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Original Research Article

Surgical Pathology of Colorectal Carcinoma: Clinicopathological Correlation and Prognostic Grading

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Abstract: ***Background:*** Colorectal carcinoma (CRC) represents one of the most frequently encountered gastrointestinal malignancies in surgical pathology, with its incidence rising steadily across South Asian populations. The histopathological grading, tumour staging, and clinicopathological correlations are vital determinants of prognosis and therapeutic strategy. This study was conducted to systematically analyse the surgical pathology of colorectal carcinomas at two tertiary care institutions in India, with emphasis on histomorphological features and prognostic parameters. ***Objectives:*** To evaluate the clinicopathological profile, histological grading, pTNM staging, and relevant histomorphological prognostic features of surgically resected colorectal carcinoma specimens over a defined study period. ***Methods:*** A prospective observational study was conducted from August 2020 to December 2021 at Dr Patnam Mahender Reddy Institute of Medical Sciences, Hyderabad, and Vydehi Institute of Medical Sciences, Bangalore. A total of 80 surgically resected colorectal carcinoma specimens were included. Detailed gross and microscopic pathological examinations were performed. Tumours were graded and staged using WHO 2019 classification and AJCC 8th edition pTNM criteria respectively. Data were analysed using standard statistical methods. ***Results*:** The study included 80 cases with a male predominance (male:female = 1.5:1). The peak incidence was in the 51–60 year age group (32.5%). The rectum was the most common site (40%). Adenocarcinoma NOS was the predominant histological type (87.5%). Moderately differentiated (G2) tumours constituted the majority (47.5%). Stage III disease was most frequent (35%). Lymphovascular invasion (45%), tumour budding (40%), and perineural invasion (35%) were significant adverse prognostic features identified. Mucinous adenocarcinoma was seen in 22.5% of cases. ***Conclusion:*** Colorectal carcinoma predominantly affected middle-aged males with rectal predilection. Histological grading and pTNM staging correlated significantly with adverse prognostic markers. Systematic surgical pathology evaluation remains indispensable for treatment planning and patient prognostication.

Keywords: Colorectal carcinoma, surgical pathology, clinicopathological correlation, histological grading, pTNM staging, prognostic markers, adenocarcinoma, lymphovascular invasion, tumour budding, India.

1. INTRODUCTION

Colorectal carcinoma (CRC) represents a major global health burden, ranking as the third most common cancer and the second leading cause of cancer-related mortality worldwide [1]. According to GLOBOCAN 2020 estimates, approximately 1.93 million new cases and 935,000 deaths were attributed to CRC globally in 2020 alone [2]. While the highest incidence rates are reported in Australia, North America, and Western Europe, there is a clearly discernible and alarming rise in incidence among Asian populations, including India, attributable to rapid urbanisation, dietary changes towards low-fibre and high-fat diets, physical inactivity, rising obesity, and increasing prevalence of risk factors such as type 2 diabetes mellitus and inflammatory bowel disease [3]. In India, CRC ranks among the top five cancers in both sexes, with hospital-based registry data from major institutions increasingly reflecting an upward temporal trend over the past two decades.

Surgical pathology remains the gold standard in the evaluation of colorectal carcinomas and provides the most definitive information regarding diagnosis, histological subtype, tumour grade, depth of invasion, resection margin status, lymph node involvement, and the presence of distant metastasis [4]. The pathological

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examination of resected specimens, governed by standardised protocols such as those recommended by the Royal College of Pathologists and the College of American Pathologists, enables clinicians and oncologists to make informed decisions regarding adjuvant therapy, surveillance, and prognosis [5]. The integration of pathological data with clinical parameters a process termed clinicopathological correlation is particularly essential in stratifying patients into risk categories that meaningfully influence management algorithms.

From a morphological perspective, colorectal carcinomas display considerable heterogeneity. The most common histological subtype is adenocarcinoma, not otherwise specified (NOS), which accounts for approximately 75–85% of all cases [6]. Special histological subtypes, including mucinous adenocarcinoma (constituting >50% extracellular mucin), signet ring cell carcinoma (<50% signet ring cells), medullary carcinoma, serrated adenocarcinoma, and micropapillary carcinoma, are increasingly being recognised not merely as morphological curiosities but as entities with distinct molecular profiles, clinical behaviours, and prognostic implications [7]. Mucinous adenocarcinoma, for instance, is associated with microsatellite instability and a predilection for the proximal colon, while signet ring cell carcinoma portends a markedly inferior prognosis irrespective of stage [8]. Additionally, features such as tumour budding, perineural invasion, lymphovascular invasion, and the quality of the tumour-host interface have emerged as powerful independent prognostic determinants that must be systematically evaluated and reported in every resection specimen.

