Small Intestine and Appendix

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F. Billmann, T. Keck (eds.), *Essentials of Visceral Surgery*,
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2.1 Anatomy of the Small Intestine

2

Key Points

- Longest part of the gastrointestinal tract
- Difficult endoluminal access
- Surgical exploration: one of the diagnostic modalities
- New diagnostic techniques available: non-invasive assessment by double balloon endoscopy, imaging techniques (CT/MRI), capsule endoscopy

2.1.1 Measured Values

- Length = 270–290 cm (from pylorus to cecum)
  - Duodenum = approx. 20–25 cm
  - Jejunum = approx. 100–110 cm
  - Ileum = approx. 150–160 cm
- Diameter = 1.8–2.5 cm
- Surface:
  - Small intestine tube (cylinder) = 0.69 m^2 (for a 5 m long small intestine)
  - Functional resorptive surface = 120–900 m^2 (depending on author)

2.1.2 Limits

- Duodenum: from pylorus to duodenojejunal flexure
- Jejunum: Oral border = from duodenojejunal flexure (Treitz ligament)
- Ileum: No clear boundary between jejunum and ileum; ileum to ileocecal junction

2.1.3 Wall Structure of the Small Intestine

Four layers (from the outside to the inside):

- Serosa:
  - Consisting of visceral peritoneum
  - Coating of jejunoileum + anterior surface of duodenum
- Muscularis propria:
  - Smooth muscles
  - Fine longitudinal outer + thicker circular inner layer
  - Plexus myentericus: between the two layers
- Submucosa:
  - Fibroelastic connective tissue
  - Includes vessels + nerves (Meissner's plexus)
- Mucosa:
  - Muscularis mucosae + lamina propria + epithelial cell layer
  - Epithelial cell layer = goblet cells, Paneth cells, enterocytes and enteroendocrine cells

Surface Multiplication (► Sect. 2.1.1)

- Plicae circulares (Kerck ring folds): Transverse folds of the mucosa (prominent in the distal duodenum + jejunum) lead to an increase in surface area from 0.69 to 1 m^2
- Villi: surface multiplication factor up to 30-fold
- Microvilli: surface multiplication factor = 30

2.1.4 Circulation

Arterial Blood Flow

- Excluding superior mesenteric artery
- Exception = Proximal duodenum through branches of the truncus coeliacus
- Division pattern of the superior mesenteric artery:
  - Specific branches for pancreas
  - Specific branches for distal duodenum
  - Specific branches for small intestine
  - Specific branches for ascending and transverse colon
- Collateral system = vascular arcades of the mesentery
- For the jejunum: long vasa recta of one or two arcades
- For the ileum: short vasa recta of 4–5 arcades (ileum: better blood circulation)

Venous Drainage

- Superior mesenteric vein
- Drainage (with V. splenica) in V. portae hepatis (behind the neck of the pancreas)

Lymphatic Drainage

- From the mucosa through the small intestine wall
- Draining of mesenteric lymph nodes
- Main drainage pathway of fats into the bloodstream
- Immunological role + role in the distribution of cells in the case of malignant intestinal neoplasms

Mesenteric Base

- Fixed to the posterior abdominal wall
- From the left view of LWK 2, oblique to the right and caudal to the right sacroiliac joint

2.1.5 Innervation

- Innervation of the small intestine = autonomic nervous system

Parasympathetic Component

- Fibres of the vagus nerve
- Function: influence on secretion, motor function + all phases of intestinal activity

Sympathetic Component

- Nerve ganglia: Collected in the plexus around the superior mesenteric artery.
- Function: vascular contractility, intestinal secretion and motor function and pain sensation

2.1.6 Small Intestine Functions

Digestion and Nutrient Absorption

- Small intestine: main role in absorption of nutrients + water + electrolytes + minerals
- Peristalsis = intestinal contractions from oral to aboral 1–2 cm/s
  - Main function: transport of the chyme through the intestine
  - Motor pattern different between digestive phase and sobriety

Endocrinological Function

- Small intestine = largest endocrine organ in the body
- Products: Hormones + Peptides
- Paracrine + autocrine functions + neurotransmitter function

Immunological Function

- Antigen processing, humoral and cellular immunity
- Lymphoid tissue: in the Peyer's plaques, the lamina propria + intraepithelial lymphocytes

2.2 Diseases of the Small Intestine

2.2.1 Clinical Presentation

Key Points

- Small intestine diseases = broad spectrum
- Most frequent small bowel disease = small bowel ileus after previous surgery
- Exploratory laparoscopy/laparotomy = often the optimal solution:
  - Free preparation of the intestine
  - Resection or bypass
  - Well accepted: Hardly any postoperative restrictions, resection mostly limited
- Imaging: key role in diagnosis + optimal decision making in treatment of small bowel disease

General

- Mostly unspecific Clinical Presentation
- Broad spectrum of clinical signs: From simple chronic pain to acute peritonitis
- Clinical picture depends on the etiological underlying disease:
  - Inflammatory bowel disease (Crohn's disease) = most common small bowel lesion
  - Neoplastic lesions
  - Small bowel obstruction (in the context of adhesions) (► Sect. 2.2.5)
  - Other rare pathologies (e.g. Meckel's diverticulum)

Inflammatory Bowel Disease

Development

- Onset: Often insidious; rarely also acute
- Medical history: Slow + protracted
- Alternatively symptomatic phases (abdominal pain + diarrhoea) and asymptomatic phases
- Progressive increase in symptomatic phases: More frequent, longer and with more pronounced symptomatology

Symptoms

- Inflammatory symptoms of the gastrointestinal tract
- Typical triad: Chronic recurrent episodes of diarrhoea + abdominal pain + weight loss
- Possible symptoms:
  - Pain in the right lower abdomen (differential diagnosis: appendicitis)
  - Hematochezia: blood in the stool
  - Urge to stool
  - Abdominal cramps and abdominal pain
  - Feeling of incomplete evacuation
  - Constipation (up to ileus)
- General Symptomatology:
  - Fever
  - Loss of Appetite
  - Weight loss
  - Fatigue
  - Night sweats
  - Menstrual irregularities
- Extraintestinal manifestations (30% of patients):
  - Manifestation: GI (gastrointestinal) symptoms, dependent or independent
  - Skin lesions: Erythema nodosum and pyoderma gangraenosum…
  - Arthritis/arthralgias
  - Uveitis and iritis
  - Hepatitis and pericholangitis
  - Aphthous stomatitis
  - Amyloidosis
  - Pancreatitis
  - Nephrotic syndrome

