Guidelines

Update in version 2021 of CSCO guidelines for colorectal cancer from version 2020

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Colorectal cancer (CRC) is one of the major cancers threatening life and health of Chinese residents. According to the latest data released by the National Cancer Center in 2015 (1), there were 387,000 new cases and 187,100 deaths of CRC in China, accounting for 9.87% and 8.01% of all malignancies. The first version of the Chinese Society of Clinical Oncology (CSCO) guidelines was released in April 2017, and has been updated annually based on the latest clinical research data and the availability of new drugs (2-4). Here, we present the main updates of the 2021 version compared to 2020 version.

Updates related to CRC screening

In this part, there are four points updated based on the new evidence and expert opinions (1). The terms "general population" and "high-risk group" for CRC screening were modified to "general-risk population" and "high-risk population", respectively (2). In recent years, a number of domestic guidelines for early diagnosis and screening of CRC have taken colonoscopy as the main screening method. Chinese guideline for the screening, early detection and early treatment of CRC (2020 version) formulated by National Cancer Center has carried out systematic review and systematic evaluation to evaluate the effect of colonoscopy screening in reducing the incidence and mortality of CRC (5). The analysis results showed that colonoscopy screening was associated with 56% of lower risk of disease and 57% of lower risk of death compared with no screening. Therefore, the recommendation of "direct colonoscopy for individuals aged 50–74 years" in general-risk population screening was modified from class II recommendation to class I recommendation, and the restriction of "in eligible areas" was added (3). Fecal immunochemical test (FIT)-DNA is used to detect DNA mutations in fecal cells and combined with FIT to form an individual comprehensive risk score. For subjects whose comprehensive score exceeds the preset threshold, they are defined as high-risk population and colonoscopy is required. A prospective validation study of 9,989 participants in the United States and Canada reported a diagnostic sensitivity of 92.3% and 42.4% for CRC and advanced adenoma, respectively, via this multi-target fecal FIT-DNA test (6). Due to the high price of FIT-DNA testing, the 2021 version of the guidelines recommends that it could be considered when medical resources are sufficient. For individuals with positive fecal occult blood, adding fecal DNA test before colonoscopy can improve the detection rate. This year, for the first time, the Fit-DNA test was added as class III recommendation for screening of

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general-risk population (4). Computed tomography (CT) colon imaging technology refers to that the client expands clean colon with gas after intestinal preparation, and performs thin-slice CT scan of the whole colon in the supine and prone position, and carries out three-dimensional reconstruction on the obtained two-dimensional images to observe the situation of the whole colon. The 2020 version of the Chinese guideline for the screening, early detection and early treatment of CRC systematically evaluated the diagnostic accuracy of CT colon imaging for CRC and precancerous lesions. Based on meta-analysis, the sensitivity and specificity of CT colon imaging for CRC were 0.95 and 0.98, respectively. The sensitivity and specificity of CT colon imaging for precancerous lesions was 0.88 and 0.95, respectively (5). Therefore, the 2021 version of the guideline recommends CT colon imaging for individuals with contraindicated colonoscopy. This year, also for the first time, CT colon imaging was added as class III recommendation for screening of general-risk population.

Updates related to treatment of non-metastatic unresectable colon cancer

The Keynote 177 study compared the clinical efficacy and safety of pembrolizumab and standard two-drug chemotherapy with or without targeted therapy as first-line therapy for microsatellite-instability-high (MSI-H) or mismatch-repair-deficient (dMMR) metastatic CRC (mCRC) patients. A total of 307 patients with MSI-H/dMMR mCRC who had not previously received treatment were randomly assigned, in a 1:1 ratio, to receive pembrolizumab at a dose of 200 mg every 3 weeks or chemotherapy (mFOLFOX6 or FOLFIRI with or without bevacizumab or cetuximab). Pembrolizumab was superior to chemotherapy with respect to progression-free survival (PFS) (16.5 *vs.* 8.2 months; P=0.0002). Based on response evaluation criteria in solid tumors (RECIST) 1.1 criteria, the objective response rate (ORR) was 43.8% in the pembrolizumab group and 33.1% in the chemotherapy group (7). Pembrolizumab led to significantly longer PFS than chemotherapy when received as first-line therapy for MSI-H/dMMR mCRC patients. Therefore, for T4bM0 patients with potentially resectable or unresectable locally advanced colon cancer, a new note was added: "Based on the results of Keynote 177 study, if the patients are MSI-H/dMMR, immunotherapy of PD-1 inhibitor can be considered in conversion therapy or palliative treatment".

