

# Colorectal carcinoma

*Colorectal carcinoma (CR-CA)* is a malignant cancer that ranks third among the world's most common malignancies. In 2012, almost 1.4 million new cases were diagnosed worldwide. In the Czech Republic, the incidence of CR-CA is rising from year to year. In addition to a high and constantly increasing incidence, the disease also has a high mortality rate, mainly due to the predominant diagnosis of the disease in advanced stages, when treatment procedures are limited. Therefore, today there is an effort for effective screening for people over 50 years of age. In terms of prognosis and treatment, it is appropriate to distinguish between colon carcinoma and rectosigmoid carcinoma and rectal carcinoma.

## Epidemiology

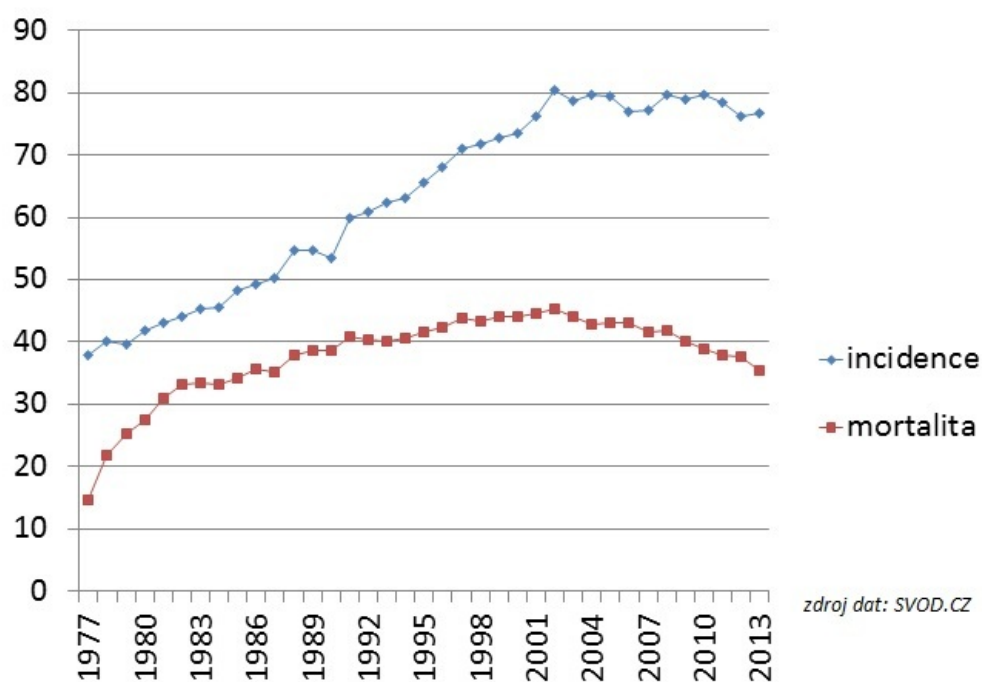
CR-CA is a disease that occurs mainly in developed countries. The highest incidence in terms of continents is in Europe and Oceania, while the lowest is in Africa and Asia. The four countries with the highest worldwide incidence of CR-CA of both sexes in 2012 were South Korea, Slovakia, Hungary and the Netherlands.

**The Czech Republic is at the forefront of the global incidence**, whether male (4th place in 2012) or female (16th place in 2012).

In terms of long-term development in the Czech Republic, the incidence of colorectal cancer has been growing in the last 30 years, and mortality has increased during the same period. In 2013, the incidence of colorectal cancer in the Czech Republic (diagnosis C18 - C21) was 76.74 /

100,000 inhabitants and the mortality rate was 35.35 / 100,000 inhabitants. Current information on the incidence and mortality of CR-CA in the Czech Republic can be found on the website of the Institute of Biostatistics and Analyses of Masaryk University (<https://www.svod.cz/>)

Incidence a mortalita C18–C21 v letech 1977–2013



Incidence and mortality

## Symptomatology

The clinical picture of CR-CA depends on its location in the colon and the way it grows, so it can be very **diverse**.

