

REVIEW PAPERS

COLORECTAL CANCER IN THE ELDERLY PATIENT

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It is extremely difficult to determine the limit at which the elderly age starts. According to the commonly accepted WHO definition, persons aged over 65 years are considered elderly. However, this is a very rough definition which does not take the social and economical diversity of a society into account. In addition, it seems important to consider the clinical status of a patient, namely a widely understood biological age as it determines the course of a disease and its treatment. Therefore the therapy of elderly people requires a thorough analysis and a special, interdisciplinary approach due to the concurrent or additional medical problems.

Epidemiology

The colorectal cancer morbidity increases with age peaking in the seventh decade of human life. The average age of the affected persons is 72 years at the diagnosis of colonic cancer and 70 years when the diagnosis of rectal cancer is made. Colorectal cancer is the most common malignant tumor in humans over 75 years of age (1, 2). In Europe, approximately 137,000 case of colorectal cancer are diagnosed annually. This the death cause in 85,000 of the diseased persons with over a half of them being older than 70 years of age (3). In 2007, 14,244 persons were affected with

this neoplasm in Poland and 9,372 died of this cause (4). Obviously, the number of surgical interventions undertaken in the persons over 70 years of age is increasing. In the 1940s, the disease was treated surgically in 15% of the cases, in the 1970s – in over 40% of the affected persons while in the mid-1980s this number rose to roughly 50%. In 1997, 60% of the cases were treated surgically (5, 6). In recent years, the percentage of patients who receive surgical treatment due to colorectal cancer ranges from 57 to 91% (7, 8). The colorectal cancer morbidity is still rising with an upward tendency at approximately 3.5% annually among men and 2.5% among women. Based on the recent data it is assumed that this cancer constitutes 12.4% of malignant tumors in men and 10.1% in women (4). The risk of colorectal cancer is similar in both genders and stands at approximately 4%. However, the mortality in men ranges between 5.1 and 5.5% whilst in women – from 2.2 to 2.7% (9).

Pathogenesis and clinical symptoms

The etiopathogenesis of colorectal cancer is complex. It seems that environmental factors and a genetic predisposition play the major role. The first ones include excessive amounts of fats, protein, nitrosamines, low-fiber foods

and alcohol. Vitamin A, C and D deficiencies and insufficient amounts of fiber favor the development of this neoplasm. This is of special importance in the elderly due to the prolonged exposure lasting many years as well as impaired intestinal transit and proneness to constipation. This is also associated with an increased mutation rate of the intestinal epithelial cells and a reduced activity of the immune system (4, 10, 11). The genetic predispositions include: transfer of the familial adenomatous polyposis gene, occurrence of hereditary non-polyposis colorectal cancer (HNPCC), the Lynch I and Lynch II syndromes, and higher morbidity in persons related to the patients affected with colorectal neoplasms.

The symptoms of colorectal cancer depend on a number of basic factors, namely: location, growth and size of a tumor as well as its dignity and possible metastases.

The neoplasms located in the right half of the colon (app. 15-20%) are associated with anemia, melena, and often unspecific abdominal pain. The tumor palpable through the abdominal wall is found in approximately 50% of the affected persons. If the cancer is located on the left side of the colon (app. 70-80%), the predominant symptoms are a changed nature of stools, rectal bleeding and increased intestinal spasticity associated with progressive obstruction. In addition, less specific symptoms are observed such as weight loss, weakness, flatulence or inappetence (4, 10).

Colorectal cancers metastases via lymphatic and blood vessels and by infiltrating the adjacent tissues and anchoring to the peritoneum. Rectal cancer spreads along the superior rectal veins to the liver and laterally via middle veins to the lungs. Colonic cancer metastases mainly to the liver whereas the metastatic lesions in the lungs occur later. The metastases to the liver in the elderly patients are reported in about 11% of patients and distant metastases – in approximately 36% (12, 13, 14). The clinical symptoms are sometimes associated with metastases with a clinically silent primary tumor.

