Azienda Ospedaliero Universitaria Careggi

# VEQ ANATOMIA PATOLOGICA CICLO 2025: PRESENTAZIONE E COMMENTO DEI RISULTATI DEI PARTECIPANTI

Firenze 05 Febbraio 2026
AOU Careggi NIC 3, Aula Magna

## Caratterizzazione istopatologica dell'adenocarcinoma del colon retto

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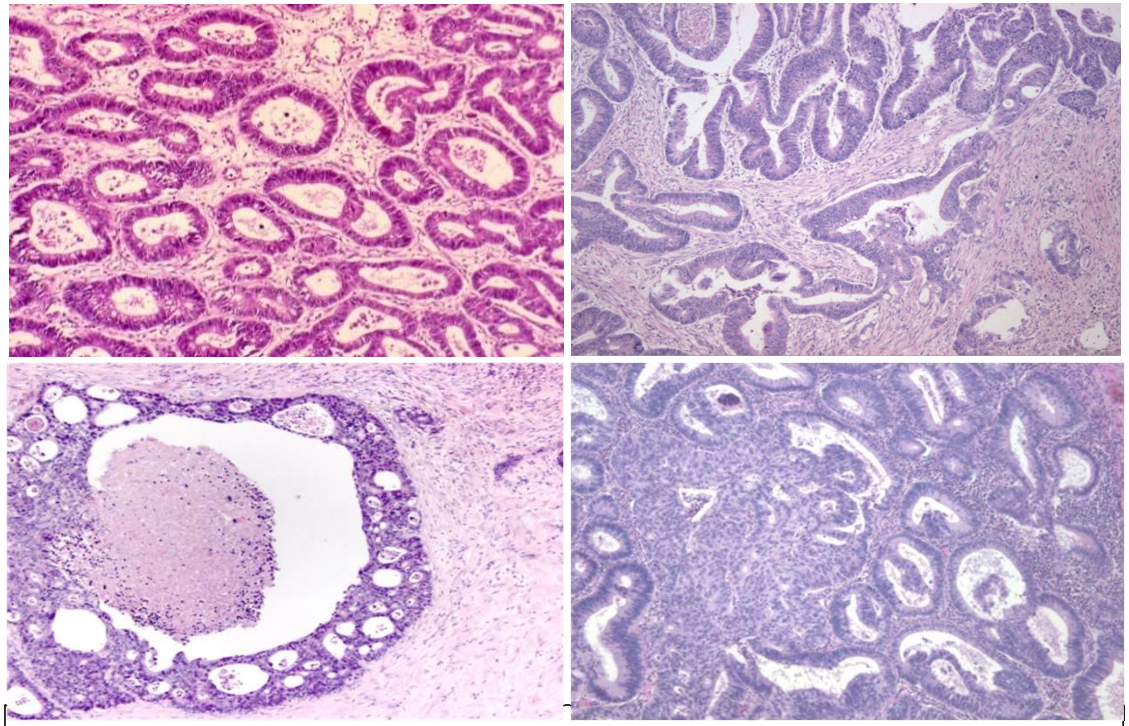
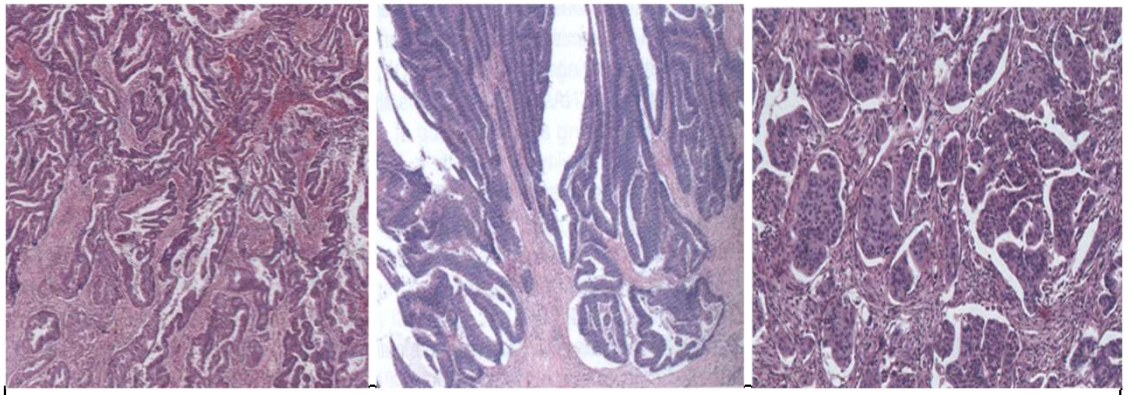
# Classification of colorectal carcinoma WHO 2019

- Adenocarcinoma NOS (80%)
- Serrated adenocarcinoma
- Adenoma-like adenocarcinoma
- Micropapillary carcinoma
- Mucinous adenocarcinoma
- Signet-ring cell carcinoma
- Medullary carcinoma
- Adenosquamous carcinoma
- Carcinoma undifferentiated NOS
- Others

