Gastrointestinal Polyps

Prof. Dr. Ömer ŞENTÜRK

Colorectal Polyps

- Neoplastic mucosal lesions
- Non-neoplastic mucosal lesions
- Submucosal lesions

Colorectal Polyps

- **Neoplastic mucosal lesions**
  - **Benign (adenoma)**
    - Tubular adenoma
    - Tubulovillous adenoma
    - Villous adenoma
  - **Malign (carcinoma)**
    - Noninvasive CA
      - Carcinoma insutu
      - İntramucosal CA
    - İnvasive CA
- Non-neoplastic mucosal lesions
- Submucosal lesions

Colorectal Polyps

- Neoplastic mucosal lesions
- **Non-neoplastic mucosal lesions**
  - Hyperplastic (metaplastic) polyp
  - Normal epithel (polypoid appearance-mucosal polyps)
  - Juvenil polyp (retention polyp)
  - Peutz-Jegher polyp
  - Inflammatory polyp
    - IBD
    - Bacterial infection
    - Schistosomiasis
    - Cap polyposis
- Submucosal lesions

Colorectal Polyps

- Neoplastic mucosal lesions
- Non-neoplastic mucosal lesions
- **Submucosal lesions**
  - Colitis cystica profunda
  - Pneumatosis cystoides intestinalis
  - Lymphoid polyps
  - Lipoma
  - Metastatic neoplasm
  - Others

Colorectal Polyps

- Adenomatous polyp is the result of inadequate levels of cell proliferation and apoptosis
- Initial abnormality starts from a single colonic crypt
- The histological type of adenoma is determined by the reaction of the lower mesenchyma (connective tissue and capillaries)
- Mesenchymal proliferation is minimal in tubular adenoma
- In villous adenoma, mesenchymal proliferation accompanies epithelial proliferation, resulting in large polyps

Colorectal Polyps

- Most colon cancers originate from benign adenomas
- Colon cancer can rarely originate from a flat, non-adenomatous epithelium
- Adenomatous polyps need 5-10 years for the development of cancer
- The development of benign adenomas from familial polyposis syndromes requires 10-12 years

Colorectal Polyps

- Adenomatous polyps may be with or without stalk
- If 80% of the adenoma is tubular, tubular, and 80% of the villous structure is called villous adenoma
- Tubular adenomas constitute 80-86% of adenomas, 8-16% of tubulovillous ones, and 3-16% of villous ones

- Nearly complete of colorectal cancers originates from adenomas, while very few (less than 1 in 20) adenomas progress to cancer
- There are 3 main features that correlate with malignant potential for adenomatous polyps:
  1. Polyp diameter
  2. Hystologic type
  3. Dysplasia grade
  4. Polyp number

	Polyp Diameter	
	<1 cm	**>2 cm**
Tubular	1%	35%
Villous	10%	53%
Mild dysplasia	0.3%	42%
Severe dysplasia	27%	48%
	Malignancy Risk	

Diminutive polyps

- Polyps smaller than 5mm
- 30-50% of these polyps, previously considered non-neoplastic, were found to be **adenomatous**
- Despite the excess of adenomatous content, the risk of cancer is very low (villous character <1%)
- In 33% of asymptomatic persons with diminutive pole, synchronous proximal adenoma is present (but most of them are <5mm)
- As a result, diminutive polyps have little clinical importance

Other adenoma variants

1. Flat adenoma
   - It constitutes 10% of all adenomas
2. Serrated adenoma
   - It is characterized by adenomatous and hyperplastic polyps (mixed)
3. Aberan cripts
   - It is often hyperplastic, but may be dysplastic

Molecular Genetic and Biology

Genetic changes that may lead to the development of colorectal polyps are grouped into three groups:

1. Changes in Proto-Oncogenes
2. Loss of Tumor Suppressor Gene activity
3. Abnormalities in genes that play a role in DNA Mismatch Repair