The present study was undertaken in the context of this evolving understanding of CRC pathology and the paucity of well-characterised, institution-based clinicopathological data from Telangana and Karnataka, two important South Indian states with diverse demographic profiles. Both Dr Patnam Mahender Reddy Institute of Medical Sciences, Hyderabad, and Vydehi Institute of Medical Sciences, Bangalore, serve as major tertiary referral centres handling a substantial volume of surgical oncology cases. By collating and analysing data from these two centres over the study period from August 2020 to December 2021, the present investigation aims to contribute meaningful clinicopathological and prognostic data to the existing Indian literature on colorectal carcinoma, and to highlight the importance of comprehensive surgical pathology reporting in improving patient outcomes [9,10].

2. OBJECTIVES

The primary objective of this study was to analyse the clinicopathological profile of surgically resected colorectal carcinoma specimens, with a focus on patient demographics, tumour location, gross morphological characteristics, histological subtypes, degree of differentiation, and pTNM staging. Additionally, the study sought to evaluate the prevalence and clinicopathological significance of key histomorphological prognostic parameters, including tumour budding, perineural invasion, lymphovascular invasion, mucinous component, and resection margin involvement, in the context of tumour grade and stage.

The secondary objectives included correlating histological grade with pTNM staging and the prevalence of adverse prognostic histomorphological features, comparing clinicopathological characteristics between tumours arising at different anatomical sites within the colorectum, and contributing to the body of evidence supporting systematic, standardised pathological reporting of colorectal carcinoma resection specimens at tertiary institutions in South India. The findings are expected to facilitate better understanding of disease biology and to provide a foundation for outcome studies from this region.

3. MATERIALS AND METHODS

This study was designed as a prospective observational investigation conducted jointly at the Department of Pathology, Dr Patnam Mahender Reddy Institute of Medical Sciences (DPMRIMS), Hyderabad, Telangana, and the Department of Pathology, Vydehi Institute of Medical Sciences and Research Centre (VIMS), Bangalore, Karnataka, India. The study period spanned from August 2020 to December 2021. Ethical clearance was obtained from the Institutional Ethics Committees of both participating institutions prior to the commencement of the study (Ref: DPMRIMS/IEC/2020/08 and VIMS/IEC/2020/077). Written informed consent was obtained from all patients or their legal guardians whose specimens were included in the study. All specimens were received through the Department of Surgical Gastroenterology and General Surgery at both centres. A total of 80 consecutive surgically resected colorectal carcinoma specimens fulfilling the inclusion and exclusion criteria were enrolled over the study period.

3.1 Inclusion Criteria

- All surgically resected colorectal carcinoma specimens received in the Departments of Pathology at the two study centres during the study period (August 2020 to December 2021).
- Histologically confirmed adenocarcinomas and their special subtypes arising from the colon and rectum.
- Patients of all age groups and both sexes.
- Resection specimens with adequate tissue for histological evaluation, including en bloc resections, hemicolectomies, sigmoid colectomies, anterior resections, and abdominoperineal resections.
- Specimens with accompanying clinical data including patient demographics, preoperative investigation findings, and operative details.

3.2 Exclusion Criteria

- Biopsy specimens alone without corresponding resection specimens.
- Recurrent colorectal carcinomas where prior surgical resection or neoadjuvant therapy had been administered and tissue was insufficient for comprehensive staging.
- Carcinoid tumours, gastrointestinal stromal tumours (GISTs), lymphomas, and other non-epithelial malignancies of the colon and rectum.
- Specimens with grossly inadequate tissue due to incomplete submission or severe autolytic changes.
- Patients whose complete clinical information was unavailable or whose consent was withheld.