Complications

- Main complications = constipation + perforation
- Constipation to the point of ileus:
  - Etiology = chronic fibrosing lesions, lumen obstruction (partial to complete)
- Perforation:
  - Free (rare) vs. covered
  - Abscesses: Localized, formation in relation to the perforations…
- Fistulas:
  - Etiology = adhesions due to inflammation
  - Abnormal connection between two adjacent organs
  - From the small intestine: to the small intestine, urinary bladder, vagina, stomach, skin
  - Generalized peritonitis = rare
- Perianal lesions (fissure, fistula, stricture, abscess): For anal/rectal involvement
- Infestation of esophagus or stomach possible
- Malignant neoplasms of the small and large intestine: Crohn's disease = predisposition

Neoplastic Intestinal Diseases

- Variable onset of disease

Symptoms

- Early symptoms: mostly non-specific, over months to years
  - Dyspepsia
  - Anorexia
  - Malaise
  - Dull abdominal pain
- Pain: most frequent symptom (often due to obstruction, partly due to intussusception)
- Intestinal bleeding: most frequent symptom (haematochezia/haematemesis)
- Obstruction/Ileus: In 15–35% of patients due to tumor infiltration and adhesions.
- Palpable mass: In 10–20% of patients.
- Perforation: up to 10% of patients (especially in sarcomas/lymphomas)

GIST (Gastrointestinal Stromal Tumors)/ Carcinoid Tumors

(► Chapter 14)

- Special separate tumor entity
- Malignant carcinoid syndrome = rare (10% of cases)

  - Hemodynamic manifestations: Flushing, asthma
  - Cardiac manifestations: Cardiac lesions
  - Intestinal manifestations: Diarrhea, hepatomegaly
- Specific markers:
  - Elevated urine markers: 5-hydroxyindolacetic acid (5-HIAA, 24 h measurement)
  - Chromogranin A in serum (marker of neuroendocrine tumors)
- Metastases: Clinical presentation = as in other neoplastic diseases

2.2.2 Imaging

- Modalities:
  - Radiological imaging
  - Endoscopic imaging
- Indications:
  - Atypical symptoms
  - Complications (e.g. bleeding, obstruction)

Radiological Imaging

Conventional Abdominal Radiograph

- Obsolete, no longer primarily indicated (also due to radiation exposure)
- Allows exclusion of ileus; no information about etiology
- Ileus sign:
  - Dilated loops of small intestine (with/without colonic dilatation)
  - Multiple air-liquid levels
- Localization of the ileal height (proximal vs. distal)

CT Examination with Contrast Medium

- Gold standard for v. a. small bowel disease/ileus
- Pros:
  - Localization of the affected segments
  - Identification of the etiology (extra- or intraluminal lesion)
  - Identification of complications: Ileus, intestinal ischemia (pneumatosis intestinalis, "portal venous gas"), intestinal necrosis
- Staging examination (TNM) in the case of a malignant tumour
- Key examination for extraluminal lesions

Colon Contrast Enema

- Obsolete due to lack of meaningfulness
- Contraindicated due to risk of perforation and when surgery is indicated

CT Enterography/MRI Enterography

- High sensitivity and specificity in the diagnosis of small intestinal diseases (especially chronic inflammatory bowel diseases)
- Principle:
  - Small bowel distension (by oral intake of 1–2 L preparation 1 h before examination)
  - i.v. contrast medium

Abdominal Sonography

- Not much use in small bowel Diagnosiss
- Exception: intestinal ultrasound with contrast medium (chronic inflammatory bowel diseases)

Endoscopic Imaging

Colonoscopy/ Esophagogastroduodenoscopy (EGD)

- Very useful for CIBD (chronic inflammatory bowel disease):
  - Visualization of aphtous ulcerations
  - Cobblestone mucosa pattern
  - Discontinuity of the segments concerned
- In the setting of atypical/malignant lesions: Ideal for biopsy confirmation
- For the treatment of proximal/distal bleeding

Double Balloon Endoscopy

- Access to most of the small intestine possible
- Biopsy of a lesion possible (especially after radiological imaging)

Capsule Endoscopy

- Currently standard method of examination of the small intestinal mucosa

- Application only after exclusion of a stenosis/obstruction (CT)
- Special software for image analysis (automated analysis of anomalies)
- New generation of capsules: Integrated biopsy system

2.2.3 Crohn's Disease

Pathophysiology

- Benign lesion of the small intestine (mostly small intestine and colon)
- Chronic transmural inflammation of the intestinal tract (affected segments: all from mouth to anus possible)
- Unknown etiology
- Pathogenesis: two hypotheses:
  - Primary dysregulation of the mucosal immune system: excessive immunological response against normal microflora; as consequences:
  - Alteration in intestinal microflora or disrupted epithelial barrier function: pathologic response of the normal mucosal immune system
- Triggering/Favoring Factors:
  - Infections (Mycobacterium paratuberculosis)
  - Immunological reactions (humoral and cellular)
  - Genetic defects (IBD1 locus)
  - Environmental factors
  - Dietary factors
  - Smoking

Diagnosis

- Clinical suspicion
- Laboratory chemistry: orienting, serological markers: perinuclear antineutrophil cytoplasmic antibodies (p-ANCA) and anti-Saccharomyces cerevisiae antibodies (ASCA)
  - Atypical p-ANCA: in patients with IBD, especially ulcerative colitis
  - Atypical p-ANCA + ASCA for the differential diagnosis of ulcerative colitis (p-ANCA +) vs. Crohn's disease (ASCA +)
  - Atypical p-ANCA + ASCA prognostic for the development of IBD
- Imaging: to confirm the diagnosis by
  - CT: typical = transmural bowel wall thickening; visualization of extraintestinal complications
  - Endoscopy: typical = aphtous ulcerations with granulations; surrounding mucosa normal; biopsy: granulomas with Langerhans giant cells; systematic exploration of the ileum

Differential Diagnosis (= Other Inflammatory Bowel Diseases)

- Infectious intestinal diseases (Yersinia, Campylobacter, Salmonella, Shigella, Tuberculosis, Amoebiasis)
- Acute appendicitis
- For CIBD: Spontaneous symptom relief
- If symptoms during surgery: no resection, no biopsy (except emergency indications: abscess, perforation)

2.2.4 Small Intestinal Neoplasms

Epidemiology

- Rare + insidious tumors = diagnosis difficult
- Necessity high level of suspicion

Small bowel = 80% of GI tract, 90% of mucosal surface; small bowel tumors = rare (1–2% of GI malignancies)

- Often late diagnosis (advanced stage) = poor prognosis

Diagnosis

- Diagnosis through combined imaging modalities
- Flexible endoscopy: For lesions in the duodenum + terminal ileum
- Double balloon endoscopy: For the middle part of the small intestine
- Capsule endoscopy: contraindicated for malignant lesions with strictures
- CT:
  - For the detection of extraluminal gastrointestinal stromal tumors (GIST)

