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Primary colon cancer: ESMO Clinical Recommendations for diagnosis, adjuvant treatment and follow-up

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incidence

In 2006 there were 412 900 new cases of colorectal cancer in Europe. This is 12.9% of all cancer cases. Colorectal cancer was responsible for 217 400 deaths in Europe in 2006. This represents 12.2% of all cancer deaths.

diagnosis

The diagnosis of a colonic adenocarcinoma requires a histopathologic confirmation taken via colonoscopy/sigmoidoscopy. Risk factors including familial and/or hereditary predisposition, location, and histological evaluation of colonic tumors should be documented.

staging and risk assessment

Staging provides essential prognostic information relevant for choosing adequate therapy and should also identify patients with resectable distant metastases.

Preoperative staging consists of clinical examination, blood counts, liver and renal function tests, carcino-embryonic antigen (CEA), chest X-ray or preferably chest CT-scan, CT scan of the abdomen including the pelvis and a colonoscopy of the entire large bowel, i.e. with postoperative repeat colonoscopy if proximal parts of the colon were not accessible preoperatively.

Pathologic staging should be done according to the 2002-TNM system with optional listing of the modified Dukes stage, as described in Table 1.

Risk factors for colorectal cancer are: family history, familial adenomatous polyposis (FAP) and attenuated FAP (AFAP) syndromes, hereditary non-polyposis colorectal cancer (HNPCC) syndrome, past history of colorectal cancer or adenoma, chronic ulcerative colitis and Crohn's disease.

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prognosis

Survival rates have been published from the SEER US national cancer registry from January 1, 1991 through December 31, 2000 based on data from 199 363 patients according to the new AJCC sixth edition staging. Overall 5-year colon cancer-specific survival for this entire cohort was 65.2 %. Five-year colon cancer-specific survival by stage was 93.2% for stage I, 84.7% for stage IIa, 72.2% for stage IIb, 83.4% for stage IIIa, 64.1% for stage IIIb, 44.3% for stage IIIc and 8.1% for stage IV cancer. Another large analysis based on the US National Cancer database showed in 50 042 patients from 1987 till 1993 a 5-year survival rate of 59.8% for stage IIIa, 42.0% for stage IIIb and 27.3% for stage IIIc colon cancer.

treatment

Surgery is the mainstay in the management of patients with colon cancer. The primary goal is a wide resection of the primary tumor with all locoregional lymph nodes. Optimal surgery by experienced colorectal surgeons should be performed. An adequate number of lymph nodes should be recovered (at least 12) and resection margins have to be free. Laparoscopic resection gives similar oncologic outcome compared to laparotomy and has less postoperative morbidity in experienced surgical hands.

Adjuvant chemotherapy is recommended for stages T1-4, N1-2, M0 (i.e. stage III, modified Dukes C1-3). In stage III colon cancer adjuvant chemotherapy significantly improves the disease-free survival (DFS) and overall survival [I, A]; the absolute survival benefit is approximately 15%. Adjuvant chemotherapy can be considered in selected node-negative patients, especially if high risk factors for recurrence are found. The UK Quasar study that randomized patients postoperatively between no treatment and adjuvant 5-fluorouracil (5-FU) based therapy (mainly with leucovorin) has shown a small but statistically significant improvement in 5-year survival in unselected patients (mainly stage II).

Subgroup analyses of the stage II patients in the randomized studies comparing 5-FU/LV and 5-FU/LV/oxaliplatin (FOLFOX) suggests also an improved DFS in patients with high risk stage II colon cancer. Amongst the known high risk factors in stage II colon cancer are: T4, poorly differentiated adenocarcinoma/undifferentiated

Table 1. 2002-TNM system

TNM	Stage	Extension to	5-year overall survival
Tis No Mo	0	Carcinoma *in situ*	most likely normal
T1 No Mo	I	Mucosa or submucosa	>90%
T2 No Mo	I	Muscularis propria	>85%
T3 No Mo	IIa	Subserosa/pericolic tissue	>80%
T4 No Mo	IIb	Perforation into visceral peritoneum or invasion of other organs	72%
T1-2 N1 Mo	IIIa	< = 3 LN	60 – 83%
T3-4 N1 Mo	IIIb	< = 3 LN	42 – 64%
T1-4 N2 Mo	IIIc	> = 4 LN	27 – 44%
Any T any N M1	IV	Distant metastases	<10%

carcinoma, vascular invasion, lymphatic vessel invasion, perineural invasion, obstruction or tumour perforation at initial presentation, ≤12 regional lymph nodes examined and high CEA level [II, B].

Recent evidence also showed the possible deleterious effect of 5-FU based chemotherapy in stage II tumours with microsatellite instability (MSI). It is therefore important to determine the MSI status in stage II colon cancer. Patients with low risk stage II colon cancer should not be offered adjuvant chemotherapy.