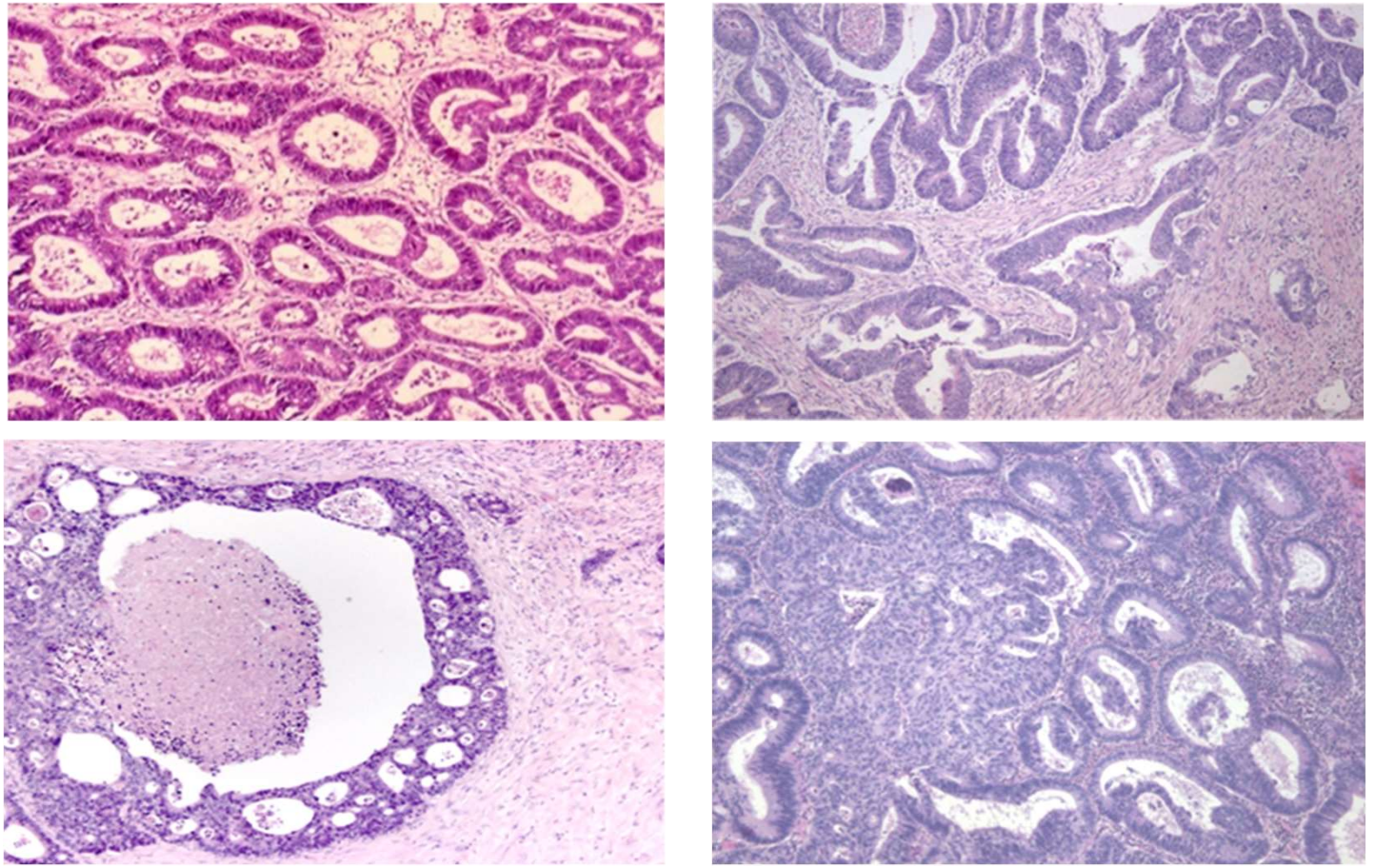


Adenocarcinoma NOS

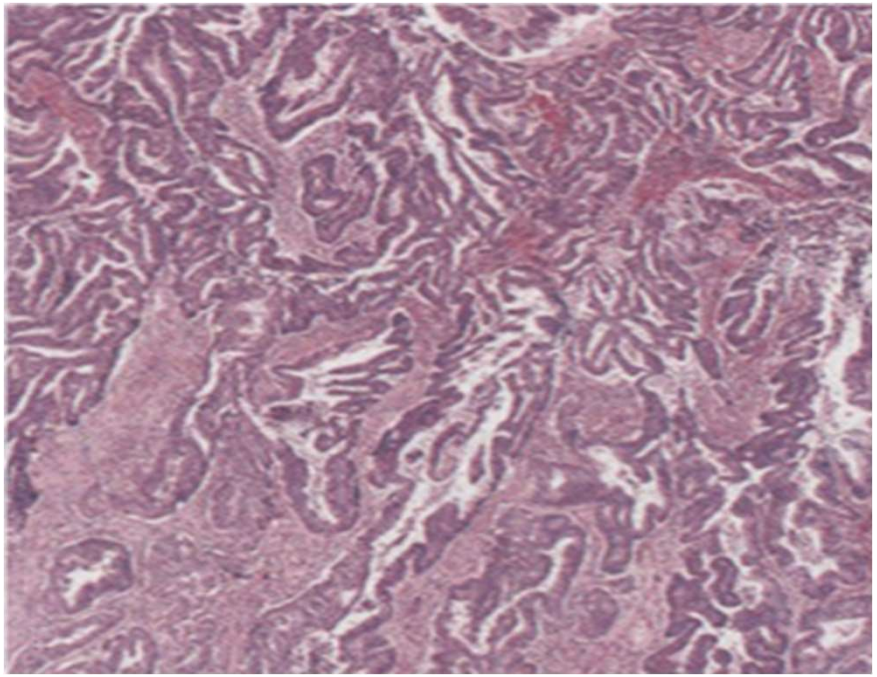


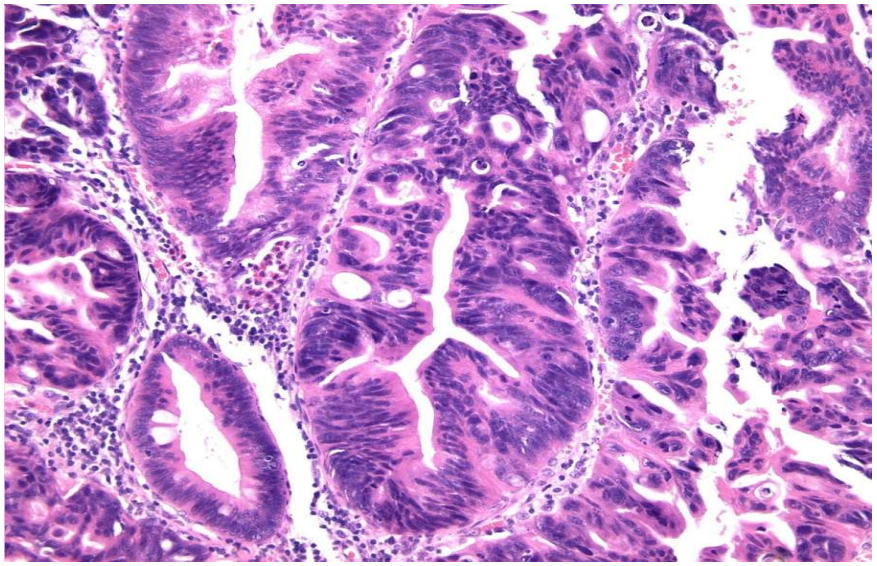
Serrated Adenoma-like Micropapillary

# Adenocarcinoma NOS



Medium or large-sized glands with moderate variability in gland size  and configuration.
Most of these adenocarcinomas are moderately to well differentiated.
Dirty necrosis.
WHO 2019