The hallmark of colorectal cancer in an elderly patient is its more frequent location in the right half of the colon as compared to younger persons. In recent papers it has been shown that the tumor occurs in this location in about 19-55% of the patients, i.e. in 42.7%

of the diseased individuals on average. A lower susceptibility of the right colon to carcinogenic substances may play a role and thus the cancer may locate at this site at later age (1, 6, 7, 8, 15). It is also believed that this neoplasm at elderly age develops much slower and the disease may have a poorly symptomatic or asymptomatic course for a long time. In the history, the duration of symptoms is usually longer than in younger patients. Colorectal cancer in the elderly demonstrates higher local aggressiveness and more frequent occurrence of primary tumors that cause obstruction, perforation or infiltration of the adjacent organs. Seemingly, it also has a lower distant metastatic potential as compared to younger individuals (16, 17, 18).

Concurrent diseases that are reported in 52-85% of the cases in the discussed patient group are an additional aggravating factor. Over a half of the diseased individuals who are over 70 years of age suffers from at least one systemic illness. Chronic obstructive pulmonary disease (COPD) affects approximately 3-26% of the elderly diseased individuals, ischemic heart disease (IHD) – about 34-72%, hypertension is reported in 20-35%, diabetes in app. 7-28%, and renal insufficiency – in 6-9% (1). According to other studies, the most common concurrent diseases from which the patients who underwent a scheduled surgical procedure for a malignant colorectal cancer suffered were: ischemic heart disease in 47%, hypertension in 42% and diabetes in 21% of the patients (19).

Diagnosics

Early diagnostic intervention and a diagnosis of a colorectal neoplasm significantly impact the good outcome of a treatment. Screening tests allow identifying persons potentially with colorectal cancer even in an asymptomatic stage of the disease. According to Dodd, screening tests reduce the mortality by approximately 30-60%, particularly in the group of patients over 65 years of age (20).

Today, two screening methods are used. The first one involves colonoscopy performed once every 10 years and the second method, a two-step procedure, involves performing a fecal occult blood test (FOBT) in feces once a year and if the result is positive, further colonos-

copy is done (4). These tests are especially important at elderly age as the morbidity of colorectal cancer is increased in this life period (10). Ongoing studies have already suggested that via early detection of a neoplasm they may improve the treatment outcomes in the elderly diseased individuals (8, 21, 22).

Unfortunately, a simple and cheap fecal occult blood test is not than widespread in the society. Its non-invasiveness, relatively low cost and wide availability may have a special importance in positive elderly people, with difficulties in independent mobility and treated in small health centers with a limited access to endoscopic procedures. However, it shall be considered that this test has a limited value due to difficulties in interpretation and, in the case of stool guaiac test, the need for a special preparation of a patient: a three-day non-meat and non-chlorophyll diet and exclusion of peroxidase-containing products and drugs, which most patients of this age take, before the test. With newer immunohistochemical methods, these limitations are not that rigid yet one should be sure as to which method is used by a given laboratory. Importantly, false positive results occur in the course of diverticular disease or with hemorrhoids (23, 24) and it should be considered that not all neoplasms induce bleeding. Therefore much hope is put on a novel screening method that involves detecting a M2-PK marker in feces. This is a sensitive and specific method that does not require any preparation of a patient such as a diet. It involves the detection of a pyruvate kinase isoenzyme type M2, typical of neoplasms (25, 26, 27). This method is not, however, widely available.

Today, endoscopic examination of the lower segment of the gastrointestinal tract is the basic diagnostic procedure. In experienced centers, it is possible to perform the endoscopic diagnostics of the caecum in 80% of patients, the right colonic flexure in 85%, and the left colonic flexure – in 90% of the examined individuals. Rectosigmoidoendoscopy allows diagnosing 50-70% of neoplasms situated in the terminal segment of the colon (24, 28).

In 1995-2002, Kirchgatterer et al. performed 1,175 colonoscopies and 213 sigmoidoscopies in the patients aged over 80 years. Colorectal cancer was diagnosed in 6% of the patients. The indications were: anemia and bleeding in half of the examined persons and

suspicion of a tumor in the abdominal USG imaging in 10% of the individuals (7).