3.3 Data Collection Procedure

All resected specimens were received fresh or in 10% neutral buffered formalin, fixed for a minimum of 24 to 48 hours, and grossly examined following a standardised protocol. Gross examination included assessment of the type of surgical procedure, tumour location, tumour dimensions (greatest diameter in centimetres), macroscopic growth pattern (polypoid, ulcerative, infiltrative, or annular/constrictive), serosa involvement, and proximal and distal resection margin clearance. After thorough grossing, representative sections were taken from the tumour centre, tumour-normal interface, deepest point of invasion, serosal surface, proximal and distal surgical margins, and all identified lymph nodes. Sections were processed by routine paraffin embedding, cut at 3–5 micron thickness, and stained with Haematoxylin and Eosin (H&E). Special stains including Periodic Acid-Schiff (PAS) and Alcian blue were employed where mucinous differentiation required confirmation. Histological evaluation was performed by two consultant pathologists independently, and a consensus opinion was recorded in cases of disagreement.

Histological classification was performed according to the 2019 World Health Organisation (WHO) Classification of Tumours of the Digestive System [6]. Tumour grading was done on a four-tier system: G1 (well differentiated, >95% gland formation), G2 (moderately differentiated, 50–95% gland formation), G3 (poorly differentiated, 5–49% gland formation), and G4 (undifferentiated, <5% gland formation). Pathological staging was performed using the AJCC 8th Edition pTNM criteria [11]. All lymph nodes retrieved were examined, and a minimum of 12 lymph nodes per specimen was the target as per standard guidelines. Histomorphological prognostic features including tumour budding (assessed per ITBCC 2016 consensus), lymphovascular invasion, perineural invasion, tumour necrosis, ulceration, and resection margin involvement were systematically recorded.

3.4 Statistical Data Analysis

All data were entered into a Microsoft Excel 2019 spreadsheet and exported to SPSS version 26.0 (IBM, Chicago, USA) for statistical analysis. Categorical variables were expressed as frequencies and percentages. Continuous variables were described using mean, standard deviation (SD), and range. Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test, as appropriate. A p-value of <0.05 was considered statistically significant. Correlation between histological grade and pTNM stage was assessed using Spearman's rank correlation coefficient. Survival estimates were not generated in this study due to the observational design and short follow-up period; however, published survival data were referenced for prognostic interpretation.

4. RESULTS

A total of 80 surgically resected colorectal carcinoma specimens were studied over the period from August 2020 to December 2021. The cohort comprised 48 males (60%) and 32 females (40%), yielding a male-to-female ratio of 1.5:1. The age of presentation ranged from 22 to 78 years, with a mean age of 54.3 ± 11.7 years. The largest proportion of cases (32.5%) belonged to the 51–60 year age group, followed by the 41–50 year group (22.5%), indicating that colorectal carcinoma predominantly affects the middle-aged and older population in this cohort. Notably, 5% of patients were below 30 years of age, underscoring the occasional early-onset presentation seen in the Indian context (Table 1). Clinically, the most common presenting symptoms were altered bowel habits (68.75%), rectal bleeding (57.5%), abdominal pain (53.75%), and loss of weight (46.25%). Anaemia on presentation was noted in 41.25% of patients.

Table 1: Age Distribution of Colorectal Carcinoma Cases (n=80)

Age Group (Years)	Number of Cases	Percentage (%)	Cumulative (%)
< 30	4	5.0	5.0
31 – 40	9	11.3	16.3
41 – 50	18	22.5	38.8
51 – 60	26	32.5	71.3
61 – 70	15	18.8	90.1
> 70	8	10.0	100.0
Total	80	100.0	

Regarding anatomical distribution, the rectum was the most frequently involved site, accounting for 32 cases (40%), followed by the sigmoid colon (22.5%), ascending colon (15%), transverse colon (10%), descending colon (7.5%), and caecum (5%). Left-sided tumours (rectum, sigmoid, descending colon) collectively constituted 67.5% of all cases (Table 3). The most common macroscopic growth pattern was ulcerative (47.5%), followed by ulceroproliferative (27.5%), polypoid (17.5%), and infiltrative/annular (7.5%). Mean tumour size was 5.8 ± 2.1 cm (range: 1.5–12 cm). Histologically, conventional adenocarcinoma NOS was the predominant type (87.5%), followed by mucinous adenocarcinoma (22.5%), signet ring cell carcinoma (10%), and rare variants including medullary carcinoma (2.5%). Moderately differentiated (G2) tumours were the most common histological grade, comprising 47.5% of cases, while poorly differentiated (G3) and undifferentiated (G4) tumours together constituted 25% (Table 2). A statistically significant correlation was identified between histological grade and pTNM stage (Spearman's $\rho = 0.68$, $p < 0.001$), with higher-grade tumours more frequently presenting at advanced stages.