Proto-Oncogens

- Most of these genes play a role in the regulation of normal cell growth and development
- Changes in expression of these genes lead to abnormal proliferation and ultimately carcinogenesis
- There are 3 ras genes in humans:
  1. K-ras
  2. N-ras
  3. H-ras

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Proto-Oncogens

- They regulate the intracellular message pathways
- RAS gene mutations (point mutations) play a role in the development of adenoma in the intermediate stage
- While the incidence of RAS gene mutations is 10% in <1cm adenomas, this rate is 58% in >1cm adenomas

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Tumor Supressor Gens

- The deletion in the long arm of the fifth chromosome (5q21) resulted in the emergence of the **APC gene**
- Abnormalities in the APC gene cause changes in cellular adhesion molecules, **E-cadherin** and **Catenin**
- These molecules disrupt cell-cell adhesion and facilitate the development of colonic neoplasia in sporadic adenomas and FAP patients

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Tumor Supressor Gens

- Another suppressor gene is the DCC gene localized on chromosome 18q
- This gene provides proper communication between cells
- Loss of function in this gene plays a role in the late period of adenoma-carcinoma development
- Allelic deletion in chromosome 17p (localized p 53 gene in this locus) is the most important region where allelic loss occurs in colorectal cancer

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DNA Mismatch Repair Gens

- HMSH2 and h MLH1 genes play a role in repairing inappropriate base mating during DNA replication
- Changes in these genes cause errors and mutations in DNA replication
- These genes play an important role in the development of HNPCRC
- In sporadic cancers, these changes are at 10-15%

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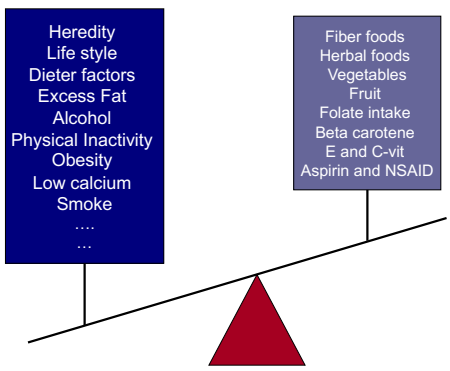
Risk Factors For Adenoma Development



Polyps: Anatomic Distrubution

- Polyps, which are large and symptomatic, have more localization on the left side
- Adenoma distribution was shifted proximally in both autopsy and colonoscopic scans in older age group (especially >60 years)

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Conditions Associated with Adenomatous Polyps

1. Ureterosigmoidostomy
   In the presence of fecal flora, adenoma occurs as a result of the development of N-nitrozamines from urinary amines
2. Acromegaly
   GH ?
3. Streptococcus bovis bacteremia
4. Skin tags
5. Atherosclerosis and cholesterol
6. Breast cancer
7. Cholecystectomy
   Increased bile acid secretion → increase in the formation of secondary bile acids from primary bile acids → increase in colonic mucosal proliferation

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Adenomatous Polyps: Diagnosis

- **Symptoms and symptoms**
  - Most have a **symptomless (asymptomatic)** or nonspecific symptom
  - The most common symptom attributable to colonic polyp is hidden or overt rectal bleeding
  - Other symptoms;
    - constipation
    - diarrhea
    - flatulence
    - abdominal pain
    - reduction of stool diameter

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Adenomatous Polyps: Diagnosis

- FOB
  - Usually <1 cm polyps do not bleed
  - Greater positivity is detected in large diameter and distal polyps
- Sigmoidoscopy
- Colon graphy
- **Colonoscopy (FUSE system)**
- Others
  - Hydrocolonic USG
  - Helical CT
  - Virtual colonoscopy

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Colonoscopy in Determining Polyps

- In the colonoscopic examination, adenomas from;
  - <5 mm 27%
  - Between 6-9 mm 13%
  - >10 mm 6%

  } **may not be seen**

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The Course of Adenomatous Polyps

- Natural course (untreated)
  - Proportional to the diameter of adenoma
  - Diminutiv polyps need 2-3 years to reach a diameter of 1 cm
  - >1 cm doubling time in polyps 4-6 months