Updates related to treatment of metastatic colon cancer

In this part, there are eight points updated based on data of clinical studies and expert opinions.

1) Treatment for patients with potentially resectable metastases: FOCULM study was a phase II clinical trial comparing the no evidence of disease (NED) rate of three-drug chemotherapy with or without cetuximab, which enrolled 101 patients with initially technically unresectable colorectal liver-limited metastases (CLM) and *BRAF*/*RAS* wild-type. The results showed that the NED rates of cetuximab plus mFOLFOXIRI group and mFOLFOXIRI group were 70.1% and 41.2% (P=0.005), respectively. The median overall survival (OS) of cetuximab plus mFOLFOXIRI group was significantly longer than that of the three-drug chemotherapy group, and the ORR was also obviously increased (95.5% and 76.5%, P=0.010) (8). Macbeth study, another phase II randomized controlled study, also showed that cetuximab plus mFOLFOXIRI regimen performed a R0 resection rate of 28.4% for patients with unresectable, previously untreated *RAS*/*BRAF* wild-type mCRC, and for the patients with liver-only metastases, the R0 resection rate was 51.9% (9). Therefore, because of the high ORR, R0 resection rate or NED rate, for *RAS*/*BRAF* wild-type mCRC patients with potentially resectable metastases, FOLFOXIRI plus cetuximab was added as class III recommendation (Level 2B evidence).

2) Palliative treatment for MSI-H/dMMR patients: Keynote 177 study showed that the efficacy of mCRC patients with MSI-H/dMMR receiving traditional chemotherapy plus targeted therapy as first-line treatment was not satisfying. Pembrolizumab was superior to chemotherapy with respect to mPFS (16.5 months *vs.* 8.2 months), PFS (NR *vs.* 23.5 months) and ORR (43.8% *vs.* 33.1%) (7). In addition, data from two phase II trials (CheckMate-142 study cohort 1 and Keynote 164 study) showed that the ORR of PD-1 inhibitors was 31%–33% for treatment-refractory MSI-H/dMMR mCRC patients (10,11). Therefore, for MSI-H/dMMR CRC patients with initial unresectable metastases, pembrolizumab was added as class I recommendation (Level 1A evidence) in the first-line palliative treatment and PD-1 inhibitors were added as class II recommendation (Level 2A evidence) in the second-line and above palliative treatment. The types of PD-1 inhibitors for second-line and above palliative treatment were not defined.

3) Second-line and above palliative treatment re-

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commendation for patients with *RAS* wild-type/*BRAF*^{V600E} mutation: At the American Society of Clinical Oncology (ASCO) annual meeting in 2020, the latest results of BEACON study were updated, of which mCRC patients with *BRAF*^{V600E} mutation received triplet combination (anti-EGFR antibody + BRAF inhibitor + MEK inhibitor) and doublet combination (anti-EGFR antibody + BRAF inhibitor) both achieved significantly longer OS (9.3 months *vs.* 9.3 months *vs.* 5.9 months), longer PFS (4.5 months *vs.* 4.3 months *vs*. 1.5 months), and higher ORR (27% *vs.* 20% *vs.* 2%) compared with the control group. And there was no difference in OS and PFS between the triplet combination and the doublet combination (12). Considering the 7% absolute increase in ORR of the triplet combination compared with the doublet combination, and the advantages of triplet combination in patients with extensive metastatic sites from subgroup analysis, for second-line and above palliative treatment for patients with *RAS* wild-type/*BRAF*^{V600E} mutation, the 2021 version revised the original "dabrafenib + trametinib + cetuximab" to "BRAF inhibitor + cetuximab ± MEK inhibitor" as class III recommendation (Level 2B evidence). A new note was added: "According to BAECON study and the 2021 version of National Comprehensive Cancer Network (NCCN) guidelines, BRAF inhibitor + cetuximab in second-line and above treatment for patients with *RAS* wild-type/*BRAF*^{V600E} mutation was recommended; BRAF inhibitor + cetuximab + MEK inhibitor can be considered for patients with extensive metastatic sites, high tumor burden or obvious tumor-related symptoms".