The most **pronounced** manifestation is **intestinal obstruction**, if the tumor mass fills the entire intestinal lumen - clinically, the patient comes in with ileum. Earlier and less clinically significant manifestations of bowel obstruction may be **early flatulence, change in defecation stereotype, colic pains, or subileus state**. It is not uncommon for a tumor to be discovered with ileal complications.

Another clinically significant manifestation is **bleeding from the tumor into the GIT**, either microscopic or macroscopic. The patient may not even notice the microscopic bleeding, so we use the occult stool bleeding test (TOKS) as a screening test, which detects even a small amount of blood in the stool. If the bleeding is more severe or prolonged, the patient may have symptoms of anemia.

**Acute peritonitis** caused by tumor perforation is one of the rarer manifestations of the disease, as well as the penetration of the tumor into the environment and the development of tactile resistance.

The specific symptom of CR-CA occurring in the rectal area is **tenesmus**.

## Etiology

CR-CA occurs in a **sporadic** and **hereditary** form, where an individual has a higher genetic predisposition to develop the disease than the rest of the population. These are mainly Lynch syndrome I and II and familial adenomatous polyposis (FAP). Hereditary background is diagnosed in about 10% of diseases, **so the sporadic incidence dominates** (90%).

However, even in the sporadic form of CR-CA, we know **risk factors** (RF), which increase the probability of the disease even in a non-genetically loaded individual. As with most cancers also CR-CA, one of the main RF is **older age**, particularly the most vulnerable are people from 70 to 80 years. Then:

- **other colon diseases** - history of intestinal adenomas and chronic intestinal inflammation, especially ulcerative colitis ;
- **hyperinsulinemia** ;
- **obesity** ;
- **smoking** ;
- **eating habits** - frequent consumption of red meat, excessive intake of animal fats and insufficient intake of fiber in the diet are especially risky.

In addition to RF, let's name **protective factors**. These include the already mentioned fiber, omega-3 polyunsaturated fatty acids, folic acid and the use of hormonal contraception .


## Screening

As with all other malignancies in the population, colorectal cancer (CR-CA) has sought to develop effective secondary screening for early stages of the disease . Ideally, precancerous lesions ( adenomas ). One of the main problems with CR-CA's still relatively high mortality is the fact that in most cases it is diagnosed at a very advanced stage. Today, CR-CA can be described as one of the three malignancies for which we have a comprehensive screening (breast cancer and cervical cancer), which effectively reduces the morbidity and mortality of this disease in the population.

### Screening methods

The basic CR-CA screening methods in our country include:

- Stool Occult Bleeding Test (FOBT) - According to four randomized trials, the introduction of TOKS has reduced mortality from CR-CA in people aged 50-80 by 15-33%.

 For more information see *Fecal Occult Blood Test (FOBT)*.

- Primary screening colonoscopy - also demonstrably reduces the risk of CR-CA mortality.

 For more information see *Colonoscopic examination*.

### Screening procedure

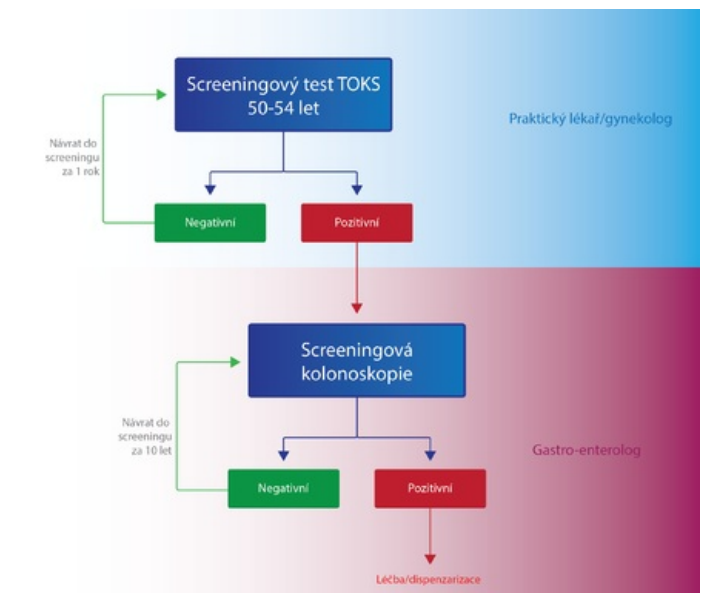
CR-CA screening is performed and covered by the insurance company for asymptomatic men and women over the age of 50. However, all high-risk patients with a positive personal or family history are excluded from the screening program, and special dispensary programs are developed for these individuals, depending on their risk.