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Multiple Adenoma and Carcinoma

- The presence of two or more adenomas is called **multiple adenomas**
- When adenoma or carcinoma is detected, the presence of a second adenoma or carcinoma is called a **synchronous lesion**
- Detection of the other one at least 6 months after the first diagnosis is called **metachronous lesion**
- Especially in older age groups, when an adenoma is found in the colon, 30-50% synchronous adenoma is present

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Preventing Polyp Formation

1. Diet
   Low fat, rich in vegetables, fruits and fiber
2. Maintaining normal body weight
   Regular exercise and limitation of caloric intake
3. Stop smoking and alcohol intake
4. Daily intake of 3 g of Calcium Carbonate

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Adenomatous Polyps: Treatment

- If polyps are detected on barium graphy, histologic diagnosis is made by colonoscopy
- If polyps are detected with rectosigmoidoscopy;
  - No need for colonoscopy if the polyp is hyperplastic
  - If the polyp is adenomatous type;
    - Diameter of adenoma
    - Histopathological features of adenoma
    - Age of patient
    - Family history

Colonoscopy is performed considering additional disease conditions

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Adenomatous Polyps: Treatment

- Not well differentiated,
- Made vascular invasion,
- Made submucosal invasion and
- Polyps that have passed out of 2 mm of polypectomy

Surgical treatment is performed

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Adenomatous Polyps: Treatment

- Adenoma **recurrence** after polypectomy;
  - 5-15% at the end of year 1
  - 20% at the end of year 5
  - 50% at the end of the 15th year

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Adenomatous Polyps: Treatment

- **Risk factors in recurrence**;
  - Multiple polyps
  - Large polyp (> 1cm)
  - Severe dysplasia
  - Villous histology
  - Advanced age

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Non-Neoplastic Polyps

- Hyperplastic (metaplastic) polyp
- Normal epithelium (polipoid appearence-mucosal polyps)
- Juvenil polyp (retention polyp)
- Peutz-Jegher polyp
- Inflammatory polyps
  - IBD
  - Bacterial infections
  - Schistosomiasis
  - Cap polyposis

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Non-Neoplastic Polyps

- Hyperplastic polyps
  - <5 mm, rarely >10 mm polyps
  - They cannot be distinguished from adenomatous polyps with macroscopically
  - There is no cytological atypia that is characteristic for adenomatous polyps
  - In 13% of hyperplastic polyps, hyperplastic and adenomatous transformation properties are found together
  - These polyps can sometimes have dysplasia and even carcinoma focus (**serrated adenoma**)

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Non-Neoplastic Polyps

- Hyperplastic polyps
  - Unlike serrated adenomas, hyperplastic polyps have no intrinsic malign potential
  - However, hyperplastic polyps and neoplastic lesions can be found in the same colon
  - Hyperplastic polyps frequency in asymptomatic individuals over 50 years of age is 9-10% and this rate is 20-35% in autopsy series
  - The presence of hyperplastic polyps in distal colon is not an alarm finding especially in elderly patients

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Non-Neoplastic Polyps

- Mucosal polyps
  - No clinical significance
  - It is seen in 8-10%

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Non-Neoplastic Polyps

- **Juvenile polyp (Retention polyp)**
  - Acquired
  - The most common polyp type of childhood
  - Spontaneous regression
  - They are often single and have stalk
  - Their sizes range from 0.3-2 cm

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Non-Neoplastic Polyps

- **Juvenile polyp (Retention polyp)**
  - Sometimes they prolapse with defecation
  - It is recommended to remove due to prolapse and bleeding
  - They are not malignant when they are single (when they are multiple -juvenile polyposis- there is a risk of developing cancer)
  - 18-20% of patients with juvenile polyps in the rectum may also have proximal polyps, but adenoma is rare

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Non-Neoplastic Polyps

- **Peutz-Jeghers polyp**
  - It is characterized by a single hamartomatous lesion
  - When multiple, Peutz-Juggers syndrome is called

