Colorectal cancer/therapy

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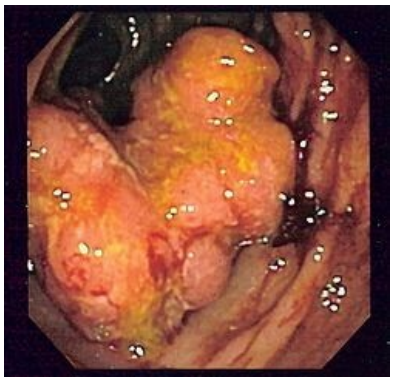
Colorectal cancer

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

Treatment modalities used to treat KR-CA include **endoscopic**', **surgical** and **oncological** methods. As a rule, the tumor mass is removed first, either endoscopically or, more often, surgically, followed by systemic oncological treatment. In the case of extensive tumors, surgery is preceded by neoadjuvant oncological therapy.

Therapy procedures for KR-CA located in the colon and in the rectum differ slightly.

Endoscopic treatment

Its importance is irreplaceable, especially in the *diagnosis* of diseases and the subsequent *dispensary* of patients after treatment. It is mainly used for **curative treatment of precancers**' (adenomas) or **very early stages *of KR-CA (carcinoma in situ, pT1), or for*** *palliative treatment* to open intestinal stenoses caused by a tumor (insertion of a stent).

Curative treatment Depending on the extent of the lesion, we use:

- **polypectomy**' (EPE),
- **endoscopic mucosal resection**' (EMR),
- **endoscopic submucosal dissection** (ESD) - removal of the polyp together with the submucosa.

In patients with a diagnosis of KR-CA pT1, we decide between an endoscopic or surgical solution based on other parameters. Endoscopic treatment is sufficient for benign tumors, however, for so-called high-risk pT1 carcinomas, we proceed with a subsequent surgical solution. High-risk cancer criteria:

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

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

Palliative treatment

The application of a metallic stent is used either for acute intestinal obstructions to **wait out the time *for an operative solution, or for inoperable and generalized carcinomas 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 biological treatment **bevacizumab** have been shown to have a higher risk of perforation. [1]

Surgical treatment

Still the only curative treatment for colorectal cancer is ``oncoradical resection *(with the exception of very early stages that can be resolved endoscopically, see the previous paragraph). It is indicated whenever it is possible to perform a* ***curative radical (R0) resection*****, i.e. to remove the entire tumor mass. Possibly also for palliative reasons, similar to endoscopic treatment, to open the intestinal lumen and thereby prolong and improve the patient's quality of life.**

Resection of the colon

For colon cancer, we use *radical resection* of the affected section of the intestine together with the removal of the hinge (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 limitation of postoperative tumor spread. Radicality is observed even in the earlier stages (T1, T2). If the tumor is unfavorably located in the watershed 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 arterial trunks (high ligature):

- **right hemicolectomy' *- ligature of* a. ileocolic'**, *a. colica dextra* and *ramus dexter arteriae colicae mediae* (tumor of the ascending colon);
- **extended right hemicolectomy** - ligature of *a. ileocolic'**,* **a. colica dextra *and additionally* a. colica media *(for tumors 'flexura coli dextra*);**
- **left hemicolectomy** - ligature of *a. colica sinistra* (descending colon tumor);
- **extended left hemicolectomy** - ligature of *a. colica sinistra* and *a. colica media* (tumor at the *flexura coli sinistra*);
- **sigma resection** - ligatures *a. mesenterica inferior*.[2]

Laparoscopic approach is a used alternative to the classic procedure, especially for left-sided colon tumors. [3]

Resection of the rectum

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

- **Curative powers'** (potentially):

1. standard operation – resection recta (+ mesorecta), can be with sphincter amputation, but also sphincter-preserving (even that is sufficiently oncoradical);
2. extensive surgery – resection of the rectum, mesorectum and abdominopelvic lymph nodes and vessels;
3. ultra-extensive surgery - additionally with resection of the internal iliac vessels.[2]

- **Palliative procedures** consist of:

1. tumor removal - in most cases it is better to remove the tumor, even if curative resection is excluded due to the staging of the disease or the general condition of the patient, every growing tumor threatens the patient with the formation of an ilea, perforation of the intestinal wall, tumor disintegration (necrosis);
2. solving an obstruction in the passage of the intestine (it is a tumor) - with a stoma or bypass;
3. pain treatment.