Individuals within the CR-CA screening are divided into two groups according to age and the examination procedure differs within these two groups:

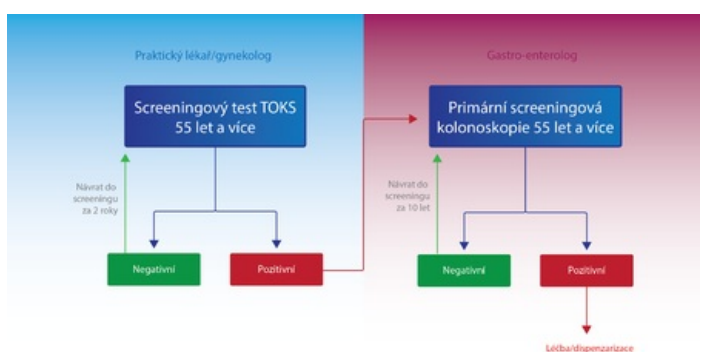
#### Persons aged 50-54

Once a year, the patient is examined either by a general practitioner or a gynecologist. If the test result is negative (FOBT-), the same test is performed on the patient again after one year. In case of a positive result (FOBT +), the patient is sent to a specialized facility for a screening colonoscopy . If the finding on a colonoscopy is negative, the patient will come for another screening examination after 10 years, if it is positive, the patient is included in the high-risk group with a special dispensary program in terms of CR-CA screening.

#### Persons over 55 years



Screening schema till 55 years



Screening schema over 55 years

In addition to FOBT, primary screening colonoscopy is used for these individuals. The patient has a choice.

- FOBT - in the case of FOBT - either the test is repeated after two years or a primary screening colonoscopy is performed. In the case of FOBT +, the patient is sent for screening colonoscopy as in the previous group.
- Primary screening colonoscopy - is an alternative method to FOBT. In the case of a negative result, it is performed again in 10 years; in the case of a positive result, the patient is included in the high-risk group with a special dispensary program in terms of CR-CA screening.

The importance of colonoscopy in screening is likely to increase with the development of non-invasive virtual colonoscopy methods.

Molecular genetic screening techniques, which have significantly higher sensitivity, are being introduced into practice. They are based on the detection of mutations and aberrant methylations typical of adenocarcinoma cells or advanced adenoma .

 For more information see *Colorectal carcinoma/screening*.

## Diagnostics

### Anamnesic data

Although it may seem that in the age of modern technologies such as CT , MRI and PET CT, taking anamnesis is something archaic, there is a whole set of symptoms that can lead a general practitioner to a correct diagnosis. Symptoms often stem from the location of the colon tumor:

- visible fresh blood in the stool - occurs mainly in aborally localized tumors (diff. dg .: hemorrhoids , IBD );
- anemia - a relatively common phenomenon, caused by small-scale chronic bleeding from an exulcerated tumor, typical mainly of tumors of the cecum and right half of the colonies, where the intestine has more lumen and therefore has sufficient time to grow before causing passage disorders;
- changes in the frequency of defecation - it can be both constipation and diarrhea, again it is more typical for the left half of the colon (descendens, sigmoid, rectum, which have a narrower lumen than previous parts of the colon), for example, the patient tells a doctor that he used to go to the toilet every day and in the last 2 months he goes barely twice a week;
- tenesmus - in rectal cancer ;
- weight loss - a rather non-specific symptom, but common in many oncological diseases (not only GIT);
- dyspeptic disorders, general weakness, cachexia,...
- Bowel perforation or ileus can unfortunately also be a condition that leads to malignancy, this is an advanced case, it is a very negative prognostic sign. Sigma cancer, colonoscopy

### Investigation methods

#### Physical exam

Symptoms of general anemia such as conjunctival and pale pallor, catechization . Examination per rectum alone may reveal a tumor in the rectum or reveal blood in the stool, so it should not be neglected by general practitioners and not by surgeons at all if GIT pathology is suspected. The importance of per rectum examination as a screening examination has not been documented, but in the case of a symptomatic individual it is a basic examination which should always be performed.