4) Third-line treatment in the palliative treatment group: Trifluridine/tipiracil (TAS-102) plus bevacizumab was added as class III recommendation (Level 2B evidence). Data from several studies with limited sample suggested that TAS-102 plus bevacizumab significantly benefit the survival of refractory mCRC patients (13,14). The DANISH study was a phase II clinical study evaluating the safety and efficacy of TAS-102 in combination with bevacizumab *vs*. TAS-102 monotherapy in patients with refractory mCRC, of which the latest data released in February 2020 in the Lancet (15). All patients were randomized to receive TAS-102 plus bevacizumab or TAS-102 monotherapy. A total of 93 patients were evaluable with a median follow-up of 10 months. The results showed that the ORR of TAS-102 plus bevacizumab groups and TAS-102 groups was 2.2% *vs.* 0, with a median PFS of 4.6 months *vs.* 2.6 months (P=0.0015) and a median OS of 9.4 *vs.* 6.7 months (P=0.028). Subgroup analysis showed that the efficacy of TAS-102 plus bevacizumab treatment was not affected by previous bevacizumab treatment. Based on these studies, TAS-102 plus bevacizumab was added as class III recommendation (Level 2B evidence) in the third-line palliative treatment for initially unresectable mCRC patients.

5) Third-line treatment in the palliative treatment group: cetuximab + irinotecan (after prior treatment with cetuximab) was added as class III recommendation (Level 3 evidence). Cricket study was a phase II, single-arm study which enrolled 28 *RAS*/*BRAF* wild-type mCRC patients with acquired resistance to cetuximab and irinotecan-based therapy in first-line treatment were assigned to cetuximab combined with irinotecan in third-line retreatment (16). The results showed an ORR of 21% and a DCR of 54%. The median PFS was 3.4 months and the median OS was 9.8 months. No *RAS* mutations were detected in samples from patients who achieved confirmed partial response. Patients with RAS wild-type ctDNA had significantly longer PFS than those with *RAS* mutated ctDNA. Therefore, in the third-line palliative treatment of mCRC patients with initially unresectable metastases who previously treated with cetuximab, cetuximab + irinotecan was added as class III recommendation (Level 3 evidence).

6) TJCC005 study was a single-arm study in China that enrolled 47 patients with confirmed wild-type RAS mCRC. The patients were recruited to receive fluorouracil-based cytotoxic agents combined with cetuximab followed by capecitabine + cetuximab for maintenance therapy. The study suggested that capecitabine combined with cetuximab as maintenance treatment achieved a median maintenance PFS of 7.2 months and a median maintenance OS of 22.2 months. The median overall PFS was 12.7 months and the median OS was 27.4 months (17). The CLASSIC study of cetuximab combined with capecitabine for first-line maintenance treatment in mCRC patients with *RAS*/*BRAF* wild-type is also ongoing. Therefore, the 2021 version deleted the note: "Capecitabine combined with cetuximab is not recommended".

7) For treatment of mCRC with initially unresectable metastases, a new note was added: "When the metastases are unresectable, there is still no consensus on whether the asymptomatic primary lesions need to be resected or the best time to do resection. Therefore, it is necessary to make individual decisions for each case under the multiple disciplinary team (MDT). A comprehensive analysis of multiple factors, such as tumor progression rate, expected survival time, site and size of primary lesions, circum-

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ference of intestinal cavity/degree of intestinal stenosis, willingness and feasibility to receive systemic treatment, should be carefully evaluated to decide whether to do the primary lesion resection."

