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**Clinical characteristics and prognosis of younger patients with colorectal cancer in eastern China**

Fu JF *et al*. Colorectal cancer in eastern China

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**Abstract**

**AIM:** To explore the clinical characteristics and prognosis of the young patients with colorectal cancer patients in eastern China.

**METHODS:** A total of 1335 patients with colorectal cancer treated from December 1985 to December 2005 in the Second Affiliated Hospital of Zhejiang University School of Medicine were studied retrospectively. The patients were divided into two groups, the younger group (aged ≤ 30 years) and the older group (aged > 30 years), and comparison was made in the clinical characteristics and prognosis between the two groups. Chi-square test was used for data analysis of all categorical variables, and overall survival (OS) was calculated by the Kaplan-Meier method. A multivariate analysis was performed using the Cox model.

**RESULTS:** There were 42 (3.1%) and 1293 (96.9%) cases in younger group and older group, respectively. The univariate analysis showed that the 5-year and 10-year OS in younger group were 33.9% and 26.1%, respectively, those in older group were 60.1% and 52.2%, respectively. Younger group had poor survival (*χ2* = 14.146, *P* = 0.000). Multiple variance analysis revealed that age was not a dependent factor for prognosis, with OR = 0.866 (95%CI: 0.592-1.269, *P* = 0.461). Stratified analysis indicated that in stage III and IV disease, the 5-year and 10-year OS were 24.6% and 14.8% in younger group, and 40.4% and 33.3% in older group, respectively, with significant difference between the two groups (*χ2* = 5.101, *P* = 0.024). In the subgroup of radical surgery, the 5-year and 10-year OS were 44.3% and 34.2% in younger group, and 69.6% and 60.5% in older group, difference being significant between the two groups (*χ2* = 7.830, *P* = 0.005).

**CONCLUSION:** Compared with older patients, the younger patients have lower survival，especially in the subgroups of stage III and IV disease and radical surgery.

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**Key words:** Colorectal cancer; Young; Clinicopathologic feature; Prognosis; Radical surgery.

**Core tip:** We firstly described the clinical characteristics and prognosis of young patients with colorectal cancer in eastern China. The incidence rate of colorectal cancer in the young patients was higher than that in other reports. Younger patients with colorectal cancer had more poorly differentiated and advanced tumors, and had worse prognosis, especially the stage III and IV patients.

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**INTRODUCTION**

As a kind of common cancer, colorectal cancer severely threatens the health of people. Colorectal cancer is the fourth common cancer and the second leading cause of cancer death in the world[1]. The majority of patients are affected in their the 50s to 70s, but the age at diagnosis is getting younger[2]. The annual percentage of colorectal cancer in young people is increasing[2]. There has been an increasing number of reports about the young colorectal cancer patients in recent years. The outcomes of the young colorectal cancer patients varied widely among different regions[2-4]. The incidence rate of colorectal cancer in young patients has also been increasing in the recent years in China[5]. Nearly all reports showed that the young colorectal cancer patients had specific clinicopathologic characteristics, including poor histological feature, and more mucinous tumors, signet ring cell tumors, and advanced tumors[6-8]. However, the relationship between the age and survival was not confirmed. Some reports documented that the young colorectal cancer patients had worse survival compared with the older counterparts[2,7-9]. But the others indicated opposite results[10-15]. There are still controversies about the definition of the age of young population. This study was to retrospectively analyze the data of patients with colorectal cancer who received surgery at our center over the past 30 years. Based on the distribution of the age, the population with colorectal cancer aged < 30 years were considered as a special subgroup in our center. Therefore, the young population was defined as those aged ≤ 30 years in our study. This study was designed to explore the clinicopathologic characteristics and prognosis of young colorectal cancer in eastern China.