#### Colonoscopy

The benefit of this examination is almost invaluable, it is a first choice examination . In addition to diagnostics (visualization and biopsy collection), in some special cases it also enables curative intervention consisting in the suffering of precancerous lesions or even a tumor (T1). With the help of colonoscopy, an endosonographic probe can also be used, thanks to which the depth of infiltration in the intestinal wall or other organs can be determined during staging (rectal cancer in particular). In addition, colonoscopy can be used to apply ink to the tumor site, making it easier for surgeons to search during surgery.

#### Two-contrast irigography

This is an X-ray examination of the abdomen with double contrast (barium suspension and air), and is performed at times when colonoscopy is not possible due to lumen obstruction or poor anatomical conditions. The examination must be supplemented with rectoscopy, due to possible tumors of the rectum. The main disadvantage is the fact that it is not possible to take biopsy samples or remove any polyps.

#### Laboratory Sigmoid cancer, abdominal ultrasound

In addition to signs of anemia (hypochromic, microcytic) from chronic bleeding there are obvious tumor markers. In the case of colorectal cancer, these are mainly serum concentrations of CEA and Ca 19-9. It is very important to realize that their contribution is not in the diagnosis of the disease, because they are non-specific. For example, elevated Ca 19-9 occurs not only in pancreatic and biliary tract cancer, but even in benign biliary obstruction. Thus, the benefit is in monitoring the effects of therapy (decreasing = effective chemotherapy, increasing = relapse of the disease) and then also the prognostic benefit. High CEA at the time of diagnosis is a negative prognostic factor.

## CT

CT examination is important in the detection of nodal and distant metastases , especially in the liver , lungs , bones and CNS . Therapy strategies (curative resection versus palliation, use of neoadjuvance, adjuvant) are definitely determined. We perform CT of the abdomen and, in rectal cancer, preoperative CT of the small pelvis, to evaluate the extent of the tumor and possible metastatic spread. According to the results, a decision is made on possible neoadjuvant radiotherapy for more extensive rectal cancers.

## MRI

Magnetic resonance imaging predominates in rectal cancer. Here it is essential to find out the degree of infiltration of small pelvic organs (bladder, ureter, vagina, but also the sacrum), do staging and decide on the type of resection.

## Ultrasonography

Classical abdominal sonography is important in the detection of liver metastases , especially preoperatively and for the evaluation of retroperitoneal nodes.

## Endosonography

Endoscopic sonography is especially important for rectal cancers. Thanks to this technique, it is possible to determine the depth of invasion of the tumor, ie to which layer of the intestinal wall it reaches, or if it does not affect the nearby lymph nodes or surrounding organs. It thus serves to determine the staging of the disease and to plan the subsequent surgical procedure.



Sigma cancer, abdominal ultrasound

## Chest X-ray

It serves to exclude metastatic lung involvement , we perform it in the anterior projection. Also as a preoperative examination.