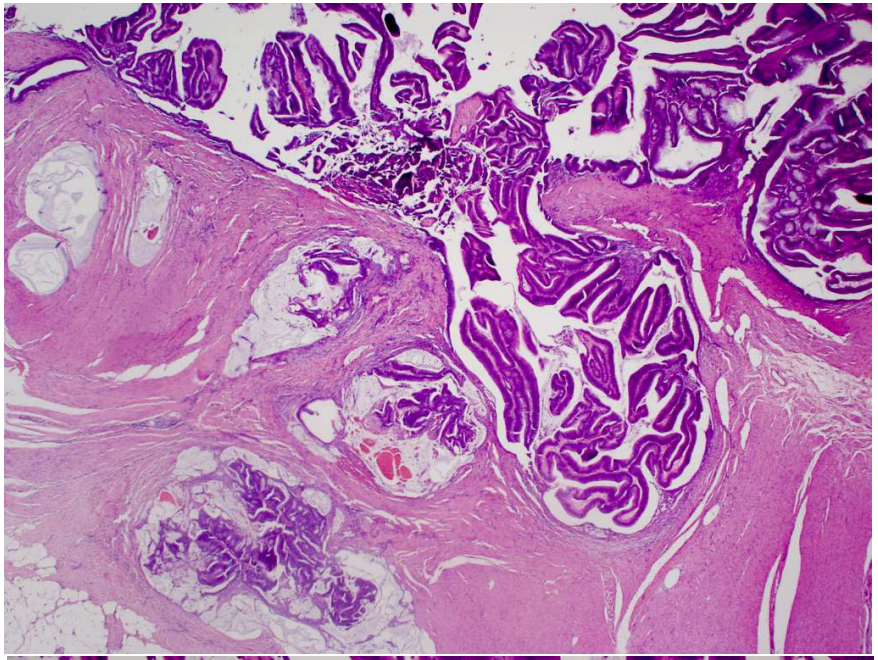
## Serrated adenocarcinoma

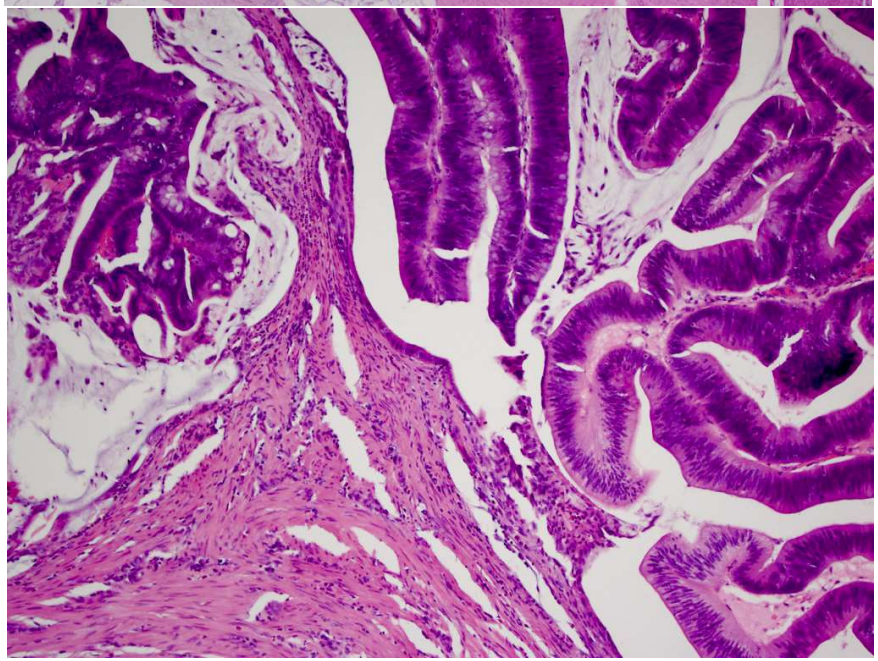
This rare variant (<10% of CRC) has architectural similarity to a sessile serrated polyp with glandular serration that can be accompanied by mucinous areas.

Cytoplasmic eosinophilia

Right colon (20%)

KRAS 35%, BRAF 45%, MSI30%.





## Adenoma-like adenocarcinoma

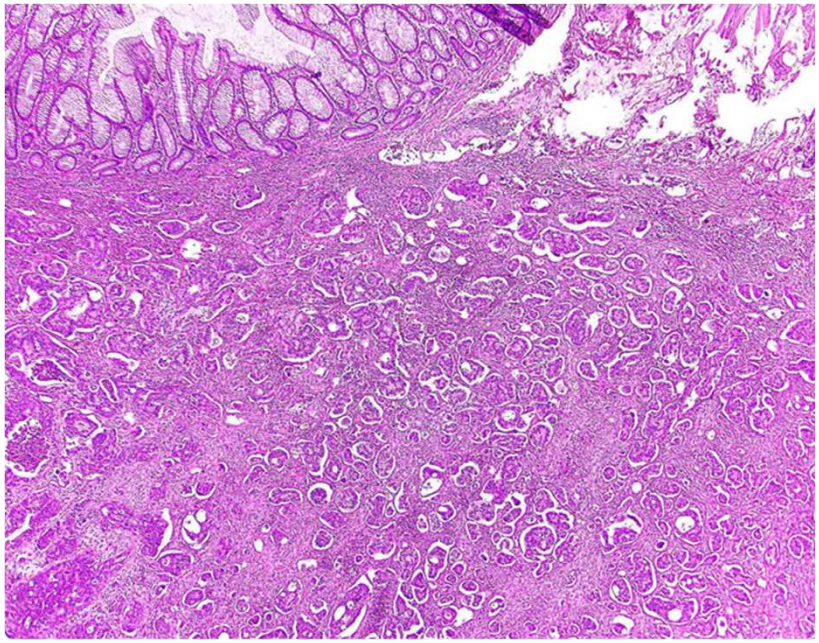
1-5% of CRC

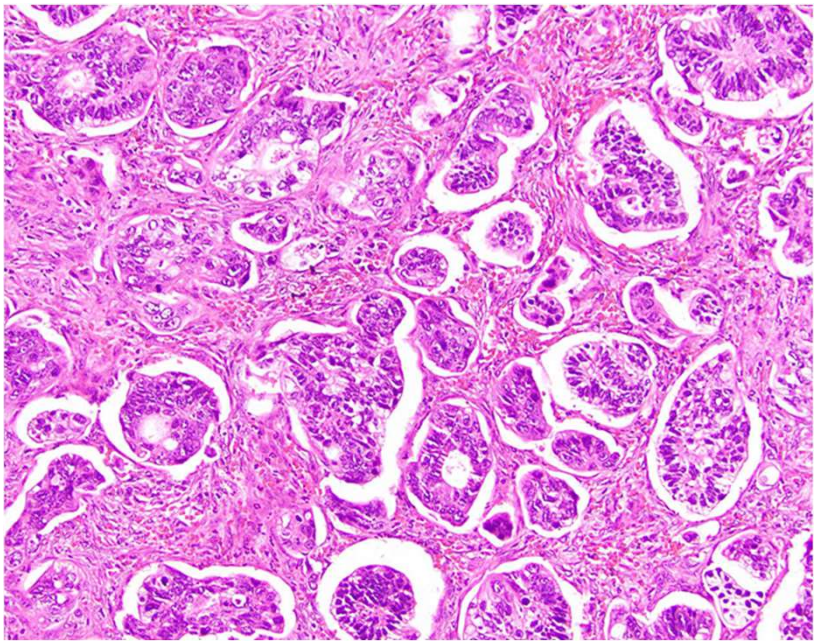
Is characterized by ≥ 50% of the invasive component having an adenoma-like appearance with low-grade villous

Low incidence of lymph-node or distant metastases

Favourable prognosis.

High KRAS mutation rate





## Micropapillary adenocarcinoma

1-5% of CRC

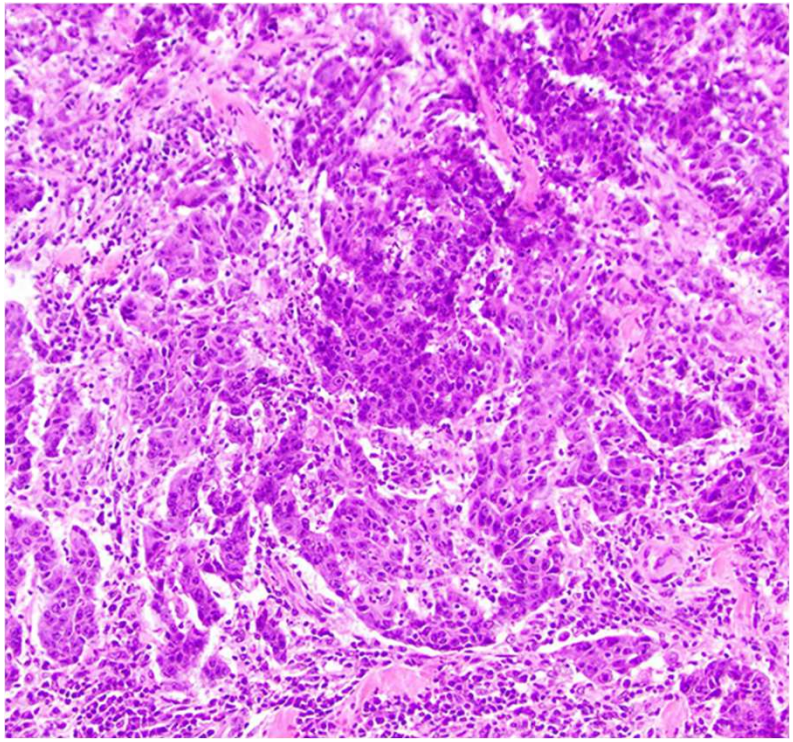
Small clusters of tumor cells within stromal spaces mimicking vascular channels .