Standard adjuvant treatment consists of fluoropyrimidine-based chemotherapy which has shown a statistically significant survival benefit [I, A].

Options for adjuvant treatment include infusional 5-fluorouracil (5-FU)/LV-regimens without or with oxaliplatin and capecitabine with and without oxaliplatin. Capecitabine has been shown to be at least as effective and less toxic as bolus 5-FU/LV [I, A].

The combination of 5-FU/LV plus oxaliplatin significantly improves the DFS in high risk stage II and III colon cancer and improves also the overall survival in stage III colon cancer compared to 5-FU/LV [I].

The combination of a fluoropyrimidine plus oxaliplatin has therefore become the standard adjuvant treatment for stage III colon cancer in patients fit for combination chemotherapy [A]. The recommended duration of adjuvant chemotherapy is 6 months, starting as soon as the patent is recovered from the surgery and optimally within 6 weeks after the surgical intervention.

The adjuvant treatment after complete resection of metastatic disease is a specific situation addressed in ESMO clinical recommendations on advanced colorectal cancer.

A good correlation has been shown between the 3-year DFS and 5-year survival in the adjuvant treatment of colon cancer. Three-year DFS is therefore now considered as an appropriate endpoint in the adjuvant treatment of colon cancer [III].

follow-up

There is no strong proof that regular follow-up after successful treatment improves the outcome of patients with colorectal cancer.

However, it may be clinically beneficial to identify recurrence of colon cancer in a stage at which its diagnosis will have therapeutic implications (i.e. surgery for metastatic disease or for local recurrence).

In the absence of an evidence-based standard, a provisional recommendation to identify patients in need of salvage surgery and to prevent second colorectal cancers is the following:

- History and physical examination and CEA determination (if initially elevated) every 3–6 months for 3 years and every 6–12 months year 4 and 5 after surgery. Colonoscopy at year 1 and thereafter every 3 years to look for metachronous adenomas and cancers.
- CT scan of the chest and abdomen every 6 months for 3 years can be considered in patients who are higher risk for recurrence.
- Other laboratory and radiological examinations are of unproven benefit and shall be restricted to patients with suspicious symptoms.

note

Levels of evidence [I–V] and grades of recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the experts and the ESMO faculty.

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1 Annals of Oncology 24 (Supplement 6): vi7 vi23, 2013 doi: /annonc/mdt284 Published online 22 August 2013 Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up E. Senkus 1, S. Kyriakides 2, F. Penault-Llorca 3,4, P. Poortmans 5, A. Thompson 6, S. Zackrisson 7 & F. Cardoso 8,9, on behalf of.Â After neoadjuvant systemic treatment, the response to treatment and amount of residual disease are important prognostic factors but need as much standardisation as any of the other biological markers, and no uniform guidelines exist for the evaluation of response to neoadjuvant treatment, although some guidance is provided by the FDA recommendation for accelerated drug Adenocarcinoma; Antineoplastic Combined Chemotherapy Protocols; Carcinoma, Squamous Cell; Combined Modality Therapy; Female; Humans; Neoplasm Staging; Treatment Outcome; Uterine Cervical Neoplasms. More. External sources.Â Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology , 23(suppl_7), vii27-vii32 - October 2012. https://doi.org/10.1093/annonc/mds268.

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@article{Labianca2010PrimaryCC, title={Primary colon cancer: ESMO Clinical Practice Guidelines for diagnosis, adjuvant treatment and follow-up.}, author={Roberto Labianca and Bernard Nordlinger and Giordano Beretta and Antoine Brouquet and Anthony Cervantes}, journal={Annals of oncology : official journal of the European Society for Medical Oncology}, year={2010}, volume={21 Suppl 5}Â Primary colon cancer: ESMO Clinical Practice Guidelines for diagnosis, adjuvant treatment and follow-up R. Labianca, B. Nordlinger, G. D. Beretta, A. Brouquet & A. Cervantes On behalf of the ESMO Guidelines Working Group Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. â€ N. Colombo. 1.Â The optimal adjuvant treatment (Table 4) of intermediate risk endometrial cancer is still to be dened. External beam radiation has been shown to reduce the rate of locoregional recurrence in intermediate risk endometrial cancer.Â follow-up and long-term implications. Most recurrences will occur within the rst 3 years after treatment. The suggested frequency of follow-up is every 3â€“4 months with physical and gynaecological examination for the rst 2 years, and then with a 6 month interval until 5 years. Further investigations can be carried out if clinically indicated. Early colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. â€ R. Labianca. 1.Â Despite optimal primary treatment, with adequate surgery with or without adjuvant chemotherapy, 30%â€“50% of patients with colon cancer will relapse, and most of those patients will die from their disease. Detecting relapse in advance is the main goal of surveillance after primary treatment, but this is clinically meaningful only if it improves survival. Furthermore, follow-up can be expensive and resource-consuming in terms of both money and procedures for a national health system, so intensive surveillance needs to be justied with a good level of evidence.