# Pathology

## Precancerous lesions

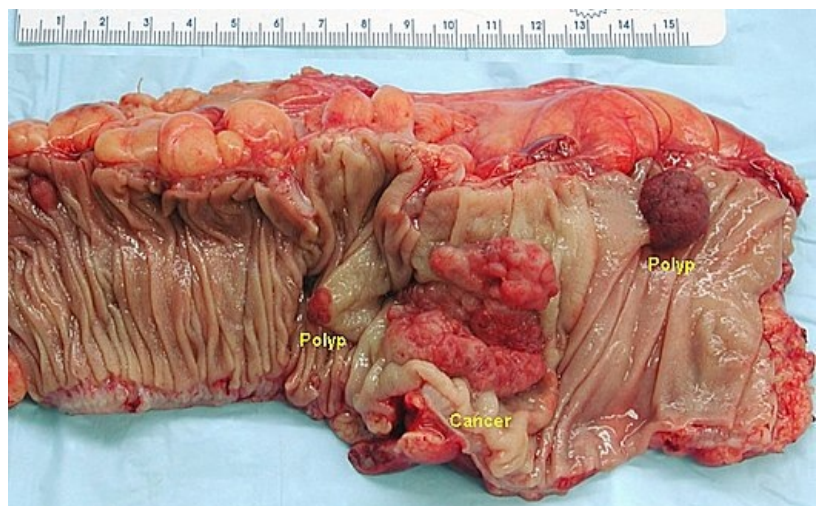
Dysplastic adenomas (tumor polyps) and other intraepithelial neoplasms, such as DALM (Dysplasia Associated Lesions or Masses) in ulcerative colitis , are considered precancerous . The risk of their malignant reversal is closely related to the degree of dysplasia .

## Macroscopy

Based on the nature of the growth, possible complications of the disease can be deduced. In terms of macroscopy, we divide CR-CA into three groups:

- exophytic (polyposis) - the main risk is intestinal lumen obstruction ( ileus ) and rarely intestinal invagination;
- exulcerated - the risk is mainly bleeding and perforation of the intestinal wall with subsequent peritonitis ;
- flat (infiltrating) - may remain clinically silent for a long time.

As annular carcinoma, we mainly call left carcinomas growing around the entire perimeter of the intestine, leading relatively early to stenoses with all the consequences. In contrast, right-sided cancers grow primarily exophytic.



Colorectal resection, visible one exophytic carcinoma and two adenomatous polyps

## Tumor localization by frequency

- left colon - 64%;
  - rectum - 30%;
  - sigmoid - 26%;
  - descending colon - 8%;
- colon transverse - 13%;
- ascending colon - 9%;
- caecum - 14%.



## Microscopy

Histology: tubular adenocarcinoma, stained with HE Microscopically, it is mainly adenocarcinoma (in 95% ), we distinguish their differentiation :

- G1 - well differentiated (tubular or papillary);
- G2 - moderately differentiated;
- G3 - low differentiated (solidly arranged) - with worse prognosis.

We also have several rarer types of CR-CA - mucinous (mucus-forming) adenocarcinoma (for which, as the name suggests, the formation of extracellular mucus is typical), adenosquamous carcinoma and ring cell carcinoma.

## Staging

We commonly use 2 classification systems to classify CR-CA

- TNM classification ,
- Dukes system .

Stage	Description
Stage A	tumor bounded by the intestinal wall
Stage B	the tumor invades or penetrates the serosis
Stage C1	tumor + positive pericolic lymph nodes
Stage C2	tumor + positive perivascular nodes
Stage D	distant metastases

### Comparison of TNM classification and Dukes system

Stage 0	Tis	N0	M0	Dukes A
Stage 1	T1	N0	M0	Dukes A
	T2	N0	M0	DukesA
Stage 2	T3	N0	M0	Dukes B
	T4	N0	M0	Dukes B
Stage 3	T1-4	N1-3	M0	Dukes C
Stage 4	T1-4	N1-3	M1	Dukes D

*See the Colorectal Cancer / Staging page for more information .*

## Metastasis

CR-CA metastasizes, like most cancers, primarily lymphogenically - to local lymph nodes. Later to the distant lymph nodes and hematogenously most often to the liver and lungs . Advanced disease can spread through the peritoneum (so-called peritoneal carcinomatosis ). Rectal carcinomas tend to grow into the surrounding organs (vagina, uterus, ureter, bladder, but also the sacrum). In women it is typical of metastases in the ovaries . The metastatic process and its complications can in some cases be detected before the primary tumor itself.