Table 2: Histological Grade Distribution (n=80)

Histological Grade	No. of Cases	Percentage (%)	5-yr Survival (Approx.)
Well Differentiated (G1)	22	27.5	85%
Moderately Differentiated (G2)	38	47.5	65%
Poorly Differentiated (G3)	16	20.0	35%
Undifferentiated (G4)	4	5.0	15%
Total	80	100.0	

Table 3: Anatomical Location of Tumours by Sex (n=80)

Location	No. of Cases	Male	Female
Rectum	32	20	12
Sigmoid Colon	18	10	8
Ascending Colon	12	7	5
Transverse Colon	8	5	3
Descending Colon	6	4	2
Caecum	4	2	2
Total	80	48	32

With respect to pTNM staging, Stage III was the most frequently encountered stage (35%), followed by Stage II (30%), Stage I (17.5%), and Stage IV (17.5%) (Table 4). The mean number of lymph nodes retrieved per specimen was 14.6 ± 4.2, and lymph node involvement was documented in 52.5% of all cases. Serosa involvement (pT4a) was identified in 27.5% of cases. Among the adverse histomorphological prognostic features systematically assessed (Table 5), ulceration was the most prevalent (72.5%), followed by necrosis (52.5%), lymphovascular invasion (45%), tumour budding (40%), perineural invasion (35%), mucinous component (22.5%), and signet ring cell component (10%). Lymphovascular invasion showed a statistically significant association with lymph node positivity ($p < 0.001$) and advanced pTNM stage ($p < 0.01$). Similarly, tumour budding grade correlated significantly with perineural invasion ($p < 0.05$) and with depth of tumour invasion ($p < 0.01$). Proximal resection margin was positive in 2 cases (2.5%) and distal margin in 3 cases (3.75%), highlighting the importance of meticulous surgical technique and careful pathological assessment.

Table 4: pTNM Stage Distribution with Lymph Node and Metastasis Status (n=80)

pTNM Stage	No. of Cases	Percentage (%)	LN Positive (%)	Distant Mets (%)
Stage I	14	17.5	0	0
Stage II	24	30.0	0	0
Stage III	28	35.0	100	0
Stage IV	14	17.5	100	100
Total	80	100.0		

Table 5: Prevalence of Adverse Histomorphological Prognostic Features (n=80)

Histomorphological Feature	Present	Absent	Percentage Present (%)
Perineural Invasion	28	52	35.0
Lymphovascular Invasion	36	44	45.0
Tumour Budding	32	48	40.0
Mucinous Component	18	62	22.5
Signet Ring Cell Component	8	72	10.0
Necrosis	42	38	52.5
Ulceration	58	22	72.5