This diagnostic procedure, as the only one, allows taking a biopsy of potential tumors in order to perform a histopathology examination and receive an essential confirmation of a neoplastic disease. In the days of modern diagnostics, we shall not forget the effective and simple rectal examination that may detect up to 30% of colorectal neoplasms. The majority of rectal cancers develops within the range accessible with a finger. Overlooking this examination is in fact a medical error (24).

Computed tomography imaging in a protocol of virtual colonography (otherwise known as virtual colonoscopy) is a less invasive procedure than standard colonoscopy and takes less time to perform. The disadvantage is the exposure of a patient to a high dose of radiation and a relatively low sensitivity in the diagnostics of lesions smaller than 5 mm. High-resolution magnetic resonance imaging, which allows a detail assessment of the mesorectum tissues, is one of the imaging techniques used for pre-operative evaluation of the dignity of rectal cancer (29). In addition, X-ray or CT of the thorax should be taken to exclude distant metastases.

Ultrasonography plays an important role in the diagnostics of colorectal cancers as it is low-invasive and cost-efficient. This involves in particular intrarectal endosonography mainly applied to assess local dignity of a tumor and post-surgical monitoring. The sensitivity of this examination is even 97% (4, 30). A double-contrast enema into the large bowel is also an accurate, cost-efficient and safe procedure with sensitivity in detecting adenomas and cancers with the diameter of over 1cm exceeds 90% (31).

Methods involving detection of neoplastic markers have been known for years. In colonic and rectal neoplasms, carcinoembryonic antigen (CEA) is most commonly tested as there it shows the highest diagnostic values yet its increased level is also reported in breast cancer or lung cancer. Its increasing level in the serum associated with the development of a neoplastic process or is the first signal of a recurrence in 50% of the patients who underwent surgical resection (32).

Thanks to their high sensitivity of 89% and specificity of app. 83%, relatively novel proteomic and genomic tests based on the assess-

ment of a protein profile may – as screening procedures – restrict the indications for endoscopic examinations only to a separated risk group. These examinations are low-invasive and highly efficient, which is especially important for the elderly patients. The sensitivity of these methods in identifying the dignity of colorectal cancer was approximately 90% in comparison with 25% that were characteristic for carcinoembryonic antigen (4, 33).

Treatment

Surgical treatment for this neoplasm is a therapy of choice. It is used to perform a definitive procedure or as a palliative treatment. The resection rate of colorectal cancer in the elderly patients is high and reaches 82.9-97%, depending on a medical center (6, 8, 12, 34). In older papers, the reported resection rate is usually lower or much lower in the elderly individuals. According to Braun, it was 69-94% and in people over 80 years of age – only 75% (35). Other authors reported the resection rate for the diseased persons older than 65 years ranging from 43% to 74% (36). In more recent studies carried out in 2000-2001, Marusch et al. found an over 90% resection rate for colorectal cancer in people older than 80 years. However it should be emphasized that it was still significantly lower than in younger affected individuals (96.8% vs. 92,7%) (37).

The way of treatment depends of a location and dignity of the tumor. It thus seems necessary to perform abdominal imaging (ideally CT) to assess the dignity of the tumor and presence of distant metastases. With cecal and ascending colon tumors, right-side hemicolectomy shall be performed. Transverse colon neoplasms are treated surgically by a partial resection of the transverse colon or an extended right-side hemicolectomy. In case of malignant tumor located in the splenic colonic flexure, descending colon and sigmoid colon, it is necessary to perform left-side hemicolectomy, Hartman's procedure or resection of the sigmoid colon. Subtotal colectomy is undertaken in synchronic tumor or, for instance, in the case of obstruction with a proximal perforation. Rectal tumors are treated surgically by an anterior resection of the rectum with the sphincters saved or with

abdominal-perineal resection of the rectum (APR) (4). In selected cases it is also possible to locally resect a rectal cancer. The procedures according to Park's, Kraske's, York-Mason's techniques or with TEM method generate comparable results for long-term survival and local recurrence and the ones with abdominal-perineal resection of the rectum (38).