## Therapy

The method of CR-CA treatment can be determined only after a complete examination of the patient and determination of the staging of the disease. Each patient should be consulted at the indication seminar and the resulting treatment should be the result of the consensus of the oncologist, surgeon, gastroenterologist, or pathologist. The therapeutic procedure must also always depend on the overall health of the patient and his wishes.

The treatment modalities used to treat CR-CA include endoscopic , surgical and oncological methods . As a rule, the tumor mass is first removed, either endoscopically or more often surgically, followed by systemic oncological treatment. In the case of large tumors, neoadjuvant oncological therapy precedes the surgical solution .

Therapeutic procedures for colonic and rectal CR-CA differ slightly.

### Endoscopic treatment

Its importance is irreplaceable, especially in the diagnosis of the disease and the subsequent dispensarization of patients after treatment. It is mainly used for the curative treatment of precancerous lesions ( adenomas ) or very early stages of CR-CA (carcinoma in situ, pT1), or for palliative treatment to clear bowel stenoses caused by tumors (stent insertion).

### Curative treatment

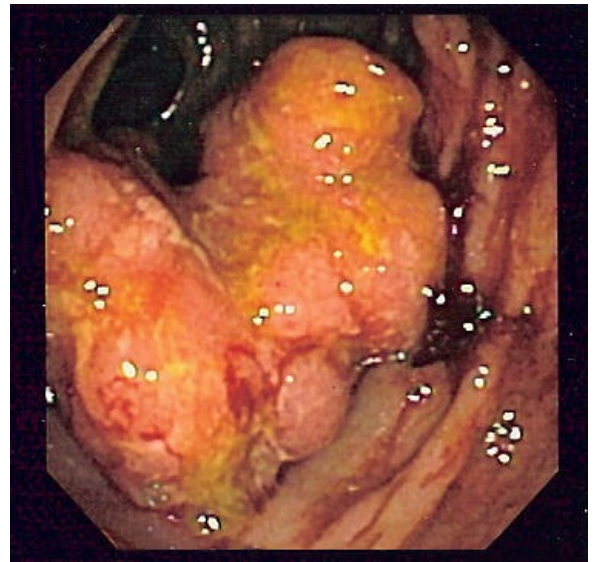
Depending on the extent of the lesion, we use:

- polypectomy (EPE),
- endoscopic mucosal resection (EMR),
- endoscopic submucosal dissection (ESD) - removal of polyps together with submucosa.

In patients diagnosed with CR-CA pT1, we decide between endoscopic or surgical solutions according to other parameters. Endoscopic treatment is sufficient for favorable tumors, however, we approach the subsequent surgical solution for the so-called high-risk pT1 carcinomas. Criteria for high-risk cancer:

- incomplete removal or removal in parts (not en block);
- distance from resection edges 1 mm and less;
- low differentiation;
- evidence of lymphatic vessel invasion in a histological specimen.

In these patients we perform surgical resection with radical lymphadenectomy as well as in more advanced stages of CR-CA.



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### Palliative treatment

The application of a metallic stent is used either in acute intestinal obstruction to survive the surgical solution, or in inoperable and generalized cancers in the last stages to improve the patient's quality of life. However, according to various studies, the usefulness of these procedures is somewhat questionable. It should only be used in carefully indicated cases after interdisciplinary consultation. Patients indicated for biologic therapy with bevacizumab have a higher risk of perforation.

### Surgical treatment

Still the only curative treatment for colorectal cancer is oncoradical resection (except for the very early stages that can be treated endoscopically, see the previous paragraph). It is indicated whenever it is possible to perform a curative radical (R0) resection, ie to remove the entire tumor mass. Possibly also for palliative reasons, similarly to endoscopic treatment, to pass the intestinal lumen and thus to prolong and improve the patient's quality of life.