8) Regimens and dosages of TAS-102 monotherapy, TAS-102 + bevacizumab, raltitrexed monotherapy, pembrolizumab monotherapy, trastuzumab + pertuzumab, trastuzumab + lapatinib, vemurafenib + irinotecan + cetuximab (VIC regimen), dabrafenib + cetuximab + trametinib were added in the commonly used systemic treatment for mCRC.

Updates related to treatment of rectal cancer

In this part, there are four points updated based on data of clinical studies and expert opinions.

1) Treatment of cT1–2N0 rectal cancer: A new note in therapeutic principles was added: "If patients are considering non-radical surgery, conventional fractionation and concurrent chemoradiotherapy (CFRT) (50–54 Gy/25–30 times) and consolidation chemotherapy after CFRT for qualified hospitals are recommended. For the evaluation of treatment response, pelvic magnetic resonance imaging (MRI), abdominal/pelvic CT, colorectal endoscopy, and anal examination are strongly recommended 2–3 months after completion of treatment. For patients received non-radical surgery, close follow-up examination is recommended, with colorectal colonoscopy and anal examination every 3 months for 2 years after the end of treatment, followed by examination every 6–12 months; Perform MRI every 3–6 months within 2 years after the end of treatment and every 6–12 months thereafter; Follow-up should last for at least 5 years. Because anal examination is simple, convenient and painless, patients can increase the frequency of it."

2) Treatment of cT3/cT4 or N+ rectal cancer: Consolidation chemotherapy refers to the delivery of chemotherapy at intervals between concurrent chemoradiotherapy (CRT) and surgery. It usually takes 6–11 weeks of rest after CRT before surgery can be performed. Without treatment, there is a risk of cancer progression. In a multicenter phase II clinical trial published by Memorial Sloan-Kettering Cancer Center (MSKCC) in 2015, 259 patients with locally advanced rectal cancer who received CRT were divided into four groups. Group 1 received surgery directly 6–8 weeks after CRT, and groups 2–4 received mFOLFOX6 regimen for 2 cycles, 4 cycles, and 6 cycles after CRT, followed by surgery. Results showed that 11 (18%) patients, 17 (25%) patients, 20 (30%) patients, and 25 (38%) patients achieved pathologic complete response (pCR) in the four groups, respectively, suggesting that consolidation chemotherapy can increase the pCR rate (18). Another phase II clinical trial affiliated to Fudan University Shanghai Cancer Center enrolled patients with locally advanced rectal cancer and performed XELOX regimen for 1 cycle after neoadjuvant CRT. The results published in 2017 showed that the pCR rate was 23.7%, the 3-year local recurrence rates was 14.6%, 3-year disease-free survival (DFS) rate was 63.8%, and 3-year OS rate was 77.4% (19). Therefore, in the treatment guidelines for cT3/cT4 or N+ rectal cancer, the original class I recommendation of "concurrent chemoradiotherapy + transabdominal resection + adjuvant chemotherapy (Level 1A evidence)" was modified to "concurrent chemoradiotherapy +/– interval chemotherapy (re-evaluation) + radical resection of rectal cancer + adjuvant chemotherapy (Level 1A evidence)."

3) Treatment of cT3/T4 or N+ rectal cancer: "intensive concurrent chemoradiotherapy regimen (concurrent chemoradiotherapy of capecitabine combined with irinotecan) (re-evaluation) + radical resection of rectal cancer + adjuvant chemotherapy" regimen was added as class II recommendation (Level 1B evidence). The CinClare study was a randomized controlled phase III clinical trial for the Chinese population, which was designed to evaluate the therapeutic benefit of capecitabine-based neoadjuvant CRT with that of irinotecan + capecitabine-based CRT in patients with locally advanced rectal cancer (20). The control group (group A, n=180) received radiation of 50 Gy/25Fx with concomitant capecitabine (825 mg/m^2 bid, d 1–5, qw), followed by oxaliplatin and capecitabine for 1 cycle. The experimental group (group B, n=180) received radiation of 50 Gy/25Fx with concomitant capecitabine (625 mg/m^2 bid, d 1–5, qw) combined with weekly irinotecan (80 mg/m^2 for patients with *UGT1A1*1*1* or 65 mg/m^2 for patients with *UGT1A1*1*28*), followed by irinotecan and capecitabine for 1 cycle. The expected positive results were obtained. The pCR rates were 15% and 30% in the control and experimental groups (P=0.001). Therefore, based on the Chinese CinClare study, for patients with cT3Nany, mesorectal fascia (MRF) negative, or cT1–2 N+ patients who have difficulty in preserving the anal sphincter, and patients with cT3Nany, MRF positive or cT4Nany patients, "intensive concurrent chemoradiotherapy (capecitabine combined with irinotecan) (re-evaluation) +