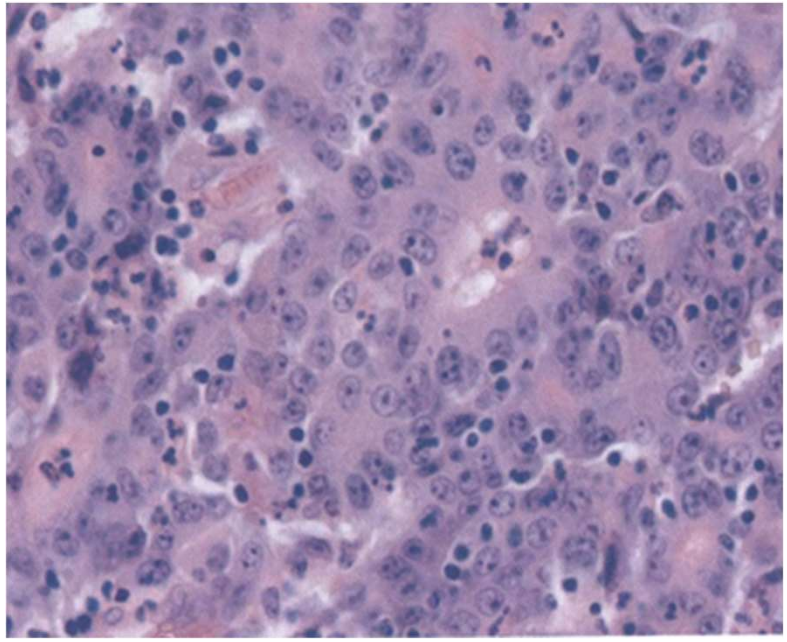
Micropapillary component ≥5%

Lymph-nodes metastases, lymphatic, venous and perineural invasion are frequently present.

Poor prognosis

KRAS, p53 (< MSI)



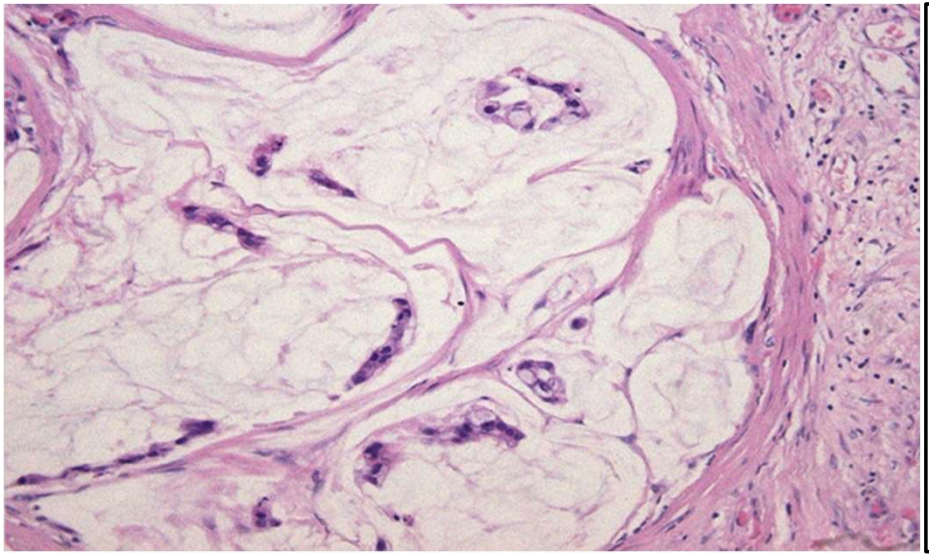


## Medullary carcinoma

2-4% of CRC
Sheets of malignant cells with vescicular nuclei, prominent nucleoli, prominent infiltration by lymphocytes.
Right colon
Good prognosis.

CK20+ 30-60%, CDX2 +20%, CK7+15%
Calretinin+ 75% (+10% in G3 CRC)
SATB2+ 85%

MSI, BRAF-V600E mutation.



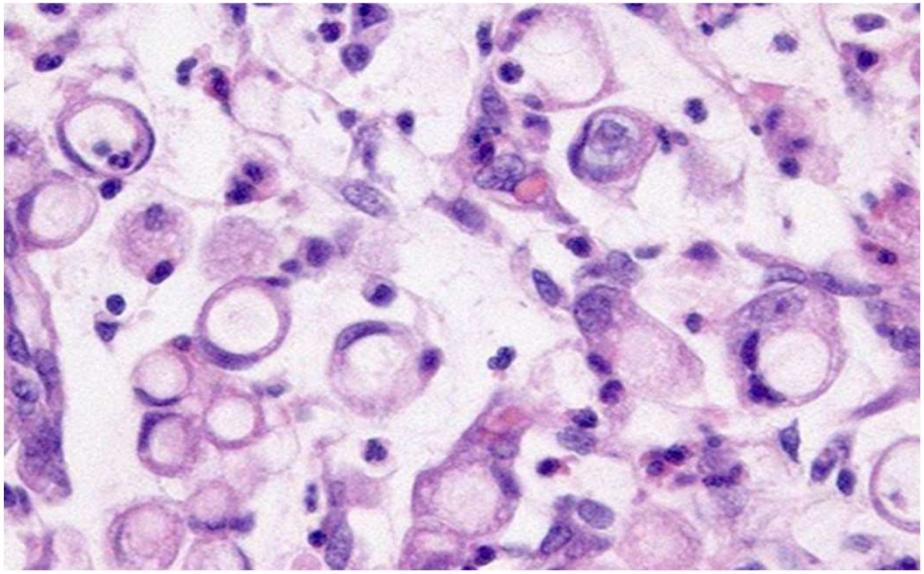
## Mucinous adenocarcinoma

10-15% of CRC

>50% of the lesion is composed of pools of extracellular mucin that contain malignant epithelium. Predilection for right colon.

Carcinomas with mucinous area ≤ 50% are categorized as having a mucinous component.

MSI 40%, KRAS 60%.



## Signet-ring cell carcinoma

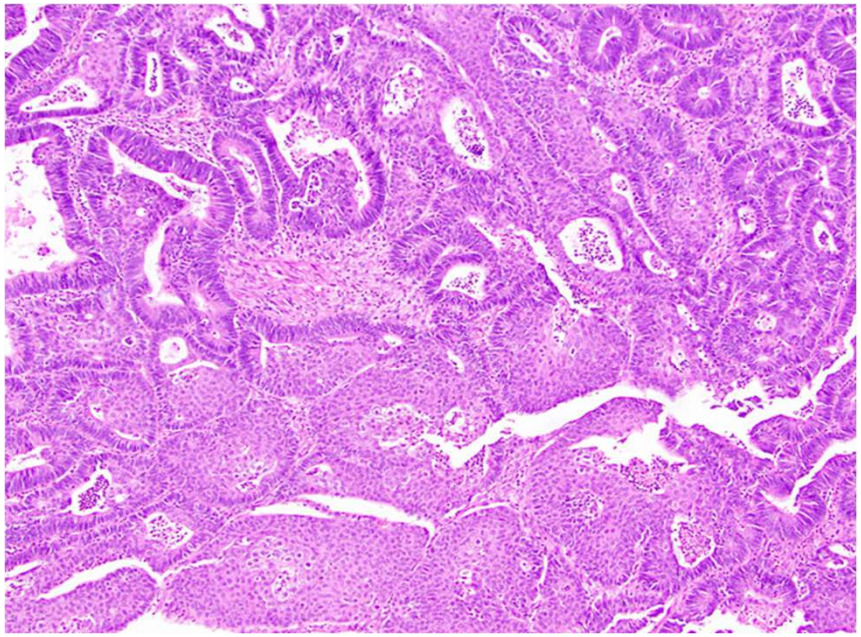
<1% of CRC (>right colon)

Signet-ring cells >50% of the tumor cells.

