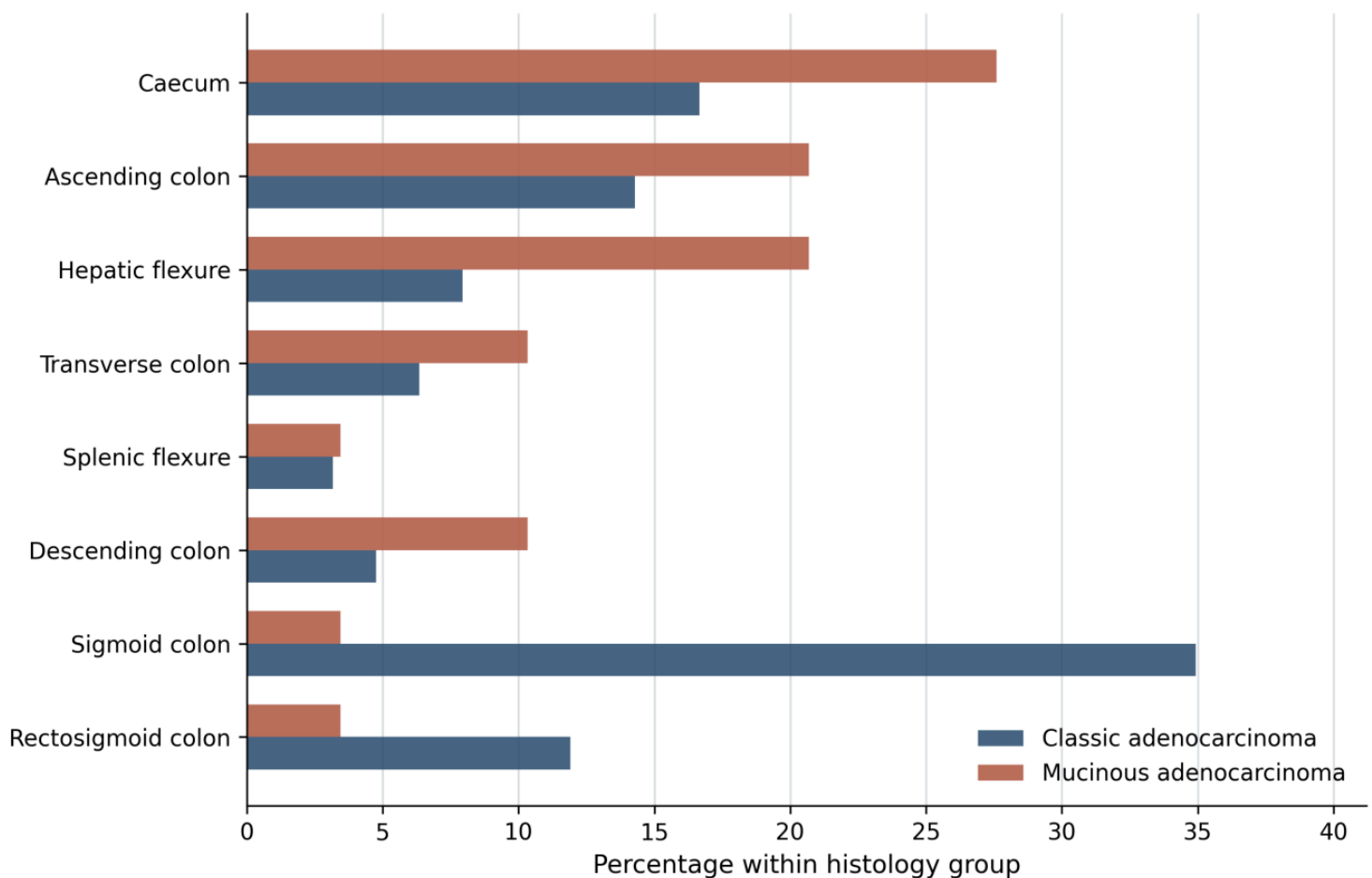


Figure 1

Detailed colonic subsite distribution by histology

Bars show the percentage distribution within each histology group; the overall comparison across subsites was significant (p=0.015).