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radical resection of rectal cancer + adjuvant chemotherapy" was added as class II recommendation (Level 1B evidence). In addition, in the subsequent concurrent chemo-radiotherapy regimen for rectal cancer, "radiotherapy + irinotecan combined with capecitabine" was added: the dose of irinotecan for *UGT1A1*1*1* (6/6 type) and *UGT1A1*1*28* (6/7 type) was recommended to be 80 mg/m^2/w and 65 mg/m^2/w, respectively; Capecitabine 625 mg/m^2, twice a day, 5 days a week."

4) Treatment of cT3/cT4 or N+ rectal cancer: for patient with cT3Nany, MRF positive or cT4Nany patients, "short-course radiotherapy + chemotherapy of 12–16 weeks + radical resection of rectal cancer" was added as class II recommendation (Level 1B evidence). Based on total neoadjuvant therapy pattern, the RAPIDO study is a multicenter phase III clinical trial which enrolled 920 patients with locally advanced rectal cancer (classified as high risk on MRI), randomly assigned (1:1) into two groups. The experimental group received short-course radiotherapy (5×5 Gy) followed by 6 cycles of CAPOX chemotherapy or 9 cycles of FOLFOX4 chemotherapy, and then followed by total mesorectal excision (TME). The control group received long-course chemoradiotherapy with concomitant capecitabine followed by TME and adjuvant chemotherapy. The results showed that the 3-year cumulative probability of disease-related treatment failure was 23.7% in the experimental group, significantly lower than that of the control group (30.4%, P=0.019). The rate of distant metastasis was also lower (20.0% *vs.* 26.8%, P=0.0048). The pCR rate of the experimental group was higher than that of the control group (28.4% *vs.* 14.3%, P<0.001). There was no significant difference in local recurrence rates between the two groups (21). Based on the RAPIDO study, for patient with cT3Nany, MRF positive, or cT4Nany patients, "short-course radiotherapy + chemotherapy of 12–16 weeks + radical resection of rectal cancer" was added as class II recommendation (Level 1B evidence)."

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Zheng RS, Sun KX, Zhang SW, et al. Report of cancer epidemiology in China, 2015. Zhonghua Zhong Liu Za Zhi (in Chinese) 2019;41:19-28.
2. Chinese Society of Clinical Oncology (CSCO) diagnosis and treatment guidelines for colorectal cancer working group. Chinese Society of Clinical Oncology (CSCO) diagnosis and treatment guidelines for colorectal cancer 2018 (English version). Chin J Cancer Res 2019;31:117-34.
3. Yuan Y, Wang X, Chen G, et al. Updates in version 2019 of CSCO guidelines for colorectal cancer from version 2018. Chin J Cancer Res 2019;31:423-5.
4. Weng SS, Yuan Y, Wang XC, et al. Updates in version 2020 of CSCO guidelines for colorectal cancer from version 2019. Chin J Cancer Res 2020; 32:403-7.
5. National Cancer Center, China, Expert Group of the Development of China Guideline for the Screening, Early Detection and Early Treatment of Colorectal Cancer. China guideline for the screening, early detection and early treatment of colorectal cancer (2020, Beijing). Zhonghua Zhong Liu Za Zhi (in Chinese) 2021;43:16-38.
6. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitarget stool DNA testing for colorectal-cancer screening. N Engl J Med 2014;370:1287-97.
7. André T, Shiu KK, Kim TW, et al. Pembrolizumab in microsatellite-instability-high advanced colorectal cancer. N Engl J Med 2020;383:2207-18.
8. Hu H, Wang K, Huang M, et al. Modified FOLFOXIRI with or without cetuximab as conversion therapy in patients with RAS/BRAF wild-type unresectable liver metastases colorectal cancer: The FOCULM multicenter phase II trial. Oncologist 2021;26:e90-e98.
9. Cremolini C, Antoniotti C, Lonardi S, et al. Activity and safety of cetuximab plus modified FOLFOXIRI followed by maintenance with cetuximab or bevacizumab for RAS and BRAF wild-type metastatic colorectal cancer: A randomized phase 2 clinical trial.