  - For staging malignant tumors (mesenteric lymph nodes, liver involvement, abdominal wall infiltration)
  - Very sensitive (90% diagnostic certainty)
- Somatostatin receptor scintigraphy: higher sensitivity in the localization and extension balance of these tumors

- Intestinal MRI is increasingly used
- Despite imaging modalities, diagnosis mostly during elective or emergency surgery (e.g. carcinoid tumors)

Histological Classification

- GIST = most frequent tumour in the small intestine (mostly asymptomatic)
- Adenomas = most frequent benign tumor in autopsy series
- Benign tumors = majority of small bowel neoplasms (mostly asymptomatic + incidental findings)

Adenomas

- 15% of all tumours of the small intestine
- Incidence in ileum, jejunum, duodenum = 50%, 30%, 20%
- Symptoms (if symptomatic, but usually autopsy findings): obstruction, bleeding
- Classification:
  - True adenomas
  - Villous adenomas: Mostly in the duodenum, possibly associated with FAP (familial adenomatous polyposis); possible malignancy
  - Brunner's gland adenomas: hyperplastic lesions in the proximal duodenum; can cause peptic ulcer; non-malignant = endoscopic treatment

Hamartomas

- Part of the Peutz-Jeghers syndrome
- Heritable dominant pattern with high penetrance
- Mucocutaneous melanotic pigmentation + gastrointestinal polyps
- Small lesions (1–2 mm), brown-black, in the circumoral region of the face, oral mucosa, forearms, palm, plantar, fingers and perianal region
- Complete jejunum + ileum affected; more rarely rectum, colon, stomach
- Clinical Presentation: abdominal colic (intermittent intussusception); bleeding rare

Hemangiomas

- Submucosal vascular proliferation
  - Mostly in the jejunum
- 3–4% of benign tumours of the small intestine; multiple in 60% of cases
- Possibly part of Osler-Weber-Rendu disease or Turner syndrome
- Symptoms: Often bleeding
- Treatment: Limited resection sufficient

Gastrointestinal Stromal Tumors (GIST)

- Most frequent mesenchymal tumors of the GI tract
- Pathogenesis:
  - GIST cell: development of precursor cell of Cajal cell (myenteric plexus)
  - Activating mutation of KIT protein kinase receptor (CD117) or platelet-derived growth factor receptor α (PDGFRA)
  - Expression of CD117 and CD34
- Benign/malignant GIST = 3–4/1
- Localization: Throughout the GI tract; more common: stomach, small intestine
- Symptoms:
  - Intramural growth: obstruction (ileus)
  - Extramural growth: larger mass, bleeding
- Risk of recurrence: mitotic index >2/50 "high-power fields" = increased local recurrence/metastasis risk
- Malignant GIST:
  - 20% of malignant tumours of the small intestine
  - More frequent in the jejunum and ileum
  - Mostly >5 cm diameter at diagnosis
  - Origin = Muscularis propria: extramural growth
  - Symptoms = obstruction, hemorrhage, perforation (due to hemorrhagic necrosis)
  - Metastasis: Hematogenous: Liver, lung, bone; lymphatic = rare

- Prognosis dependent on:
  - Tumor size
  - Mitotic index
  - Invasion of the lamina propria

Adenocarcinomas

- 50% of malignant tumours of the small intestine
- Localization: Mostly duodenum + proximal jejunum
- Risk factors:
  - FAP
  - "Hereditary non-polyposis colorectal cancer" (HNPCC)
  - Peutz-Jeghers syndrome
  - Crohn's disease
  - Gluten Intolerance Enteropathies
  - Biliary diversions
  - Smoking
  - Alcohol consumption (>80 g/dL ethanol)
  - Consumption of red meat or food preserved in salt
- Prognosis dependent on:
  - Disease stage
  - Time of diagnosis: Usually late

Lymphomas

- Manifestation: Primary lesion or part of a systemic disease
- Lesion often in the ileum
- Often associated with celiac disease of immunodeficiency status
- Lesions usually large (>5 cm) with infiltration of the intestinal wall
- Symptoms:
  - Pain
  - Weight loss
  - Nausea, vomiting
  - Changes in bowel habits
- Complications:
  - Perforation: Frequent (25% of cases)
  - Fever = sign of systemic involvement

Small Intestine NET (Carcinoid Tumors)

Terminology: Small bowel NET = international consensus, instead of carcinoid tumor of the small bowel (Small Bowel NET, SBNET)

- Pathophysiology:
  - Carcinoid = part of the neuroendocrine tumors (NET)
  - Tumor cells (= multipotent cells) originate from enterochromaffin cells (Lieberkühn crypts of the small intestine)
  - Tumor cells can produce substances (depending on the cells' site of origin): Serotonin, P-substance etc.
  - Size growth = very slow
  - After serosa invasion: severe desmoplastic reaction, mesenteric fibrosis, intestinal kinking and intermittent obstruction
- Tumor location (in decreasing frequency):
  - Appendix (most frequent localization) 45%
  - Small intestine (second most common location, especially the last 60 cm of the ileum): Ileum 28%
  - Rectum 16%
  - Carcinoids mostly multicentric in the small intestine
  - Often coexistence with another malignancy of a different type (colon adenocarcinoma) or with multiple endocrine neoplasia type 1 (MEN1)
- Malignancy:
  - Carcinoids of the ileum/jejunum = higher malignancy than carcinoids of the appendix
  - Malignancy potential associated with: Tumor location, tumor size, invasion, growth type.
  - Carcinoids <1 cm: 2% are metastatic
  - Carcinoids of 1, 2 or >2 cm: metastases in 50%, 80% and 90% of cases
- Forecast:
  - Carcinoid = best prognosis of all malignant tumors of the small intestine
  - 5-year survival = 65% (in patients with regional disease), 35% (in patients with distant metastasis)
- Clinical Presentation:
  - 70–80% of patients = asymptomatic; carcinoid = incidental finding
  - Obstruction: In connection with intussusception due to tumor

- Carcinoid syndrome:
  - Only a small percentage of patients
  - Clinical Presentation: Episodic attacks of cutaneous flushing, bronchospasm, diarrhea, and vasomotor collapse
- Treatment:
  - Extended metastasis: palliative resection (because of slow-growing tumors)
  - NET of the midgut (high recurrence rate): Long follow-up, at least 7 years

Metastatic Lesions

- More common than primary tumors
- Mostly from intra-abdominal primary tumors
- Small bowel involvement:
  - Through direct extension
  - Due to peritoneal metastasis
- Metastases from extra-abdominal tumors rare (breast cancer, bronchial cancer, skin melanomas)