Opinions on the scope of surgical treatment in geriatric patients are divided. Some authors claim that a segmental resection is associated with a lower rate of complications and lower mortality whilst a higher survival rate has not been as yet demonstrated with a more definite and extensive procedure such as complete hemicolectomy with lymphadectomy (23). Smith et al. report that despite higher mortality and number of complications in the elderly patients, one shall attempt at definitive procedures as their long-term outcomes are satisfactory (39). The others, however, point out that the age is not a significant risk factor for the patients surgically treated for colorectal cancer and does not influence a decision on the extent of a procedure (34). To the contrary, another study indicates that the age does play a role for perioperative mortality yet not in the five-year survival rate (40). It seems that this problem warrants further analysis.

If, due to the dignity and distant metastases, a therapeutic resection is not feasible and there are technical possibilities, a palliative resection should be attempted. It improves the quality of life of a patient, prolongs the average survival time as well as eliminates preoperative clinical symptoms. It is particularly evident for tumors that are located low in the pelvis, inflicting significant pain and presenting a potential for further complications. Palliative resection is associated with a lower number of complications and lower mortality in comparison with the decompressing colostomy. It is attempted in 19-28% of the elderly diseased individuals treated surgically for a colorectal tumor (6, 12, 34). Colostomy causes significant difficulties in the everyday life of elderly people and often remains the last resort of a surgical treatment. Together with bypasses, it is performed in app. 7-17% of the patients in total. They carry a high mortality risk reaching even 45% (6, 40, 41).

While scheduling a surgical treatment for colorectal cancer in the elderly patient, a lap-

aroscopic technique should be considered. Conducted studies have demonstrated a comparable efficacy of this method as compared to a classical procedure whilst an intraoperative blood loss is smaller, the patient is earlier mobilized, and an oral diet is earlier implemented, which translates into a lower number of post-surgical complications and shorter hospitalization (42). The laparoscopic procedure carries a lower risk of death in the postoperative period and a lower number of cardiovascular and respiratory complications (43) and as such it should be treated as a method of choice in geriatric patients.

Complications of colorectal cancer in the patients over 70 years of age are reported twice as often as in younger affected individuals (19, 39). For instance, in the studies by Marusch et al. the complications in a group of patients over 80 years of age occurred in 43% of the cases whereas in a group of younger persons – only in about 34% (37%). Similar numbers have been reported in other studies: 46.4% for the group of 80 year-olds or older and 22.6% for younger people (39).

According to Wise et al., the most common complications included urinary tract infections in about 16%, pneumonia in app. 6%, and myocardial infarction and cerebral infarction making a total of 6% (41). Polish studies carried out in 1990-1994 and 2001-2002 report the most common complications of scheduled surgical procedures for colorectal cancer: abscessation of a wound in 30% of cases, evisceration in 21%, pulmonary complications in 10%, and cardiac complications in about 5% (16). It should be bear in mind that in geriatric patients the complications often affect the respiratory tract, cardiovascular system and also depend on concurrent diseases. Leakiness of the anastomosis, a specific complication of resection procedures, does not occur more often in the elderly than in younger patients.

However, internal complications carry a high risk. They significantly increase mortality that differs much depending on a medical center (37, 39). Postoperative mortality is presented in the table.

The elderly patients qualified for a scheduled surgery are often placed in a higher ASA group (American Society of Anesthesiologists) that assesses the risk of serious complications or death. It should be considered that over