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JAMA Oncol 2018;4:529-36.
10. Overman MJ, McDermott R, Leach JL, et al. Nivolumab in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142): an open-label, multicentre, phase 2 study. Lancet Oncol 2017;18:1182-91.
11. Le DT, Kim TW, Cutsem EV, et al. Phase II open-label study of pembrolizumab in treatment-refractory, microsatellite instability-high/mismatch repair-deficient metastatic colorectal cancer: KEYNOTE-164. J Clin Oncol 2020;38:11-9.
12. Kopetz S, Grothey A, Cutsem EV, et al. Encorafenib plus cetuximab with or without binimetinib for BRAF V600E-mutant metastatic colorectal cancer: Quality-of-life results from a randomized, three-arm, phase III study versus the choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC). J Clin Oncol 2020;38(4 suppl):8.
13. Kuboki Y, Nishina T, Shinozaki E, et al. TAS-102 plus bevacizumab for patients with metastatic colorectal cancer refractory to standard therapies (C-TASK FORCE): an investigator-initiated, open-label, single-arm, multicentre, phase 1/2 study. Lancet Oncol 2017;18:1172-81.
14. Satake H, Kato T, Oba K, et al. Phase Ib/II study of biweekly TAS-102 in combination with bevacizumab for patients with metastatic colorectal cancer refractory to standard therapies (BiTS Study). Oncologist 2020;25:e1855-e1863.
15. Pfeiffer P, Yilmaz M, Möller S, et al. TAS-102 with or without bevacizumab in patients with chemo-refractory metastatic colorectal cancer: an investigator-initiated, open-label, randomised, phase 2 trial. Lancet Oncol 2020;21:412-20.
16. Cremolini C, Rossini D, Dell'Aquila E, et al. Rechallenge for patients with RAS and BRAF wild-type metastatic colorectal cancer with acquired resistance to first-line cetuximab and irinotecan: A phase 2 single-arm clinical trial. JAMA Oncol 2019; 5:343-50.
17. Wang L, Liu Y, Yin XL, et al. Effect of reduced-dose capecitabine plus cetuximab as maintenance therapy for RAS wild-type metastatic colorectal cancer: A phase 2 clinical trial. JAMA Network Open 2020; 3:e2011036.
18. Garcia-Aguilar J, Chow OS, Smith DD, et al. Effect of adding mFOLFOX6 after neoadjuvant chemoradiation in locally advanced rectal cancer: a multicentre, phase 2 trial. Lancet Oncol 2015;16: 957-66.
19. Zhu J, Liu F, Gu W, et al. Concomitant boost IMRT-based neoadjuvant chemoradiotherapy for clinical stage II/III rectal adenocarcinoma: results of a phase II study. Radiat Oncol 2014;9:70.
20. Zhu J, Liu A, Sun X, et al. Multicenter, randomized, phase III trial of neoadjuvant chemoradiation with capecitabine and irinotecan guided by UGT1A1 status in patients with locally advanced rectal cancer. J Clin Oncol 2020;38:4231-9.
21. Bahadoer RR, Dijkstra EA, van Etten B, et al. Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial. Lancet Oncol 2021;22:29-42.

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