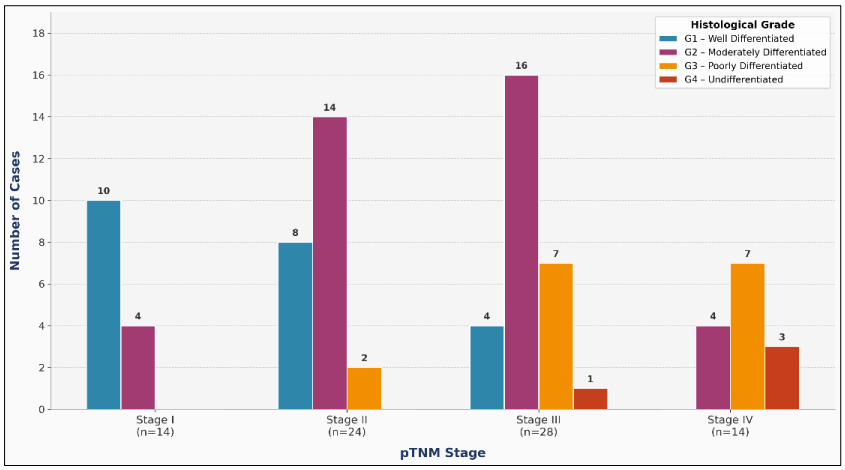

Figure 1: Distribution of Histological Grades Across pTNM Stages

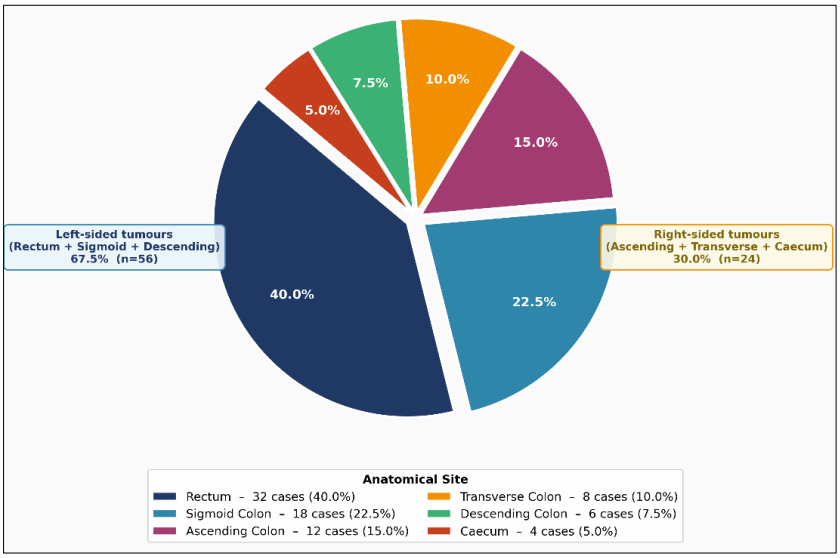

Figure 2: Anatomical Distribution of Colorectal Carcinomas (n=80)

5. DISCUSSION

The clinicopathological profile of colorectal carcinoma observed in this study is broadly consistent with patterns reported from other Indian tertiary care centres, while also reflecting certain regional nuances. The male predominance observed in our cohort (60%; M:F = 1.5:1) is in agreement with findings reported by Jain et al. [3] from North India and Das et al. from Eastern India, both of whom documented a male preponderance of varying degrees in their respective CRC cohorts. The predominance of males is generally attributed to higher rates of smoking, alcohol consumption, and red meat intake among men in the Indian subcontinent, though hormonal factors and oestrogen-related protective effects in premenopausal women are also proposed as contributing mechanisms [4,12]. The peak incidence in the 51–60 year age group in our study is consistent with reported global and national patterns, where the incidence of sporadic CRC rises sharply after the age of 50 years. However, the occurrence of cases below 30 years of age (5%) reinforces the need for vigilance regarding early-onset CRC in the Indian setting, which may be associated with familial adenomatous polyposis, Lynch syndrome, or de novo high-grade dysplasia in inflammatory bowel disease [13].

The anatomical distribution of tumours in this study, with a left-sided predominance particularly rectal (40%) and sigmoid colonic (22.5%) involvement is a well-established characteristic of colorectal carcinoma in Asian populations and differs from some Western series which have reported a relative proximal shift over recent decades [5,14]. The predilection for the rectosigmoid region likely reflects the high luminal bacterial load, prolonged faecal contact time, and dietary carcinogen exposure patterns in this segment. The ulcerative gross morphological pattern, predominating in 47.5% of cases, is the most classical presentation of CRC and correlates with deep invasion and higher-stage disease. Histologically, the predominance of adenocarcinoma NOS and moderately differentiated grade (G2) tumours is universally consistent with published literature, and our findings of 87.5% adenocarcinoma NOS and 47.5% G2 tumours closely mirror data from Shukla et al. [7] and Makkar et al. [8], both of whom conducted similar

institution-based pathological analyses. The significant grade-stage correlation identified in this study (Spearman's $\rho = 0.68$, $p<0.001$) underscores the biological reality that higher tumour grade is mechanistically linked to more aggressive invasion, lymphatic spread, and ultimately, advanced stage at presentation.