#### Colon resection

For colon cancer, we use radical resection of the affected section of the intestine together with the removal of the curtain (mesocolon). The advantage of this procedure is the removal of a larger number of lymph nodes (at least 12), the removal of potentially tumor-damaged tissue and the reduction of postoperative tumor spread. We observe radicality even in earlier stages (T1, T2). If the tumor is unfavorably located in the basin of two supplying arteries, we proceed to even more radical procedures - extended resection, or subtotal colectomy (removal of the entire colon, leaving the rectum and establishing an ileorectal anastomosis). The distance at the aboral end should be at least 5 cm from the tumor. The extent of resection is determined by the extent of dissection of the lymph nodes (and vessels) along the arterial supply, when the ligation occurs near the distance between the arteries of the arteries (high ligation):

- right hemicolectomy - ligation of the *ileocolic artery*, *a. colic dextra* and *ramus dexter arteriae colicae mediae* (ascending colon tumor);
- dilated right hemicolectomy - ligation of the *ileocolic artery*, *a. colica dextra* and in addition a *. colica media* (for tumors in the *flexura coli dextra*);
- left hemicolectomy - ligation of the *colic sinistra* (descending colon tumor);
- dilated left hemicolectomy - ligation of the *a. colica sinistra* and *a. colica media* (tumor in the *flexura coli sinistra*);
- sigma resection - *inferior mesenteric* artery ligatures.

The laparoscopic approach is a used alternative to the classical procedure, especially in tumours of the left colon.

#### Rectal resection

The most commonly used procedure is total mesorectal excision (TME), which significantly reduces the incidence of local recurrences. The prognostic factor for the success of TME is mainly the positivity of the resection margins. Today, we use modern mini-invasive, robotic and laparoscopic methods, which are still radical enough, but at the same time less mutilating for the patient. Surgical procedures can be divided into:

- Curative performances (potentially):

1. standard operation - resection of the rectum (+ mesorectum), it can be with amputation of the sphincter, but also the sphincter preserving (even that is sufficiently oncoradical);
2. extensive surgery - resection of the rectum, mesorectum and abdominopelvic lymph nodes and vessels;
3. ultraextensive surgery - in addition with resection of the internal iliac vessels.

- Palliative performances consist of:

1. tumor removal - in most cases it is better to remove the tumor, even if curative resection is ruled out for

- staging the disease or the overall condition of the patient, any growing tumor of the patient threatens the formation of ileum , perforation of the intestinal wall, tumor disintegration ( necrosis );
- 2. solving an obstacle in the passage of the intestine (obstacle is a tumor) - stoma or bypass;
- 3. pain treatment.

## Resection of liver metastases

The liver is the organ where we most often find CR-CA metastases and their treatment is closely related to the patient's prognosis.

*For more information, see Treatment of liver metastases in colorectal cancer .*

## Standard preoperative examination

- Colonoscopy with biopsy - if two-contrast irigography is not possible ,
- liver sonography

CT of the liver - in case of unclear finding or finding of liver metastases on sono,

- CT of the small pelvis ,
- Lung X-ray

CT of the lungs - when X-rays of metastases are found  
bronchoscopy - if metastases are suspected, to avoid duplication,

- urological examination - in case of hematuria or urological problems with suspected disease progression,
- gynecological examination ,
- determination of oncomarkers - CEA, CA 19-9,
- in rectal cancer: transrectal sonography , anorectal manometry .

*You can find more detailed information on the page Importance of tumor markers in the treatment of cancer .*

## Oncological treatment

Almost every patient with CR-CA undergoes oncological treatment in some of its forms - radiotherapy , chemotherapy , biological treatment . According to the treatment sequence, we distinguish between neoadjuvant, adjuvant and independent oncological treatment. Radiotherapy is used especially for rectal cancer, because it is highly sensitive to it and in addition has a high susceptibility to locoregional spread (colon cancer causes rather distant metastases), we apply a dose of 30 Gy.

### Neoadjuvant treatment

We use neoadjuvant treatment especially for rectal cancer - either radiotherapy alone or in combination with chemotherapy (ie chemoradiotherapy). In large tumors (T3 – T4, N +) during neoadjuvant (preoperative) treatment, the tumor mass decreases (so-called downstaging) , and thus better operability of the finding (higher percentage of sphincter-preserving surgery), increased percentage of curative resections and lower incidence of local recurrences . However, the overall longer survival of patients undergoing neoadjuvant therapy has not been confirmed. The combination of chemo- and radiotherapy is accompanied by slightly higher toxicity. In general, the indication of neoadjuvant therapy must be considered in relation to the patient's condition, so as not to significantly impair his quality of life. The chemotherapeutic of choice is 5-fluorouracil (5-FU), alternatively capecitabine (po), optionally in combination with oxaliplatin or irinotecan . Especially in combinations such as FOLFOX (leucovorin, 5-FU, oxaliplatin).