75% of the patients aged 75-84 years suffers from more than one internal disease. The more concurrent diseases, the higher the mortality, disability risk and risk of postoperative complications. It is thus essential to provide an appropriate therapy for concurrent diseases in order to optimally prepare a patient for a surgery (44). Diabetes presents a special risk factor as currently we are witnessing the epidemics of this disease. The prevalence of diabetes in the population of over 65-year-olds reaches 40% (45). Insufficiently controlled glycaemia in the perioperative period may result in life-threatening complications, such as electrolyte disturbances, dehydration or finally impaired healing of a surgical wound or its infection. The elderly age creates specific conditions impacting a further outcome of treatment. In addition to the primary disease and concurrent medical problems, the whole of a treatment is significantly impacted by such factors as immobilization time, decreased intake of fluids and food (common among elderly people), and reduced sensation of stimuli (46, 47). In the preoperative period, nutrition status in particular shall be considered. Geriatric patients show a tendency towards both quantitative and qualitative malnutrition, especially in terms of proteins. The nutritional status of a given patient should be thoroughly analyzed, body mass changes should be assessed in a period preceding hospitalization, and protein deficiencies should be corrected. Malnutrition or poor nutrition is a straightforward way to such complications as anastomosis dehiscence, pneumonia, a need for prolonged mechanical ventilation, longer wound healing, and a higher infection and death risk (48).

Table. Post-surgical mortality in the patients over 80 years of age treated for colorectal cancer (7, 8, 15, 19, 37, 40, 41)

Author	Number of patients	Post-surgical mortality (%)
<i>Agarwal</i> (1990)	64	25
<i>Spivak</i> (1996)	103	8,7
<i>Krasnodębski</i> (2000)	108	18,5
<i>Markert</i> (2006)	36	39
<i>Marusch</i> (2005)	2932	8
<i>Kirchgatterer</i> (2005)	54	2
<i>Ong</i> (2008)	90	1,1

Proper dietary supplementation in the postoperative period is also crucial; enteral nutrition should be introduced as soon as possible or, in case of contraindication or poor nutrition status in the preoperative period, perioperative parenteral nutrition shall be implemented (49). The optimization of body homeostasis in a diseased individual prepared for a surgical procedure is critical for its success.

Systemic treatment

Surgical resection is the basic treatment option in colorectal cancer. However, this is not the only one method. Systemic treatment with radiotherapy and chemotherapy should not be overlooked as they are aimed at improving the outcome. The preoperative neoadjuvant therapy shall initiate an early destruction of micrometastases, reduce the size of a tumor and infiltration zone. Postoperative chemotherapy (adjuvant) carries a chance to reduce the number of recurrences and deaths by 20% and to increase the survival rate by 10%. Cytotoxic drugs such as 5-fluorouracil with folic acid, capecitabine, irinotecan and oxaliplatin or a targeted therapy aimed at inhibiting the molecular pathways are used. It involves the monoclonal antibodies such as bevacizumab and cetuximab. The beneficial effect of nonadjuvant radiotherapy in colorectal cancer involves tumor regression, which increases the chances to resect the whole rectum saving the sphincters.

The decision on the most beneficial therapeutic option and specifying the indications for possible radiotherapy or preoperative chemotherapy are very important for the whole treatment process and prognosis as to the complete

remission. It should be taken by a multidisciplinary senior staff case meeting consisting of surgeons, radiologists, clinical oncologists, radiotherapists and, if needed, specialists in cardiology, critical care or other disciplines, depending on the severity of concurrent diseases. Unfortunately, due to the coexistence of numerous diseases, in particular cardiovascular problems, and multiorgan failure, the indications for chemotherapy are often limited in geriatric patients (4). Any unambiguous evidence supporting the elimination of chemotherapy is missing. It seems feasible to implement a targeted and customized treatment of a given patient depending on the nature of a disease, physiological status and patient's preferences (50). Therefore the elderly patients require special care and informed therapeutic decisions.

Summary

Colorectal neoplasms present a serious diagnostic and therapeutic problem. Continuously increasing morbidity affects the elderly people in particular and considering the aging of the society and enhanced impact of the factors with a proved role in carcinogenesis, this tendency is predicted to remain unchanged in the near future. Therefore, it seems justified to thoroughly analyze the specificity of this patient group accordingly adjust the diagnostic and therapeutic procedures. The elderly patients require an interdisciplinary care both in the preparation and postoperative period. A multispecialty senior staff case meeting seems thus essential to determine the most beneficial treatment approach. Development of additional algorithms for the elderly patient with colorectal cancer is warranted.

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