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Non-Neoplastic Polyps

- Inflammatory polyps (pseudopolyps)
  - They do not have intrinsic neoplastic potential
  - However, they are often found in diseased areas with a high risk of developing colon cancer

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Monitoring of Polyps **(Surveillance)**

- Patient with polyps;
  - Only 1 or 2 polyps,
  - Small (<10 mm),
  - Tubular adenoma
  - Low-grade dysplasia

Colonoscopy is performed every 5-10 years

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Monitoring of Polyps **(Surveillance)**

- Patient with polyps;
  - Multiple (3-10) adenomas,
  - Adenoma >10 mm,
  - Adenom villous features,
  - High-grade dysplasia and
  - if the adenoma is completely removed

Colonoscopy is performed 3 years later

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Monitoring of Polyps **(Surveillance)**

- Follow-up colonoscopy;
  - Normal or
  - There are only 1-2 small tubular adenomas,
  - Low-grade dysplasia

Colonoscopy is performed every 5 years

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Monitoring of Polyps **(Surveillance)**

- If the patient;
  - More than 10 adenomas in one examination

COLONOSCOPIC assessment should be performed at intervals of **less than 3 years** (also taking into account the family history and clinical status of the patient)

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Monitoring of Polyps (Surveillance)

- Patient with polyps;
  - Sesil adenoma,
  - However, if the adenoma is not completely removed

Remove polyp in the shortest time period (2-6 months) with COLONOSCOPY

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Monitoring of Polyps (Surveillance)

Patient's History	Follow-up
≤2, <1cm tubular adenom, low-grade dysplasia	Don't look before five years
3-10 small adenom or >1cm, 1 adenom or Villous polyp or High grade dysplasia	3 years
>10 adenom	<3 years
Large sesil polyp, which cannot be completely removed	3-6 moth
Negative colonoscopy in follow-up	Don't look before five years
>8-10 years UC or CD	1-2 years intervals

Gastrointestinal Polyposis Syndromes

- Familial adenomatosis polyposis syndromes
- Familial hamartomatous polyposis syndromes
- Non-familial multiple polyposis syndromes

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Gastrointestinal Polyposis Syndromes

Familial adenomatosis polyposis syndromes

1. Classical FAP
2. Gardner's syndrome
3. Attenuated FAP
4. Turcot's syndrome

Familial hamartomatous polyposis syndromes

1. Peutz-jegher syndrome
2. Juvenil polyposis
3. Neurofibromatosis
4. Cowden syndrome
5. Basal cell nevus syndrome

Non-familial multiple polyposis syndromes

1. Cronkhite-Canada syndrome
2. Inflammatory polyposis
3. Lenfoid polyposis
4. Pneumatosis sistoides intestinalis

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Classical FAP

- Polyps
  - Colonic adenomas (thousands)
  - Duodenal (especially periampullary)
  - Gastric fundic gland hyperplasia
  - Jejunal and ileal adenomas
  - İleal lymphoid polyps
- Extraintestinal abnormaties
  - Mandibular osteomas
  - Dental abnormalities
- Mutation in the APC gene

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Attenuated FAP

- Polyps
  - Colonic adenomas
    - The numbers are less (than classical FAP)
    - Flat typ
    - More common in the proximal part of the colon
  - Duodenal and periampullary adenomas
  - Gastric fundic gland hyperplasia
- Ekstraintestinal
  - Mandibular osteomas (rare)
- Mutation in the APC gene

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Gardner syndrome

- Polyps → Same classical FAP
- Extraintestinal abnormalities
  - Osteomes in the mandible, skull and long bones
  - Congenital hypertophy in the retinal pigment epithelium
  - Desmoid tumors
  - Epidermoid cysts
  - Fibroma, lipoma
  - Thyroid, adrenal and hepatobiliary tumors
- Mutation in the APC gene