2.2.5 Other Diseases of the Small Intestine

Diverticula and Meckel's Diverticula

- Diverticulum of the small intestine = frequent occurrence
- Rarely symptomatic = usually no indication for surgery
- True diverticulum (congenital): Diverticulum consisting of all wall layers

Duodenum Diverticulum

- Second most frequent diverticular localization after colon
- Mostly periampullary (2-cm radius around the ampulla Vateri)
- Mostly originating from medial duodenal wall
- Mostly asymptomatic; diagnosis during endoscopy or imaging
- Complications:
  - Occlusion of the choledochal duct/pancreatic duct
  - Bleeding
  - Perforation
  - Blind Loop Syndrome
- Treatment:
  - Asymptomatic/random findings: No treatment
  - Surgical treatment: necessary in less than 5% of cases

Jejunum and Ileum Diverticula

- Rare, usually false diverticula
- Mostly multiple, protruding from mesenteric side of intestine
- Symptomatology (mostly chronic):
  - Unclear abdominal pain
  - Malabsorption
  - Functional pseudoobstruction
  - Low-grade bleeding
- Complications (rare):
  - Diverticulitis
  - Perforation
  - Abscess
  - Bleeding
  - Obstruction/Ileus
- Treatment:
  - If asymptomatic/random findings: No treatment
  - In case of complication: resection + primary anastomosis

Meckel's Diverticulum

- Most frequent congenital small intestine anomaly
- Localized antimesenteric side of the ileum, 45–60 cm proximal to the ileocecal valve
- Mostly incidental finding
- Pathophysiology
  - Origin = incomplete occlusion of the omphalomesenteric duct
  - Cells of the omphaloenteric duct = pluripotent; Meckel's diverticulum often with heterotopic tissue: gastric, colonic, pancreatic mucosa
- Clinical Presentation:
  - Bleeding (most common form of presentation)
  - Obstruction/Ileus
  - Volvulus or intussusception
  - Incarceration
  - Diverticulitis
- Treatment (symptomatic Meckel's diverticulum) = surgery (usually laparoscopic):

- Meckel's diverticulum resection: transverse stapler resection
- Small bowel segment resection of the diverticulum-bearing segment

Ulcerations and Fistulas

Ulcerations

- Rarely
- Most often associated with Crohn's disease, typhoid fever, tuberculosis, lymphoma, lesions of gastrinoma
- Drug-induced ulcerations: Coated KCl tablets, corticosteroids, NSAIDs (nonsteroidal anti-inflammatory drugs, ulceration usually in the ileum)
- Treatment (if necessary) = small bowel segment resection + anastomosis

Enterocutaneous Fistulas

- Etiology:
  - Mostly iatrogenic
  - Neighbour abscesses
  - Traumas
  - Rarely spontaneous (then in the context of Crohn's disease)
- Risk Factors/Predisposition:
  - Radiation in the anamnesis
  - Intestinal obstruction
  - CIBD
  - Mesenteric vascular disease
  - Intraabdominal sepsis
- Clinical Presentation:
  - Generalized peritonitis: Rare
  - Classification: In terms of localization and output volume (high vs. low output)
  - High-output fistula, if output ≥500 mL/24 h
  - Proximal fistulas: More serious problem due to higher output, electrolyte loss, malabsorption (distal segment eliminated)
- Poor prognostic factors (= no spontaneous healing):
  - High-Output
  - Severe interruption of intestinal continuity (>50% of circumference)
  - Active CIBD
  - Malignant disease
  - Radiation enteritis
  - Distal obstruction
  - Undrained abscess
  - Short fistula tract (<2.5 cm)
  - Epithelialization of the fistula tract
- Treatment:
  - Somatostatin: rapid reduction of output + shorter healing time of the fistula
  - Surgery: If no spontaneous healing

Small Bowel Obstruction/Ileus

- Most common disease of the small intestine

Etiology

- Postoperative adhesions (60%)
- Malignant diseases
- Crohn's disease
- Hernia

Classification of Obstruction/Ileus

- Partial vs. complete
- Simple vs. Strangulated (Trapped)

Clinical Presentation

- Abdominal pain: colicky, intermittent
  - High ileus: Briefly persistent + bilious vomiting
  - Distal ileus: progressive pain, persistent for days + abdominal distension
- Nausea, vomiting
- Diarrhoea or constipation

Complications

- Necrosis
- Perforation

Caution

Signs of necrosis/perforation are fever and tachycardia.

Diagnosis

- CT abdomen:
  - Sensitivity = 90–96%, Specificity = 96%
  - Very effective in evaluation of ileus + diagnosis of tissue damage

  - Ideal in assessing which patient can be treated conservatively vs. surgically
  - Effective in strangulation detection

- Effective detection of strangulation/complication by CT of the abdomen.
- Classic guiding paradigm of "never let the sun rise and set on an ileus" no longer appropriate
- CT diagnosis also enable conservative treatment

Treatment

- Highly dependent on Clinical Presentation + etiologies (■ Table 2.1)
- Depending on the CT findings
- Basic indication for surgery: in case of persistence of pain for hours (laparotomy vs. laparoscopy)

2.2.6 Treatment Strategies

Drug Therapy

- Must always be considered

Surgery = mostly overtherapy, unnecessary bowel resection + surgical complications.

Crohn's Disease

- Medicinal + surgical treatment = palliative
- Therapeutic objective: alleviation of acute exacerbation + alleviation of complications
- Drug therapy: induction + maintenance of remission
  - Aminosalicylates
  - Corticosteroids

■ **Table 2.1** Therapeutic strategies for small bowel obstruction (ileus)

Etiology	Type	Management
Adhesions	Partial SBO	Non-operative treatment over 24–48 h
		Intraluminal contrast medium examinations
		Surgery
	Complete and symptomatic SBO	Surgery
Neoplasia	Primary	Resection
	Secondary	Resection, bypass or stoma
Crohn's disease	Initial presentation	Bowel resection
	Perforation, phlegmon	Bowel resection
	Multiple strictures	Bowel resection, stricturoplasty
Gallstone ileus		Enterotomy
Radiation enteritis		Bypass or resection
Meckel-Divertickel		Meckel's or bowel resection
Invagination	Spontaneous	Reduction
	Tumorous	Resection
Bezoare		Enterotomy, extraction Fragmentation/propulsion into the caeca
NSAID stricture		Bowel resection, stricturoplasty, balloon dilatation

SBO small bowel obstruction

- Immunosuppressive drugs
- Antibiotics
- Anti-TNF antibody

Malignant Lesions

- Adjuvant radiotherapy/chemotherapy: Best survival rates
- Curative resection only in 50% of patients
- Metastases in 1/3 of cases already at the time of surgery
- 5-year overall survival = 25%