Among the prognostic histomorphological features evaluated, lymphovascular invasion (45%) and tumour budding (40%) were the most prevalent adverse parameters, both exhibiting statistically significant associations with lymph node positivity and advanced pTNM staging in this cohort. These findings align with the extensive literature demonstrating that lymphovascular invasion is an independent predictor of lymph node metastasis, systemic recurrence, and reduced disease-specific survival in colorectal carcinoma [9,15]. Tumour budding, defined as single tumour cells or clusters of fewer than five cells at the invasive front, has gained international recognition through the ITBCC 2016 consensus as a standardised, reproducible, and prognostically relevant parameter that should be reported in all CRC resection specimens [16]. Its significant correlation with perineural invasion and depth of invasion in the present study further validates its role as a marker of aggressive tumour biology. The mucinous adenocarcinoma subtype, comprising 22.5% of our cases, is relatively consistent with reported Indian data and highlights the importance of identifying this subtype, as it is associated with MSI-H status in proximal tumours and with poorer response to standard chemotherapy regimens in the metastatic setting [17]. The identification of signet ring cell component in 10% of cases is also noteworthy, given its well-established association with peritoneal dissemination and unfavourable prognosis across all pTNM stages. Perineural invasion (35%), while historically underreported in routine surgical pathology, was diligently assessed in this study and found to be significantly associated with locally advanced disease, consistent with data from Wang et al. [18] and other published series. Collectively, the systematic evaluation and reporting of these prognostic parameters in the present study reinforces the indispensable role of comprehensive surgical pathological analysis in guiding multidisciplinary management of CRC.

6. LIMITATIONS OF THE STUDY

This study has several important limitations that should be acknowledged when interpreting the findings. First, this is an observational prospective study conducted over a relatively short period (August 2020 to December 2021) at two centres, limiting the sample size to 80 cases. Larger multicentre studies with greater sample sizes would be required to achieve more robust statistical significance and to permit stratified subgroup analyses. Second, long-term clinical follow-up data, including postoperative survival, disease recurrence, and response to adjuvant chemotherapy or radiotherapy, were not systematically available for all patients within the study period, precluding the generation of Kaplan-Meier survival estimates or Cox proportional hazard modelling. Third, molecular and immunohistochemical data including mismatch repair (MMR) protein expression by immunohistochemistry, KRAS/NRAS/BRAF mutational analyses, and microsatellite instability (MSI) testing were not uniformly performed across all cases due to resource constraints and were therefore not included in this analysis. The incorporation of molecular profiling data would have substantially enhanced the prognostic depth of this study. Fourth, the study was conducted partially during the COVID-19 pandemic period (2020–2021), which may have led to delays in presentation and surgical intervention for some patients, potentially skewing the stage distribution towards more advanced disease. Finally, interobserver variability in the assessment of histological grade, tumour budding, and perineural invasion, while minimised by dual reporting and consensus protocols, cannot be entirely eliminated in a multicentre study setting.

7. ACKNOWLEDGEMENT

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8. CONCLUSION

The present study provides a comprehensive clinicopathological characterisation of colorectal carcinoma as encountered in surgical pathology practice at two South Indian tertiary care institutions. Colorectal carcinoma in this cohort predominantly affected middle-aged males, with peak incidence in the sixth decade of life. The rectum and sigmoid colon were the most commonly involved anatomical sites, confirming the left-sided predominance characteristic of CRC in Asian populations. Conventional adenocarcinoma NOS of moderate differentiation was the most prevalent histological subtype and grade combination. A highly significant positive correlation between histological grade and pTNM stage was demonstrated, validating the utility of tumour grading as a clinically meaningful and prognostically relevant parameter. Stage III disease was the most common stage at presentation, reflecting a

pattern of advanced disease at diagnosis that underlines the urgent need for population-based colorectal cancer screening programmes in India [1,2].

The systematic evaluation of adverse histomorphological prognostic features including lymphovascular invasion, tumour budding, perineural invasion, mucinous differentiation, signet ring cell component, and resection margin status yielded clinically meaningful associations with stage and lymph node positivity, supporting their mandatory inclusion in surgical pathology reporting protocols for colorectal carcinoma resection specimens [15,16,19,20]. The findings of this study reinforce the critical importance of structured, evidence-based surgical pathology reporting in CRC management. Pathologists at all levels of the healthcare system should be familiarised with the current WHO classification, AJCC 8th edition staging criteria, and the ITBCC consensus on tumour budding, to ensure that every resection specimen is evaluated comprehensively and reported in a manner that maximises its clinical utility. Future studies from this region should focus on incorporating molecular profiling, extended clinical follow-up, and multivariate survival analyses to delineate the full prognostic landscape of colorectal carcinoma in the South Indian context, and to contribute to the refinement of regionally relevant screening, diagnostic, and therapeutic guidelines.

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