Resection of liver metastases

The liver is the organ where we most often find KR-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 [4]

- **Colonoscopy with biopsy** - if this is not possible then double-contrast irrigography,
- **sonography of the liver**

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

- **CT of small pelvis**,
- **X-ray lung**

  CT lung – when metastases are found on X-ray
  bronchoscopy – when metastases are suspected, to rule out duplication,

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

🔎 *For more information see The importance of tumor markers in the treatment of cancer.*

Oncology treatment

Almost every patient with KR-CA undergoes oncological treatment in one of its forms - *radiotherapy*, *chemotherapy*, *biological treatment*. According to the treatment sequence, we distinguish between neoadjuvant, adjuvant and separate oncological treatment. Radiotherapy is particularly useful for rectal cancer, as it is highly sensitive to it

and, in addition, has a high susceptibility to locoregional spread (colon cancer is more likely to establish distant metastases), we apply a dose of 30 Gy. [5]

Neoadjuvant treatment

We use neoadjuvant treatment especially for rectal cancer - either radiotherapy alone or in combination with chemotherapy (ie chemoradiotherapy). In the case of extensive tumors (T3–T4, N+), during neoadjuvant (preoperative) treatment there is a '*decrease in the tumor mass (so-called downstaging)*, and thus a better operability of the findings (a higher percentage of sphincter-preserving surgeries), an increase in the percentage of curative resections and a lower incidence of local recurrences. However, the overall longer survival of patients undergoing neoadjuvant therapy was not confirmed. [3] The combination of chemo- and radiotherapy is accompanied by somewhat higher toxicity. In general, we have to consider the indication of neoadjuvant therapy in relation to the patient's condition, so that it does not significantly worsen his quality of life. The chemotherapy of choice is 5-fluorouracil (5-FU), an alternative is capecitabine (po), possibly in combination with oxaliplatin or irinotecan. . [6]Primarily in combinations like **FOLFOX** (leukovorin, 5-FU, oxaliplatin).

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

Adjuvant treatment If it is necessary after surgical treatment, systemic treatment comes next, the aim of which is to remove possible micrometastases, prevent further spread of the disease or possible relapse. The decision to start adjuvant treatment is again based on the patient's condition and tumor characteristics. It is generally recommended especially for stage III, where it increases long-term survival without signs of disease by up to 30%, and for stage II tumors with a high risk of recurrence. [3] Adjuvant chemotherapy improves 5-year survival by 10%. [4]

Separate oncological treatment

We use palliative stand-alone oncological treatment in patients with inoperable advanced findings, extending both the median of disease progression and also the median survival. [3]

Targeted treatment

A novelty in the treatment of KR-CA in the last 10 years is the introduction of targeted therapy, sometimes also referred to as biological therapy. When applied together with chemotherapy, it increases its effectiveness (increasing treatment response and prolonging the median survival of patients). The principle of targeted treatment is influencing specific signaling pathways necessary for tumor growth. In the Czech Republic, three drugs are now used for targeted treatment: "bevacizumab" (an antibody against vascular endothelial growth factor A - VEGF-A), "cetuximab" and "panitumumab" (receptor inhibitors for epidermal growth factor – EGFR). [7]

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);
- intestinal perforation or obstruction as the primary manifestation of the tumor;
- angioinvasion, lymphangioinvasion or perineural invasion;
- unknown resection margins;
- increased level of carcinoembryonic antigen (CEA);
- mucinous component of the tumor.

Treatment strategy according to disease staging at the time of diagnosis: [8]

St. I	surgical treatment
St. II	surgical treatment (in 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

Links

Related Articles

- Colorectal cancer
- Treatment of liver metastases in colorectal cancer

External links

- Česká společnost HPB chirurgie: Draft standard for surgical treatment of colorectal cancer (http://www.hpb.cz/index.php?pId=05-2-07)

References

1. ZAVORAL, Miroslav, et al. *Colorectal Cancer Therapy* [online]. Zdraví E15, ©2012. The last revision 4/6/2012, [cit. 2015-12-02]. <https://web.archive.org/web/20160331222721/http://zdravi.e15.cz/clanek/postgradualni-medicina/terapie-kolorektalniho-karcinomu-464247>.
2. ŠIMŠA, Jaromir. *Oncosurgery* [lecture for subject Surgery-pre-national internship, specialization Surgery, 1. LF UK Charles University in Prague]. Prague. 2011-10-08.
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5. LIPSKÁ, Ludmila and Vladimír VISOKAI. *Recurrence of colorectal cancer: a comprehensive approach from the surgeon's perspective*. 1st ed. Prague: Grada, 2009, 431 p.
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Recommended reading

- ČEŠKA, Richard – ŠTULC, Tomáš, et al. *Intern.* 2. edition. TRITON, 2022. 870 pp. ISBN 978-80-7387-885-6.
- KRŠKA, Zdeněk – HOSKOVEC, David, et al. *Surgical Oncology.* 1. edition. Prague : Grada, 2014. 904 pp. ISBN 978-80-247-4284-7.