GIST/Small Bowel NET (Carcinoid)

- GIST: Targeted therapies must always be considered:
  - Targeted therapy to specific molecules, e.g. imatinib with effect on KIT protein and PDGFRA protein
- Small bowel NET/carcinoids:
  - Long-acting somatostatin analogues (octreotide)
  - Effective against symptoms; no proven action on tumor inhibition
  - Also as palliative treatment for disseminated lesions

Surgical Treatment

General Principles

Segmental Small Bowel Resection + Anastomosis

- Treatment of choice in most cases
- Benign lesions: Limited resection (short segment of small bowel + limited division of mesentery).
- Malignant lesions: Oncologic resection (with control of vessels at their origin + lymphadenectomy + free small bowel resection margins)

Laparoscopic Resection

- Mostly for GIST

Surgical Procedure

Standard Procedure: Laparoscopic GIST Resection

- Lesion must be presentable laparoscopically
- Transillumination (diaphanoscopy) to visualize the vascular supply of the segment to be resected
- Incision of the mesentery, control of the vessels by ligatures or vessel sealing systems: ultrasound dissectors (Sonicision, Covidien), high-frequency thermal fusion devices (LigaSure, Covidien)
- Cutting through the intestine using a 60-mm linear stapler (e.g. EndoGIA, Covidien)
- Isoperistaltic side-to-side anastomosis to restore intestinal continuity: antimesenteric opening of the two intestinal segments, anastomosis using a linear stapler via this incision, closure of the intestinal incision

Caution

Short bowel syndrome = risk in small bowel resection due to resection of healthy tissue

Therefore, always weigh well the indication for resection

Bypass Procedures

- In selected cases of ileus/obstruction

Treatment of CIBD (E.g. Crohn's Disease)

Indications for Surgical Treatment

- Obstruction/Ileus
- Perforation
- Fistula or abscess
- Bleeding
- Complications affecting adjacent tissues

Strategy

- Preoperative imaging: essential for the clarification of multiple lesions
- Treat the affected bowel segment specifically
- Limit to one short bowel segment (recurrent resection of long segments = no better outcome + risk of short bowel syndrome)
- Obstruction/Ileus: Mostly partial/temporary

  - Drug therapy indicated
  - In targeted cases: Endoscopic dilatation
- If surgery is necessary: Segmental resection + primary anastomosis
- Intraoperatively: always careful exploration (macroscopy + palpation) of the entire peritoneal cavity (to exclude secondary lesions)
- In case of obstruction by strictures:
  - Stricturoplasty = longitudinal incision of the fibrotic tissue (preservation of the mucosa) + transverse closure
  - Indications for this technique:
    - Multiple stricture areas in long segments
    - For patients who have already undergone resection
    - If stenosis due to fibrosis: no acute inflammation
- In generalized peritonitis: external enterostomy indicated

Treatment of Benign Lesions

- Potentially malignant lesions: Resection like malignant lesions
- Symptomatic benign lesions: Endoscopic destruction/mucosal resection
- Segmental resection: laparotomy/laparoscopy; possibility of intraoperative identification of the lesion
- Always complete small bowel exploration to exclude other lesions
- Treatment of complications (obstruction/bleeding): Surgery

Treatment of Malignant Lesions

- Malignant tumors: obligatory oncological resection + regional lymphadenectomy
- Carcinoid tumors: treatment depends on tumor size + localization + presence of metastases:
  - Tumor <1 cm without local lymph nodes = segmental small bowel resection
  - Tumor >1 cm, multiple or regional LK metastases = oncological resection (wide bowel resection + mesentery)
  - Involvement of the terminal ileum = hemicolectomy on the right side
  - Cholecystectomy indicated: Because of lifelong somatostatin analogue treatment in most patients…
  - Metastases = surgery in the sense of debulking (symptom relief)

2.3 Vermiform Appendix

2.3.1 Anatomy of the Vermiform Appendix

Normal Anatomy

- Base:
  - Localized at convergence of the long taeniae (inferior surface) of the caeca
  - Anatomical relationship allows localization during surgery
- Tip: Most often retrocecal in the peritoneal space

Localization Variations (According to Wakeley and Testut & Latarjet)

- Retrocecal (65%)
- Pelvin (31%)
- Subcaecal (2%)
- Preileal (1%)
- Rare variations (1%)

The different localizations form the origin of the myriad of symptoms in acute appendicitis.

Circulation and Lymphatic Drainage

- A. appendicularis: branch of A. ileocolica
- Lymphatic drainage to the anterior ileocolic lymph nodes

Caution

Because of the prevention of postoperative bleeding, it is essential to control the appendicular artery during appendectomy (need to know the anatomy).

Histological Features

- Mucosa: goblet cells (distributed in mucosa): Mucus production
- Submucosa: Lymph follicle = important defence function (early stages of development)

2.4 Diseases of the Appendix

2

2.4.1 Appendicitis Vermiformis

Key Points

- One of the most common acute digestive diseases in children/adults
- Treatment (appendicitis and complications) as a therapeutic challenge, depending on:
  - Clinical Presentation
  - Biochemistry
  - Imaging
- Current standard = laparoscopic appendectomy
- Alternative treatment (for uncomplicated appendicitis) = conservative antibiotic treatment
- Complications: Abscess/perforation

Physiopathology

- Etiology of appendicitis = appendiceal stump obstruction
- Obstruction by stool, lymphoid hyperplasia, food debris (fibers), parasites, neoplasms.
- Obstruction:
  - Bacterial overgrowth + mucus accumulation
  - Intraluminal distension
  - Increase in wall pressure
    - Loss of the epithelial mucosal barrier
    - Perforation (after about 48 h after onset of symptoms) + abscess/peritonitis

Symptoms

Initial Symptoms

- Periumbilical pain = visceral pain (due to luminal distension)
- Nausea + Vomitus

Progressive Symptoms (Due to Inflammation of the Surrounding Structures)

- Localized pain in the right lower quadrant
- Possible vomiting
- Fever: parallel with leukocytosis + CRP elevation

Other possible symptoms: urological symptoms, diarrhoea, paralytic ileus, functional intestinal obstruction.

Clinical Presentation: Biochemistry

Clinical Presentation

- Local pain at McBurney point (possibly with defensive tension)
- Dunphy's sign: pain in the right lower abdomen during coughing
- Rovsing's sign: pain in the right lower abdomen on retrograde palpation of the colon
- Blumberg sign (= release pain): Pain in the right lower abdomen after release of pressure in the left lower abdomen
- Obturator sign: pain in the right lower abdomen on internal rotation of the hip = sign of pelvic appendicitis
- Iliopsoas sign: pain in the right lower abdomen with extension of the right hip = sign of retrocecal appendicitis
- With perforated appendicitis: pronounced intense pain + diffuse contracture

Biochemistry

- Mostly leukocytosis >11.5 × 10^3/mm^3
- Elevated CRP

In the absence of one of these two signs appendicitis is unlikely. Here, surveillance should be continued (for prophylaxis of unnecessary surgery).