Carcinomas with signet-ring cells in ≤ 50% of the tumour are categorized as having a signet-ring cells component.

Metastases develop rapidly. Bad prognosis.

MSI, KRAS, BRAF

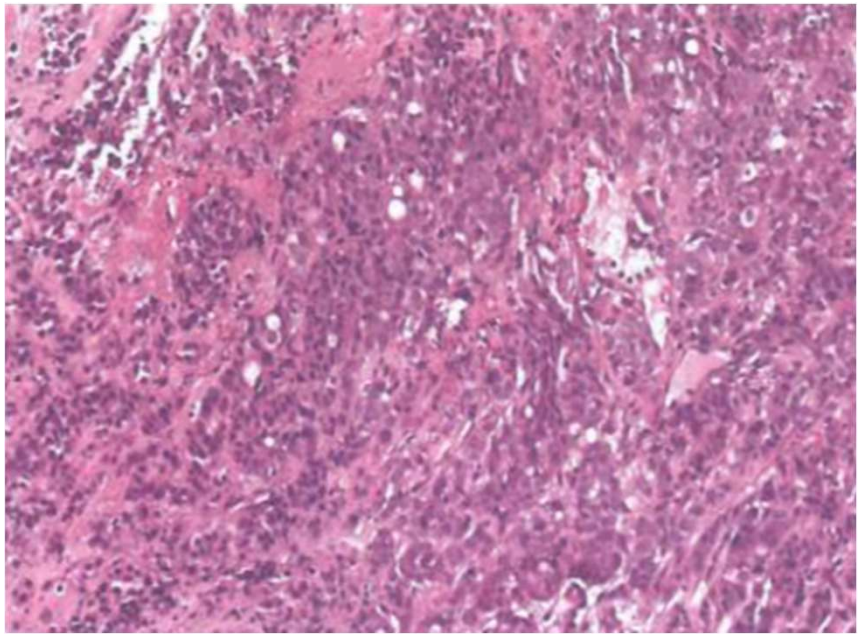


## Adenosquamous carcinoma

<1% of CRC

Admixture of distinct components of both adenocarcinoma and squamous cell carcinoma

(≥ 20% of either component)

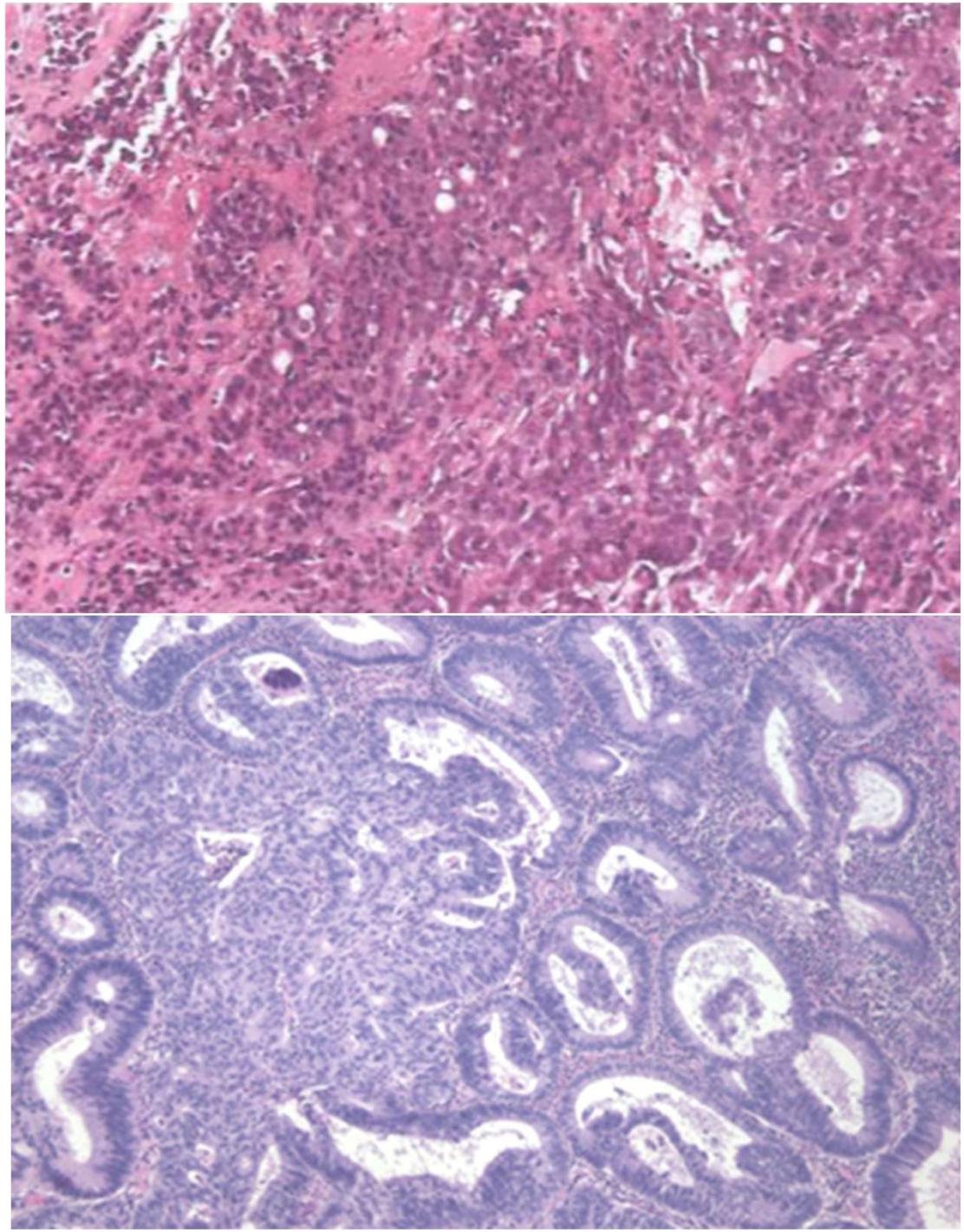


## Undifferentiated carcinoma

No or minimal gland formation (<5%)

DD Medullary carcinoma:

pushing border, lymphocytic infiltrate, vescicular nuclei, calretinin+

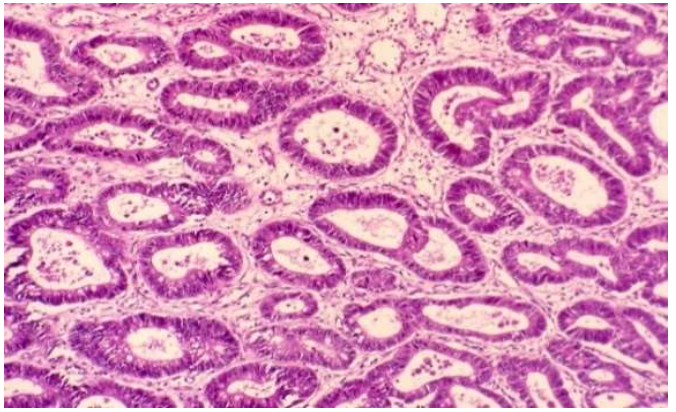


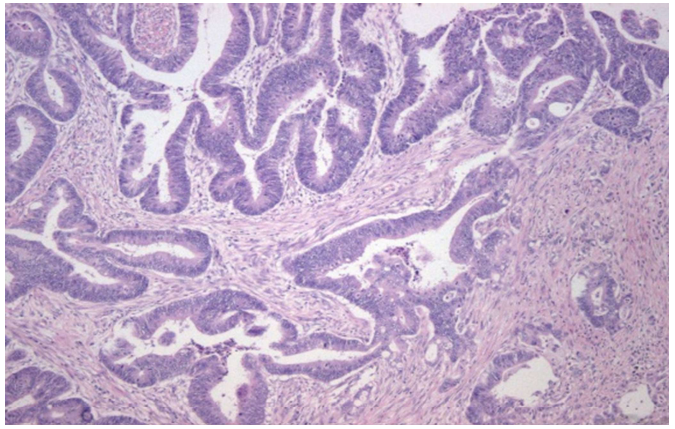
# Grading of colorectal carcinoma

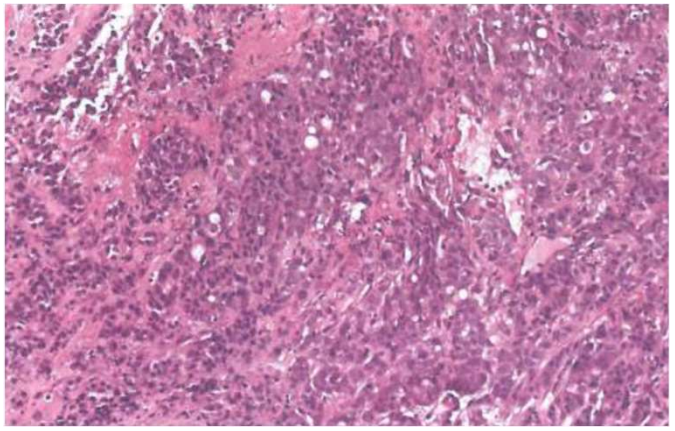
## Grading

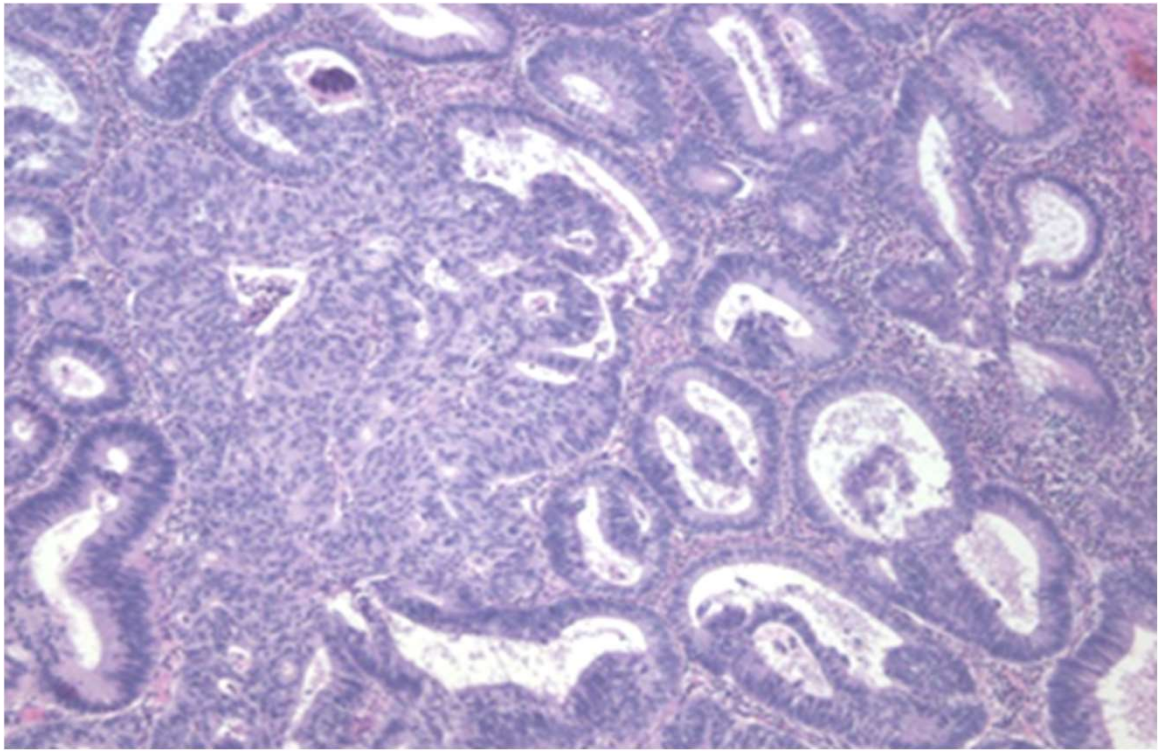
G1 >95% gland formation
G2 50-95% gland formation
G3 >5-49% gland formation
G4 <5% gland formation

- Low-grade:
  G1-G2 (≥50% gland formation)
- High grade:
  G3 (<50% gland formation)
- Undifferentiated carcinoma
  G4 (<5% gland formation)







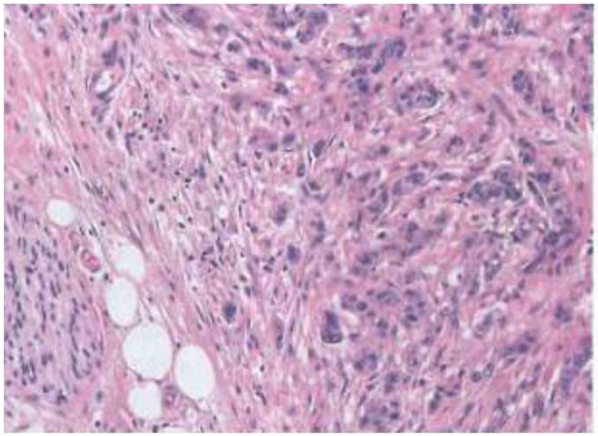


Grading of CRC is based on gland formation:

**-low-grade** (formerly well- to moderate differentiated tumours:

**-high grade** (formerly poorly differentiated tumours)

Grading is based on the least differentiated component away from the invasive edge.



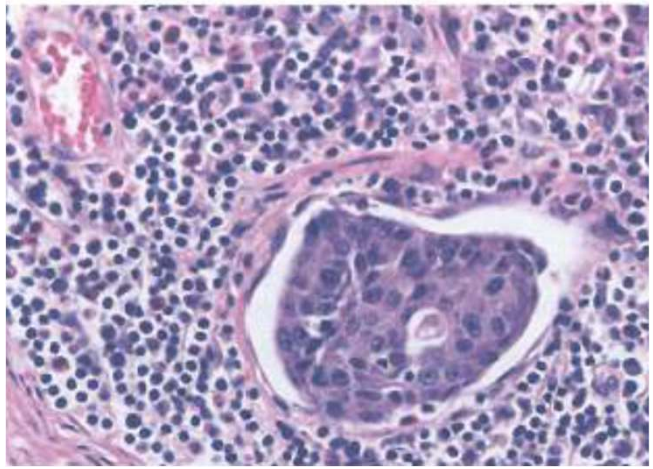
Tumor budding or poorly differentiated clusters which are found on the invasive front, should not be taken into account when grading the tumour, but should be reported separately