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Turcot's sendromu

- Colonic adenomas + central nervous system tumors
- Oto.res. / oto. dom.
- Polyps
  - Colonic adenomas (less than classical FAP)
- Ekstraintestinal
  - Medullablastoma
  - Glioblastoma multiforme
  - Congenital hypertrophy in retinal pigment epithelium

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FAP: Diagnosis and Treatment

- Nonspecific symptoms
- Hematochezia, diare and abdominal pain
- Diagnosis is usually made by genetic analysis
- Medical treatment
  - Ascorbic asid (C-vit 3-4g/day)
  - Alpha tocopherol (E-vit 400 mg/day)
  - Calcium
  - Fiber diet (supplementel fiber 22,5 g/gün)
  - NSAID's (sulindac)
- Surgical treatment
  - Total proctocolectomy and convantional ileostomy
  - Subtotal colectomy and ileorectal anastomosis (rectum protection)

TIMING OF THE SURGERY AND THE METHOD OF PROCESS ???

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Peutz-Jegher's syndrome

- Genetic mapping and responsible gene for this syndrome is not clear yet
- Gastrointestinal polyposis (hamartomatous type)
  - Polyps in the stomach, small bowel and colon
- Mucocutaneus pigmentation
  - In the mouth, hand-feet, perianal and genital regions
- Carcinoma in the pancreas and biliary tract
- Ovarian sex cord tumor
- Testis sertoli tumors
- Urinary system, nasal system and bronchi may also be polyps

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Juvenil polyposis

- It is seen in childhood
- It typically leads to gastrointestinal bleeding, intussusception and obstruction
- Risk of colon cancer increased
- Polyps can be found in the small intestine and stomach
- Juvenile polyps may be associated with adenomatous and hyperplastic polyps

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Neurofibromatosis

- Multiple submucosal neurofibromas in Upper GIS
- It can cause dyspepsia, abdominal pain and bleeding

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Cronkhite-Canada syndrome

- Cutaneous hyperpigmentation
- Alopesia
- Glossit
- Gastrointestinal polyposis
- Diare, hematochezia
- Malabsorption (due to this tetani, paresthesia, edema may occor)
- Onycholysis in nails

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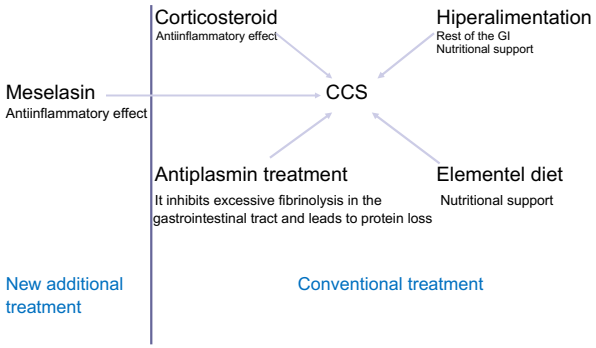
Cronkhite-Canada syndrome: Treatment



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Follow-up Polyps (Surveillance)

Familial Adenomatous Polyposis

- Starting at 10-12 years of age, if negative result is obtained, colonoscopy is performed with 12 months interval until 35-40 years of age

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Gastric polyps

1. Hyperplastic polyps
2. True neoplastic adenoma

Others;

- Multiple polyposis syndromes
- Fundic gland polyps
- Gastric hamartomas are also found

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Hyperplastic polyp

- 3-4 times more than adenomatous polyps
- Often <1 cm (rarely reach 3 cm)
- Often more than one
- Most often in antrum
- They consist of superficial gastric epithelium
- They occur due to chronic inflammation and regenerative hyperplasia
- Malignant degeneration is rare (<2%) (large and multiple)
- Hyperplastic polyps are common after gastric surgery
- Inflammatory origin may occur due to *H.pylori* (active chronic gastritis) and may be regressed by eradication

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Adenomatous polyps

- Adenomatous polyps are true neoplasms
- Tubular, villous or tubulovillous
- They contain different degrees of dysplasia (more in villous ones)
- With or without stalk
- Adenomatous polyps are most commonly found in the antrum

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