Imaging

- Necessary to ensure diagnosis (prevention of unnecessary surgery)
- Necessary in case of an uncertain diagnosis

Ultrasound (US)

- Sensitivity = approx. 85%; specificity >90%
- Signs of acute appendicitis:
  - Anteroposterior diameter of the appendix ≥7 mm
  - Thick-walled appendix
  - Noncompressible luminal structure
  - Cocard sign: Target in the transverse section of the appendix
  - Appendicolite

Computer Tomography (CT)

- Standard imaging in acute appendicitis
  - Sensitivity = 90%, specificity = 80%
  - Negative appendectomy after CT = rate < 10%
  - No increase in perforation rate

Diagnostic Laparoscopy

- In case of uncertain diagnosis
- Direct examination of the appendix + peritoneal cavity (other diseases)
- Indications: Primarily in young women with questionable US/CT findings

Differential Diagnosis

Operative Differential Diagnosis

- Invagination
- Meckel's diverticulitis

Non-Operative Differential Diagnosis

- Acute gastroenteritis
- Mesenteric lymphadenitis
- CIBD
- Constipation
- Functional pain
- Pyelonephritis
- Colitis
- Diverticulitis
- Ileus
- Tumour of the GI tract

Gynaecological Differential Diagnosis

- Tuboovarian abscess
- Torsion of the ovary
- Ruptured ovarian cyst
- Ectopic pregnancy
- Gynecological tumors (uterus, tube, ovary)

The large number of differential diagnoses (mostly non-operative) increases the importance of preoperative imaging.

Surgical Treatment Modalities

Treatment Strategy

Early Surgical Appendectomy

- In most cases of acute appendicitis

Antibiotic Treatment

- Perioperative antibiotic prophylaxis indicated: second generation cephalosporins (cover aerobic + anaerobic contamination)
- Systematic antibiotic treatment not recommended (no influence on postoperative complications)
- Non-perforated appendicitis: perioperative single dose, no postoperative antibiotics to reduce postoperative wound infection/intra-abdominal abscesses
- Perforated/gangrenous appendicitis: postoperative intravenous antibiotics until patient is afebrile (at least 5 days)

Laparoscopic Appendectomy

Minimally Invasive (Laparoscopic) Appendectomy = Currently the Gold Standard

Surgical Procedure

Laparoscopic Appendectomy

- Positioning as for open appendectomy (supine position, legs together, right arm abducted 90°, left arm along the body)
- Surgeon + assistant to the left of the patient; monitor to the right of the patient
- Standard instrumentation: Laparoscopy tray: 0° or 30° laparoscope with HD camera, lap scissors, atraumatic fenestrated graspers, monopolar and bipolar coagulation grasper, clip applicator, irrigation aspirator, Röder loops (e.g. Surgitie ligating loop, Covidien),

endoscopic salvage bag; possibly stacker (e.g. EndoGIA linear staplers, Covidien), suture material. Trocars: One 10- to 12-mm trocar (optics), and two 5-mm trocars (working trocar)
- 10-mm optic trocar placed subumbilically through open access; two 5-mm trocars suprapubically and laterally of the left rectus abdominis muscle under visual control
- Patient in Trendelenburg position + turned to the left side
- First step = exploration of the peritoneal space
  - Confirmation of the diagnosis + exclusion of differential diagnoses, especially Meckel's diverticulum, adnexa
- Second step = dissection:
  - Adequate presentation of the appendix (consequences of taenia of the caecum) + mobilization (adhesiolysis)
  - Elevation of the appendix + transection of the mesenteriolum (bipolar forceps, bipolar scissors) until adequate visualization of the appendix base
  - Control of the appendicular artery:
  - Monopolar/bipolar coagulation, vessel sealing devices (e.g., LigaSure, Covidien), stapler, suture of the artery (no technique comparatively better)
- Third step: Setting down the appendix
  - Prior to this, the base is treated with 2–3 Röder loops (e.g. Surgitie Ligating Loop, Covidien)
  - Setting down of the appendix; in case of very inflamed/necrotic stump: stapler (staple suture device) with possibly distal part of the caecum (gangrenous appendicitis, pronounced inflammation of caecal base, abscess, perforation, peritonitis)
- Fourth step: extraction of the appendix

Using a salvage bag to prevent contamination of the abdominal wall

Controversy with Normal Appearing Appendix at Laparoscopy

- Leave appendix vs. appendectomy
- Always complete exploration of the abdominal cavity to exclude differential diagnoses (e.g. Meckel's diverticulum, Crohn's disease, mesenteric lymphadenopathies, pelvic disease, abscesses, ovarian torsion, hernias)
- Current position: After exclusion of differential diagnoses = appendectomy
- Arguments for appendectomy (expert opinion):
  - Infection of the mucosa often inapparent in early phase
  - Risk for re-operation > Risk for removal of a normal appendix

- Since 1894 standard = open appendectomy (McBurney incision)
- For about 20 years standard = minimally invasive appendectomy (also for complicated appendicitis)

Advantages of the Minimally Invasive Procedure

- Less postoperative pain, shorter hospital stay, rapid recovery, low complication rate, lower readmission rate, better quality of life
- For perforated appendicitis: fewer wound infections
- Diagnostic appendectomy: Useful in cases of uncertain diagnosis
- Conversion laparoscopic open: Very rare

Resection Technique

Retrospective study (Mutter and Marescaux 2013): Consecutive series with 262 patients:
- Resection technique
  - Endoscopic ligation: 207 cases (79%)
  - Stapler appendectomy: 55 cases (21%)
- Indication for Stapler appendectomy given by the surgeon:
  - Severe inflammation: 38 cases (69%)
  - Questionable viability of the appendage base 14 cases (25.5%)
  - Necrosis of the appendix base 3 cases (5.5%)

Evidence-Based Approach

- Inverting the appendiceal stump into the caecum: No evidence of benefit
- Need for bipolar coagulation of the mucosa of the appendiceal stump (prevention of abscess by secretion); risk of local necrosis by monopolar electric current and possible postoperative fistula
- Irrigation: no evidence of benefit; risk of spreading germs (Douglas abscess); "suction only strategy" recommended
- Fascia of the 10 mm trocar must be adapted