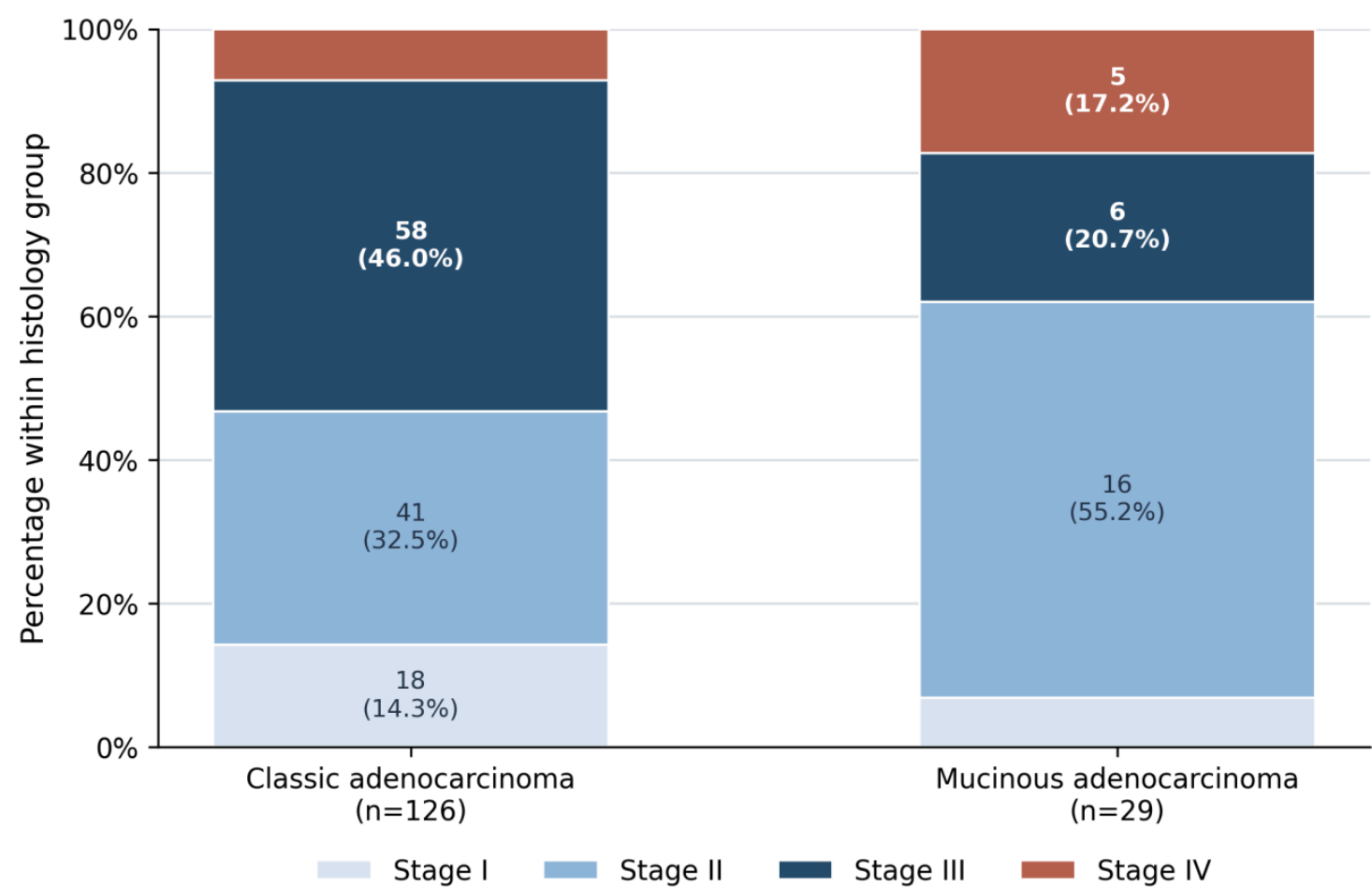


Figure 2

Stage distribution within each histology group

Each bar sums to 100% within the relevant histology group. Values printed inside the bars show the count and within-group percentage for each stage.