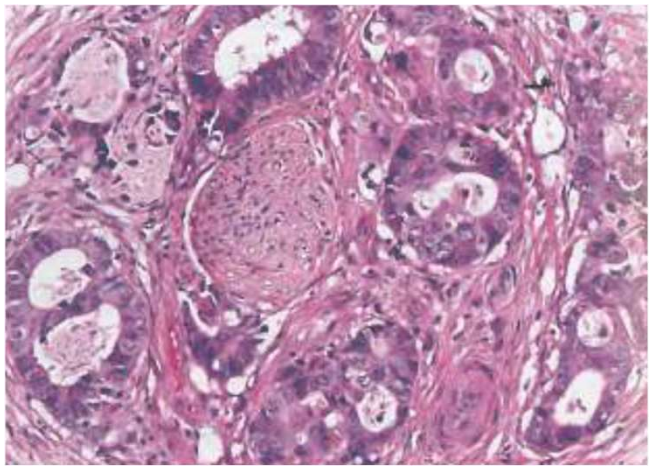
**WHO 2019**

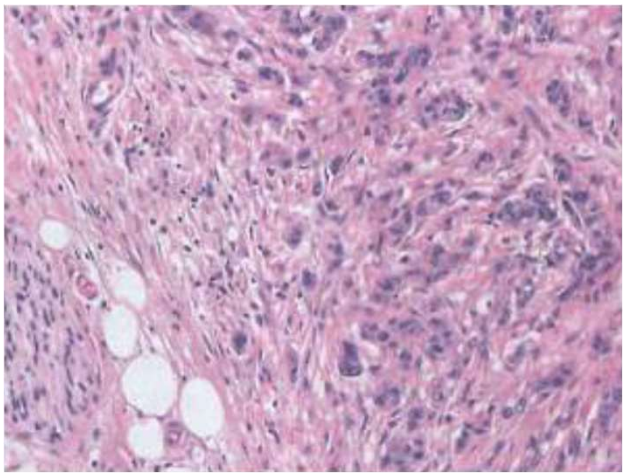
| Risk factor | HR (95% CI) univariate | HR (95% CI) multivariate | Remarks |
|---|---|---|---|
| **Subtypes** | | | |
| Mucinous carcinoma | 1.05 (1.02–1.08) | | Compared with adenocarcinoma NOS |
| Signet-ring cell carcinoma | 1.49 (1.39–1.59) | 2.66 (2.35–3.01) | Compared with adenocarcinoma NOS |
| Medullary carcinoma | 0.94 (0.80–1.00) | | Compared with adenocarcinoma NOS |

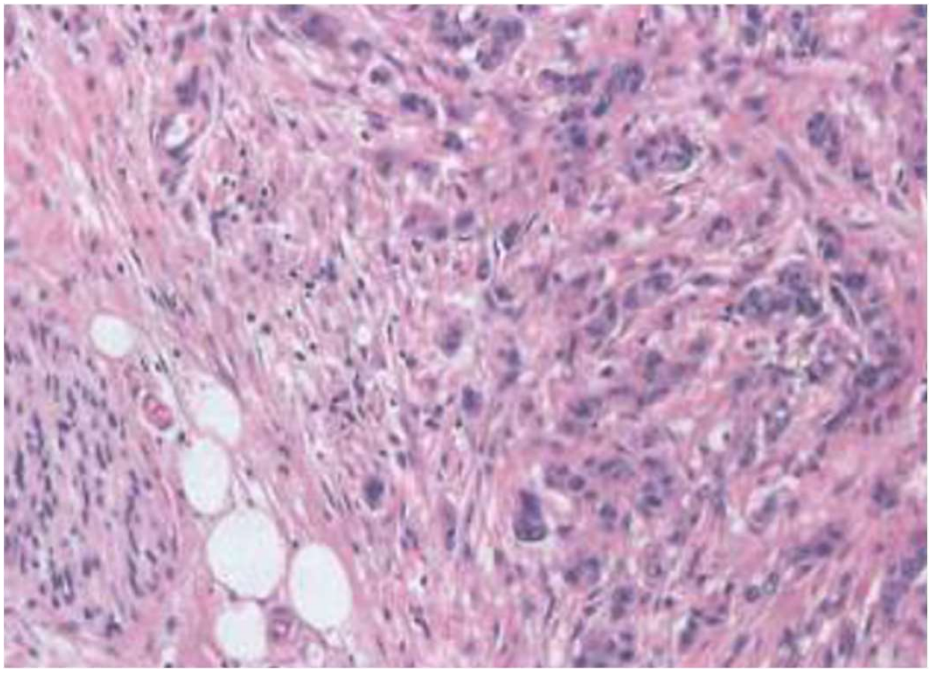
| | |
|---|---|
| Good prognosis | Adenoma-like adenocarcinoma |
| Poor prognosis | Micropapillary carcinoma<br>Undifferentiared carcinoma<br>Serrated adenocarcinoma |

| Risk factor | HR (95% CI) univariate | HR (95% CI) multivariate | Remarks |
|---|---|---|---|
| **Relevant histological features** | | | |
| Perineural invasion | 2.09 (1.68–2.61) | 1.85 (1.63–2.12) | Compared with no perineural invasion |
| Intramural vascular invasion | 2.04 (1.39–2.99) | 1.60 (1.15–2.24) | Compared with no intramural vascular invasion |
| Extramural vascular invasion | 3.6 (2.4–5.5) | 1.72 (1.39–2.12) | Compared with no extramural vascular invasion |
| Lymphatic invasion | 2.15 (1.72–2.68) | | In stage I/II colorectal cancer |
| Tumour deposits | 2.90 (2.20–3.92) | 2.19 (1.72–2.77) | Compared with no tumour deposits |
| Tumour budding | 4.51 (2.55–7.99)[a] | | Compared with no tumour budding |









**Tumour budding** is defined as the presence of tiny cords and small agregates of neoplastic epithelium (four cells or less) that detach from tumour glands at the invasive front and appear to migrate into adjacent stroma.
Tumour budding is present in 20% to 40% of all CRC.
WHO 2019

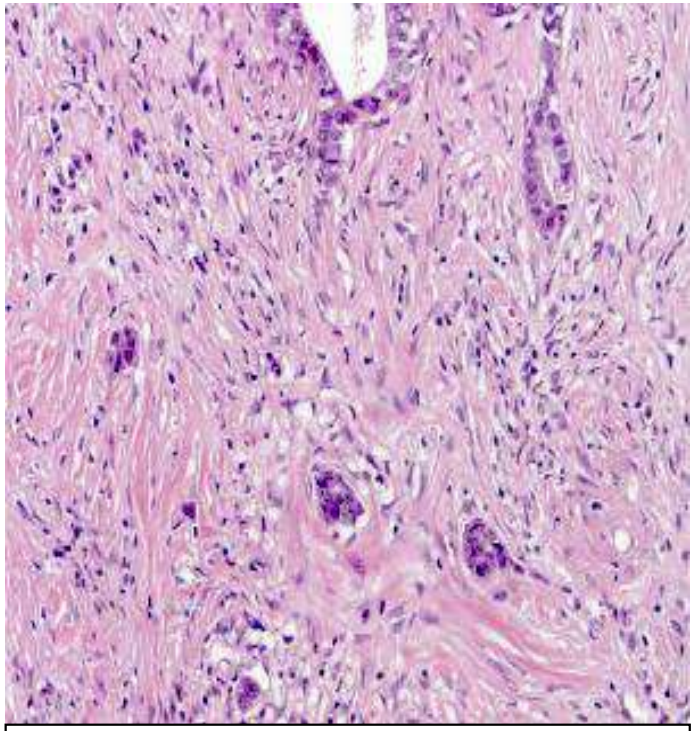
# Recommendations for Reporting Tumor Budding in Colorectal Carcinoma Based on the 2016 International Tumor Budding Consensus Conference (ITBCC)