Open Appendectomy

McBurney Incision

- McBurney incision = conventional approach
- Allows easy access to the appendix
- Limitations:
  - Complete abdominal exploration impossible
  - Impossible adnexal exploration
  - Mostly oversized incision (does not correspond to the theoretical ideal incision)

Median Laparotomy

- Indications:
  - If McBurney is insufficient for adequate exploration or if the appendix is very inflamed
  - In exceptional cases of serious intraabdominal complications (need for preoperative imaging)
  - Some of these cases can be treated with medication, interventions or conservatively

Surgical Procedure

Open Appendectomy

- McBurney incision: oblique incision in the right lower quadrant of the abdomen
- Distraction of muscles (prevention of postoperative hernias)
- Opening of the peritoneum
- Localization of the appendix (follow taenia of the caecum) + advancement in front of the abdominal wall; minimization of the risk of rupture by careful manipulation of the inflamed tissue
- Severing of the mesenteriolum between clamps + ligation
- Skeletonization of the appendix base + ligation using absorbable sutures
- Deposition of the appendix after clamping
- Abdominal wall closure; no drainage recommended

Drug Therapy

- Indicated in two situations:
  - Uncomplicated appendicitis—only (CT evidence)
  - Severe complications of appendicitis supportive

Uncomplicated Appendicitis

- Surgical therapy = still standard for complicated appendicitis
- Evidence-based:
  - Effectiveness in the treatment of uncomplicated appendicitis: antibiotic = operative
  - Need for adequate CT diagnosis: markers of uncomplicated appendicitis
  - Duration of antibiosis (e.g. amoxicillin + clavulanic acid) = 14–21 days
  - Antibiotic therapy of uncomplicated appendicitis: supported by studies (Vons et al. 2011; Spirt 2010; Varadhan et al. 2012)

Severe Complications (Depicted by Imaging)

- Perforation: 23–73% of cases
- Perforation with abscess: 10–13% of cases
- Aim of drug therapy = to prevent major/difficult surgical procedures

Treatment Strategy

- Abscesses >5 cm: Interventionally guided drainage
- Abscesses <5 cm: Antibiotic treatment (treatment of the acute phase) + appendectomy after 6–8 weeks

Caution

Periappendicular abscess:

- Surgery: increased risk of bleeding, wound infection, fistula, adhesions
- Perioperative appendiceal abscess: non-operative treatment (reduction of complications)

2.4.2 Malignant Diseases

- Primary tumors of the appendix = Rare
- Usually only diagnosed postoperatively (in cases of appendicitis) in the pathological examination
- Most common: mucinous tumors and carcinoid tumors of the appendix

Mucocele of the Appendix

Pathophysiology

- Appendiceal lumen obstruction with intraluminal accumulation of mucus: appendiceal distension and mucocele
- Histological classification (Histology appendiceal mucosa):
  - Benign epithelium with retention cyst
  - Hyperplasia/low-grade atypia = low-grade mucinous appendiceal neoplasia
  - Malignant = mucinous adenocarcinoma

Epidemiology

- Simple/hyperplastic mucoceles (acellular mucus) = 5–25% of cases
- Mucinous cystadenoma (63–84% of cases): Appendix neoplasia with dysplastic epithelium (analogous to colonic polyps)
- Mucinous adenocarcinoma (11–20% of cases): High-grade cell dysplasia and invasion of muscularis mucosae + stromal invasion

Clinical Presentation

- Mostly unspecific
- Most frequently: Clinical Presentation of acute appendicitis (► Sect. 2.4)
- Possibly palpable tumor
- Asymptomatic patients = 25–50%

Diagnosis

Tumor Marker (Preoperative)

- CEA ("carcinoembryonic antigen"): possible indication of malignancy

Sonography

- Encapsulated cystic lesion in the lower right quadrant
- Liquid content with different echogenicity (mucus density)
- Multiple echogenic layers in the dilated appendix = pathognomonic

CT Abdomen

- Cystic mass with thin low-density wall, direct communication to the caecum
- Linear/spotted calcifications of the wall = typical for mucocele of the appendix
- No calcifications of the wall in appendiceal abscesses

Colonoscopy

- Soft erythematous mass with central ulceration (= protrusion of the appendicular ostium)
- To exclude synchronous neoplastic lesions of the colon (in up to 20% of cases)

Treatment

- Surgical therapy (strategy analogous to conventional appendectomy)
- Extent of resection: Depending on histology + extent of disease

Retention Cysts

- Resulting in: chronic obstruction of the appendiceal lumen
- Mucosa: Flat cuboidal epithelium
- Surgical extent = Simple appendectomy sufficient

Appendix Mucoceles

- Appendiceal mucoceles <2 cm without intraoperative rupture = benign
- Appendiceal mucoceles >2 cm = neoplastic
- Operation Extent:

- Appendectomy: resect appendiceal mesentery (for histological examination of lymph nodes) + prevent rupture (in case of manipulation/extraction)
- Right hemicolectomy only in case of infiltration of the residual limb

Ruptured Mucocele (= Pseudomyxoma Peritonei/Mucinous Carcinomatosis)

- Rupture = displacement of epithelial cells + mucus in the peritoneal space
- Clinical Presentation:
  - Appendicitis signs
  - Increased abdominal girth
  - Ovarian mass
  - Inguinal hernia
- Treatment: CRS (cytoreductive surgery) + HIPEC (hyperthermic intraperitoneal chemotherapy)

Forecast

Prognostic Factors

- Extent of the peritoneal tumor conglomerate
- Histological grade of the tumor

Course of the Disease

- In most patients: Dissemination of tumor cells in the abdomen at the time of diagnosis
- Most of these neoplasms are noninvasive
- Metastases = rare; locoregional recurrence = frequent (ileus)

Survival

- Without treatment: Very poor prognosis (no chance of cure + very limited survival)
- With aggressive CRS + HIPEC: 5-year survival = 50–96% in selected patient groups (if no distant metastases + complete cytoreduction)
- CRS + HIPEC must be performed early in the disease history

Carcinoid Tumors: Neuroendocrine Tumors of the Appendix

- Carcinoid tumors of the appendix = part of the carcinoids of the midgut (common embryological origin)
- Terminology: carcinoids of the appendix = well-differentiated neuroendocrine tumors (NET) of the appendix
- Histology: NET = enterochromaffin cells (expression of S-100)
- NET = malignant tumours with benign behaviour pattern

Epidemiology

- Appendix-NET = 5% of all intestinal carcinoids
- Mostly in patients around 40 years of age
- Appendiceal carcinoids <1 cm + not localized in appendiceal base = 90%
  - Appendectomy = sufficient treatment
  - Mostly retrospective postoperative diagnosis

Diagnosis

- Depending on the presence of a Clinical Presentation

Non-functional NET

- Slow growing
- Mostly years until first symptoms and diagnosis
- Mostly diagnosis in the context of surgery (pathology)