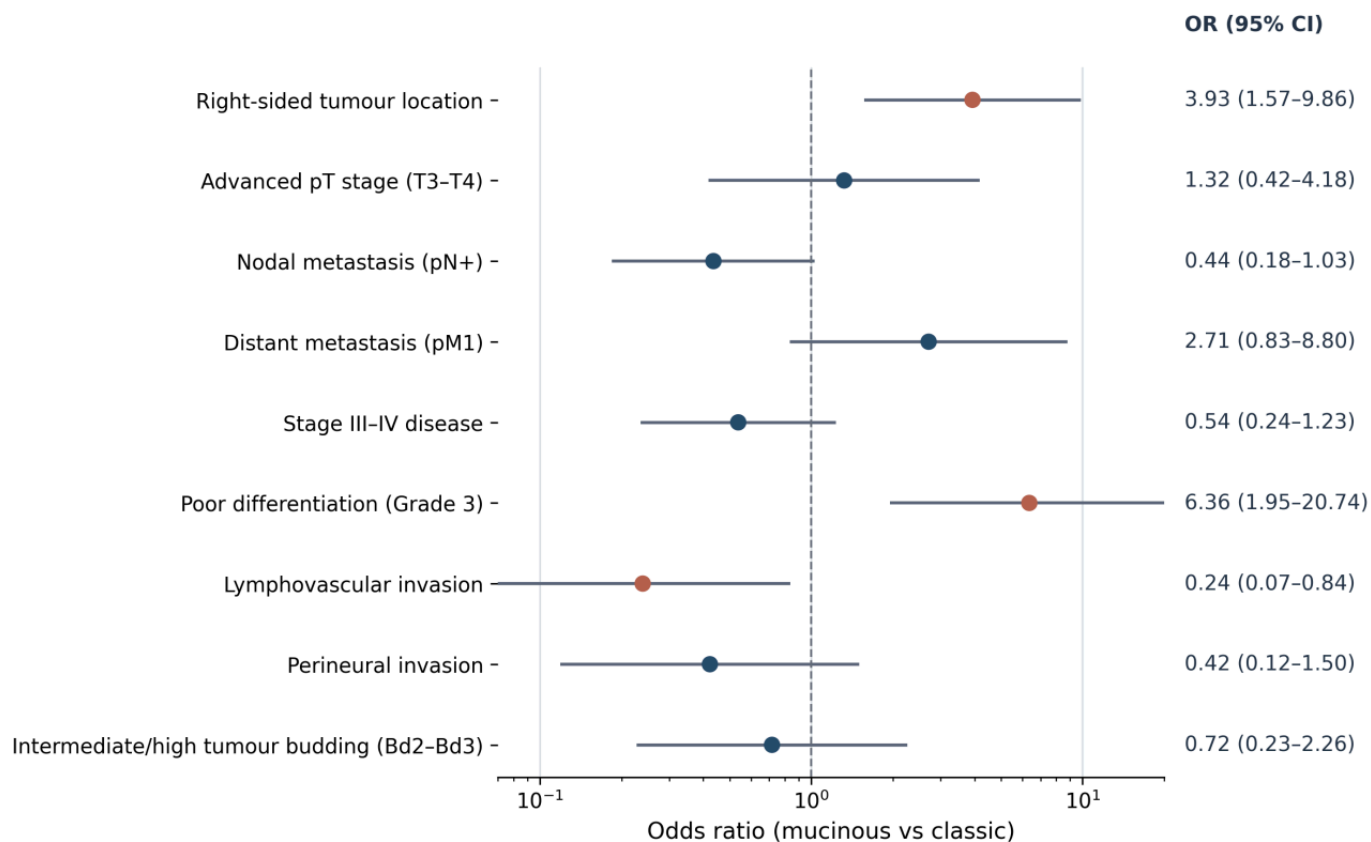


Figure 3

Forest plot of univariable odds ratios for selected clinicopathological features

Markers indicate the point estimate and horizontal lines the 95% confidence interval. Odds ratios above 1 favour a higher prevalence in mucinous adenocarcinoma.