**METHOD FOR ASSESSING TUMOR BUDDING**

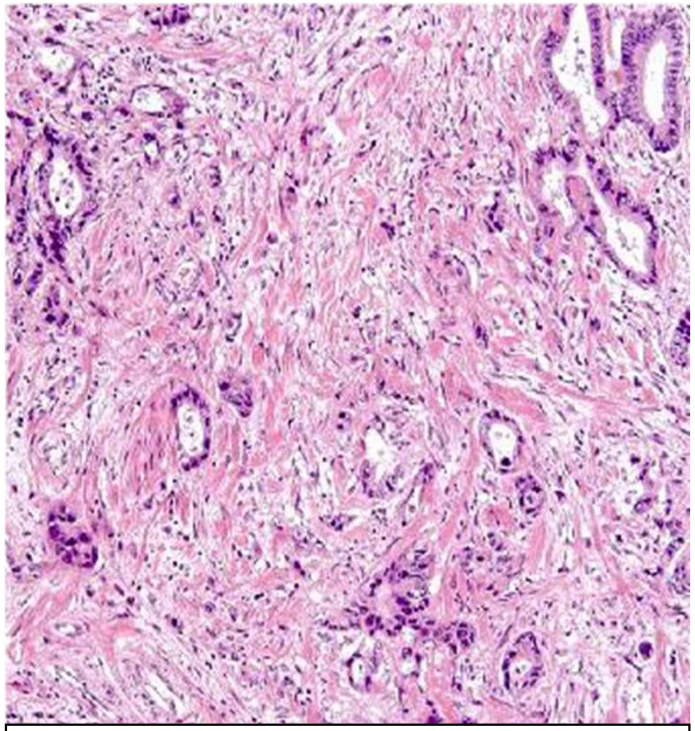
- Identify the presence of tumor budding at scanning power.
- Scan up to 10 fields at 10X to identify the field with the highest budding density “hot spot.”
- Count the number of tumor buds in a 20X field (area 0.785 mm2) of the hot spot; if the 20X field area is not 0.785 mm2, the bud count is normalized to this area.
- Grade the tumor budding.
- 0-4= low-level budding Bd1
- 5-9= intermediate-level budding Bd2
- ≥10 = high-level budding Bd3

Lugli A, Kirsch R, Ajioka Y, et al
Mod Pathol 2017 30(9):1299-1311

# Tumor budding



**LOW-GRADE BUDDING:**
**0-4 foci in a field (250x)**



**HIGH-GRADE BUDDING:**
**≥ 5 foci in a field (250x)**

***Ueno, Jass, Histopathology 2002***

PDCs are defined as cancer clusters of ≥5 cancer cells infiltrating the stroma and lacking a glandular formation

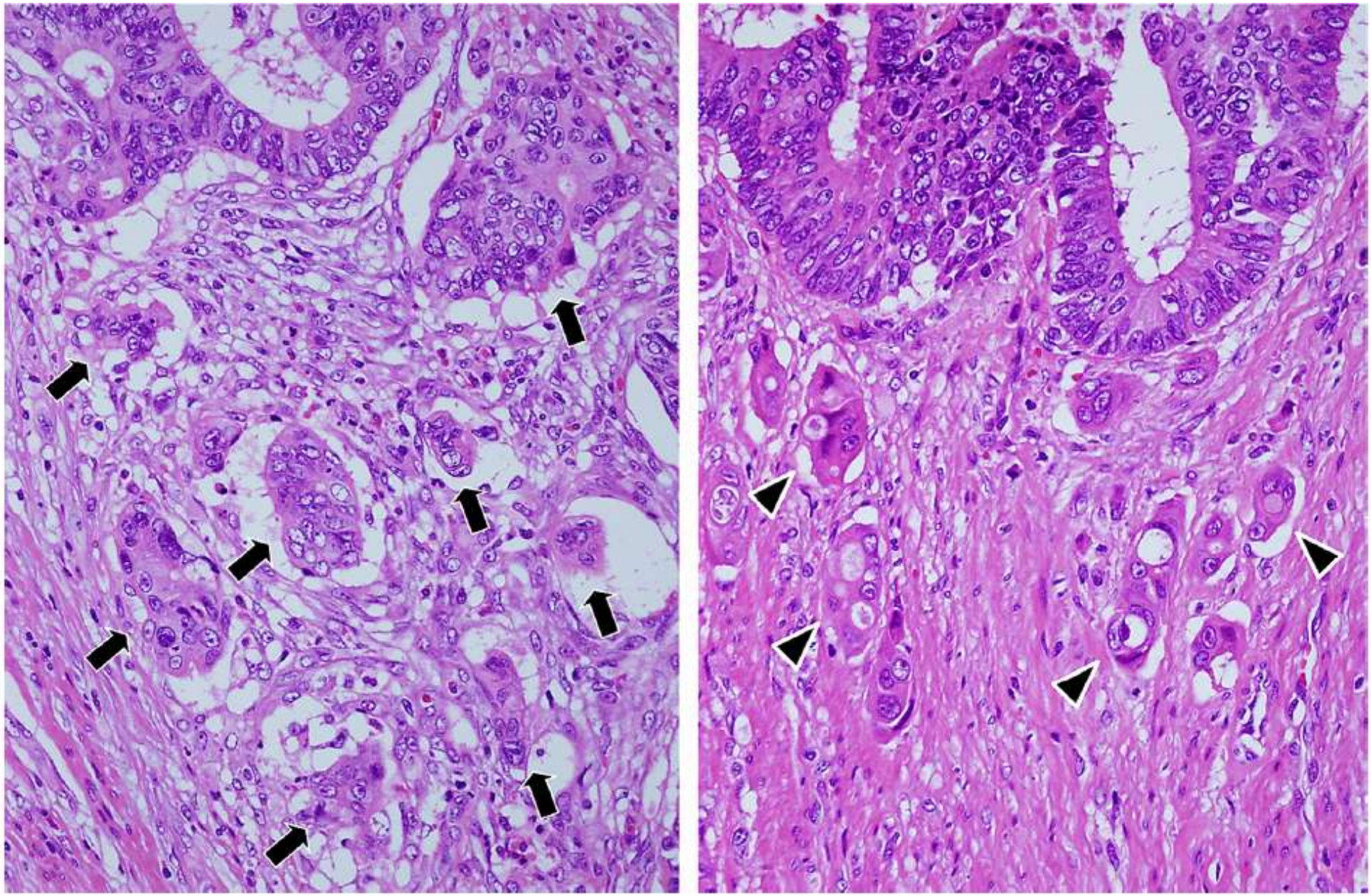


**Fig. 1** Poorly differentiated clusters (PDCs).

**Box 6.02** Essential and desirable diagnostic criteria for colorectal cancer

- Histological subtype
- Differentiation grade: Low/high
- Invasion depth: According to TNM, specify if invasion in other organs (pT4) or tumour perforation
- Presence of (lympho)vascular invasion: Intramural vascular invasion, extramural vascular invasion, lymphatic invasion
- Perineural growth: Present/absent
- Resection margin status (proximal, distal, circumferential): Positive, negative, distance in cm
- Diameter of the tumour
- Site/localization of the tumour
- Quality of the resection specimen
- Number of investigated lymph nodes
- Number of positive lymph nodes
- Presence of treatment response: Yes/no; if yes, partial or complete response
- Microsatellite status / presence of DNA mismatch repair proteins (MLH1, MSH2, MSH6, PMS2): Microsatellite-stable or -instable, staining for mismatch repair proteins present or absent
- Tumour budding status
- Immune response
- Presence or absence of relevant mutations

WHO 2019