Functional NET

- Carcinoid syndrome: hormonal production = symptoms + dosable products
- Marker:
  - 5-HIAA (degradation product of serotonin) test in urine
  - Chromogranin A
  - Serotonin

2

Environment Diagnosis

- As with other NET: possibility of other gastrointestinal genitourinary tumors
- Colonoscopy: to exclude other colon tumors
- Other screening examination depending on age and other risk factors

Treatment (According to Recommendations of the American National Cancer Institute and ENETS)

- Figure 2.1
- NET <1 cm, not in appendix base
  - Appendectomy
- NET >2 cm
  - Hemicolectomy right + ileocecal lymphadenectomy (risk of metastases)
- 1 cm < NET < 2 cm
  - Treatment controversial
  - Hemicolectomy on the right:
    - When infiltration of the mesoappendix
    - If R1 at the resection margin
    - If N+ (lymph node metastases)
    - In case of high proliferation activity (high Ki67 index), high mitotic index, angioinvasion
    - If mixed histology (goblet cell carcinoid)

Goblet Cell Carcinoid or Adenocarcinoid

- Rare variant with mixed endocrine and exocrine properties
- Associated with poor prognosis

Aftercare

- Monitoring in patients with elevated chromogranin A (indicator for extended resection)

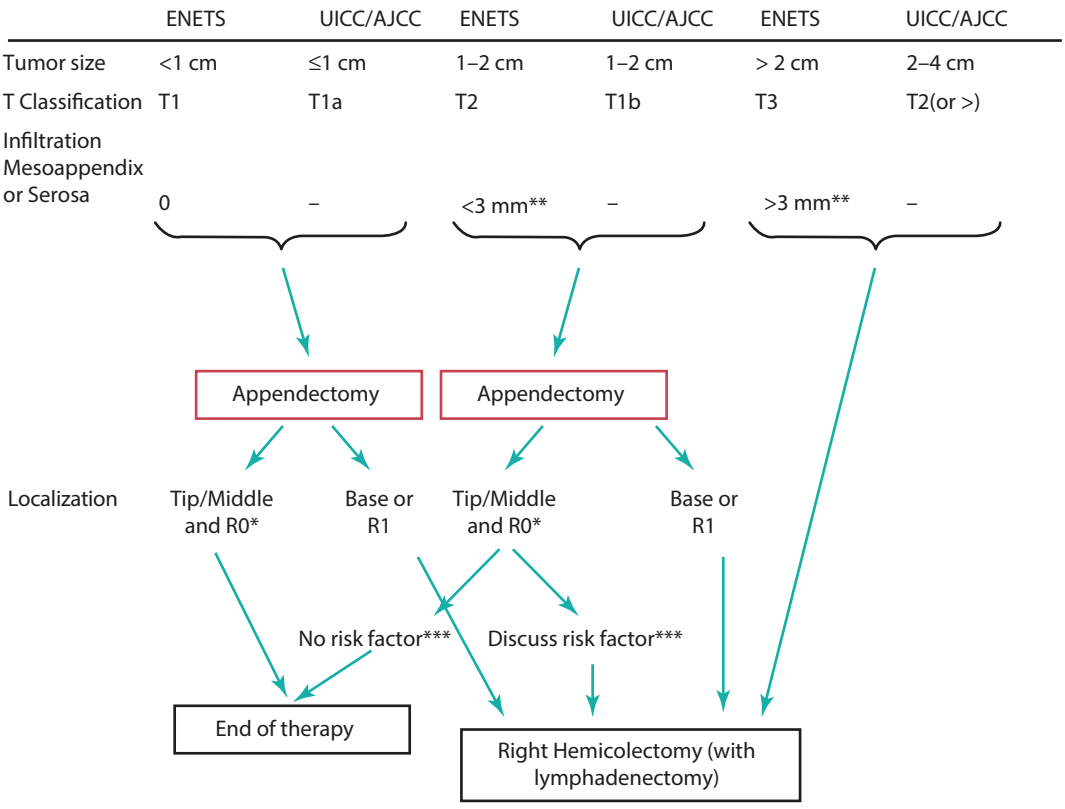

Fig. 2.1 Treatment algorithm of NETs of the vermiform appendix according to the recommendations of the American National Cancer Institute and the ENETS* R0 = tumor-free resection margins** very limited evidence*** risk factors are: V1 (histologic vascular invasion)—L1 (histologic lymphatic vascular invasion)—G2 grading—>3 mm infiltration or infiltration of the mesoappendix

- Survival:
  - Excellent for locoregional tumors
  - Tumours with distant metastases: 10-year survival = 30%

Noncarcinoid Tumors of the Appendix

- Appendix = possible location of all intestinal tumors
- Rare tumor entities

Classification According to World Health Organisation (WHO) (Table 2.2)

- Epithelial tumors
- Non-epithelial tumors

Table 2.2 Histological WHO classification of appendiceal tumours

Epithelial tumors	Non-epithelial tumors
Adenoma Tubular Villös Tubulovillous Serrated	Neuroma Lipoma Leiomyoma Gastrointestinal stromal tumor Leiomyosarcoma Kaposi's sarcoma Other
Carcinoma Adenocarcinoma Mucinous adenocarcinoma Signet ring cell carcinoma Small cell carcinoma Non-differentiated carcinoma	Malignant lymphoma
Carcinoid (well differentiated neuroendocrine neoplasia)	Secondary tumors
Tubular carcinoid	Hyperplastic (metaplastic) polyp
Goblet cell carcinoid (mucinous carcinoid)	
Mixed carcinoid adenocarcinoma	
Other	

Overview: Appendix Adenocarcinoma

- Rare: 0.08% of all carcinomas
- Mucinous appendiceal adenocarcinoma = most frequent subtype (better prognosis after resection)

Clinical Presentation

- Appendicitis in the elderly patient
- Mucocele

Treatment

- Hemicolectomy right = standard procedure
- Drug treatment/chemotherapy for specific diseases (lymphomas etc.)

References

Spirt MJ (2010) Complicated intra-abdominal infections: a focus on appendicitis and diverticulitis. Postgrad Med 122:39–51

Varadhan KK, Neal KR, Lobo DN (2012) Safety and efficacy of antibiotics compared with appendicectomy for treatment of uncomplicated acute appendicitis: meta-analysis of randomised controlled trials. BMJ 5:344

Vons C, Barry C, Maitre S, Pautrat K, Leconte M, Costaglioli B, Karoui M, Alves A, Dousset B, Valleur P, Falissard B, Franco D (2011) Amoxicillin plus clavulanic acid versus appendectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomized controlled trial. Lancet 377:1573–1579