Leucovorin is a biomodulator and is added to increase the effect of 5-FU and reduce toxicity.

### Adjuvant treatment

If it is necessary after surgical treatment, it is time for systemic treatment, the aim of which is to eliminate possible micrometastases, prevent further spread of the disease or possible relapse. We decide to start adjuvant treatment again according to the patient's condition and the characteristics of the tumor. It is generally recommended especially in stage III, where it increases long-term disease-free survival by up to 30%, and in stage II tumors with a high risk of recurrence. Adjuvant chemotherapy improves 5-year survival by 10%.

### Independent oncological treatment

We use palliative independent oncological treatment in patients with inoperable advanced findings, we prolong both the median disease progression and the median survival.

### Targeted treatment

A novelty in the treatment of CR-CA in the last 10 years is the introduction of targeted treatment, sometimes also referred to as biological treatment . When used together with chemotherapy, it increases its effectiveness (increasing the response rate and prolonging the median survival of patients). The principle of targeted treatment is to influence specific signaling pathways necessary for tumor growth. In the Czech Republic, three drugs are now used for targeted treatment: bevacizumab (antibody against vascular endothelial growth factor A - VEGF-A), cetuximab and panitumumab (epidermal growth factor receptor inhibitors - EGFR).

## Summary

General risk factors:

- less than 12 resected lymph nodes;
- low degree of tumor differentiation (grade 3 and 4);
- tumor growth through the entire intestinal wall (T4);
- bowel perforation or obstruction as a primary manifestation of the tumor;
- angioinvasion, lymphangion invasion or perineural invasion;
- unknown resection margins;
- elevated carcinoembryonic antigen (CEA);
- mucinous component of the tumor.

Treatment strategies according to the staging of the disease at the time of diagnosis:

St. AND	surgical treatment
St. II	surgical treatment (in the case of N1 NX followed by chemotherapy)
St. III	surgery and always chemotherapy
St. IV	resection or induction therapy and then resection or palliative treatment

## Prognosis

The five-year survival of individuals with CR-CA varies according to the stage at which the disease is detected.

Stage	Five years of survival
St. 0 and 1	80-90%
St. 2	60-80%
St. 3	50-60%
St. 4	4-10%

In general, individuals who are asymptomatic at the time of diagnosis are much more likely to survive five years (90%) than individuals who have difficulty lasting three (40%) or seven (25%) months at the time of diagnosis. . prevention and screening program is therefore important for this disease.

## Links

## Source

- ws:Kolektální karcinom

## Related articles

- Treatment of liver metastases in colorectal cancer
- Vienna Classification of Gastrointestinal Neoplasias (2002)

## External links

- Kolektální karcinom - článek v časopisu Onkologická péče (<https://www.linkos.cz/files/onkologicka-pece/9/86.pdf>)
- Zdravi.e15 - Terapie kolektálního karcinomu (4/2012) (<https://web.archive.org/web/20160331222721/http://zdravi.e15.cz/clanek/postgradualni-medicina/terapie-kolektalniho-karcinomu-464247>)
- Atlas patologie pro studenty medicíny - tlusté střevo ([https://atlases.muni.cz/atlas/stud/atl\\_cz/main+pgit+colon.html#coloncancer](https://atlases.muni.cz/atlas/stud/atl_cz/main+pgit+colon.html#coloncancer))
- Cancer research UK - Duke`s stages of bowel cancer (<https://www.cancerresearchuk.org/about-cancer/bowel-cancer/stages-grades>)
- Česká společnost HPB chirurgie: Návrh standardu chirurgické léčby kolektálního karcinomu (<http://www.hpb.cz/index.php?pld=05-2-07>)

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