**MATERIALS AND METHODS**

A total of 1335 consecutive patients with colorectal cancer (aged 19-92 years, mean 58 ± 13.3 years) treated from December 1985 to December 2005 in the Second Affiliated Hospital of Zhejiang University School of Medicine, located in eastern China, were studied retrospectively. The patients were divided into two groups, the younger group (42 cases, aged ≤ 30 years, average age, 26.0 ± 3.5 years) and the older group (1293 cases, aged > 30 years, average age 58.0 ± 12.3 years). The criteria for inclusion were as follows: (1) patients with pathologically confirmed colorectal cancer; and (2) patients underwent operations, including the palliative surgeries. The patients with anal cancer and the non-adenomas were excluded. Following the approval by the ethics committee of the hospital, the data including age, gender, tumor location, histological grade, approach of surgery, tumor infiltration, number of metastatic lymph node, distant metastasis and survival were obtained. Follow-up was made every 3 months for 2 years, 6 months for 5 years, then every one year. The follow-up proceeded through telephone calls or mail correspondence. The events of relapse and death in all patients were recorded.

The deadline of follow-up was November 2011. The follow-up lasted 0-302 mo (median, 57.0 ± 68.1 mo). Finally, 1335 patients who had complete data were analyzed; 267 patients (20.0%) were lost, with 5 patients (11.9%) in younger group and 262 patients (20.3%) in older group, without significant difference between two groups (*P* = 0.183). The lost patients were taken as censors when the survival was analyzed. Twenty-nine patients died of colorectal cancer in the younger group and 604 patients died in older group including 51 patients who died due to other causes. They were considered as censors when cancer related survival was calculated. All 1335 cases were included when we analyzed the clinicopathologic difference between the two groups.

The tumor was staged according to the 7th pathologic TNM stage of AJCC[16]. The tumor location was described in detail as cecum, ascending colon, liver flexure colon, transvers colon, descending colon, sigmoid, sigmorectum junction and rectum. The overall survival was calculated from the time of operation to death. The cancer-related survival was from the time of operation to the date of death because of the colorectal cancer. The causes of non-special cancer-related death included benign disease, accident, and secondary cancer. The radical surgery was classified as a procedure for no residual tumor left behind microscopically at resection margins. Palliative surgery was defined as a procedure for the residual tumor left macroscopically, which also included bypass or ileostomy. All palliative surgeries were considered as non-radical surgery.

***Statistical analysis***

Data of all categorical variables were summarized using frequencies and percentages. The data were analyzed with *χ2* test. Overall survival was calculated according to the Kaplan-Meier method. Survival rates were compared by the log-rank test. A multivariate analysis was performed using the Cox model. When *P* value was less than 0.05, the difference was considered significant. SPSS 16.0 statistics software was used for data analysis.

**RESULTS**

***Clinicopathologic characteristics***

The patient age ranged from 19 to 92 years, with a median of 58 ± 13.3 years. There were 42 (3.1%) and 1293 (96.9%) cases in younger group and older group, respectively. The ratio of male to female was 1.3:1 in both groups.

Rectum was the frequent location in colorectal cancer, with a slightly higher rate in younger group than in older group (59.5% *vs* 49.3%), without significant difference (*P* > 0.05). Compared with the older group, more patients in younger group had mucinous tumor (33.3% *vs* 13.8%), signet ring cell cancer (7.1% *vs*1.7%) and poorly differentiated tumor (59.5% *vs* 15.7%), with significant differences between the two groups (*P* = 0.000, 0.010 and 0.000, respectively).

As for tumor infiltration, no tumor *in situ* (Tis) was found in younger group, but 17 (13.1%) patients in older group were diagnosed with tumor *in situ* (Tis). Interestingly, there was no significant difference between the two groups in the tumor infiltration (*P* = 0.264). The percentages of lymph node metastasis (≥ 4 lymph nodes), distance metastasis, stage IV and stage I disease and radical surgery were 35.7%, 28.6%, 31.0%, 2.4% and 66.7% respectively in younger group, and 14.2%, 15.4%, 15.5%, 30.2% and 83.7% respectively in the older group, with significant differences (*P* = 0.021, 0.021, 0.007, 0.008 and 0.008, respectively), (Table 1).

***Overall survival***

The univariate analysis showed that there was significant difference in total overall survival between the two groups (*χ2* = 14.146, *P* = 0.000), (Figure 1, Table 2). The multivariate analysis revealed that age was not an independent factor for the prognosis of the colorectal cancer (OR = 0.866, 95%CI 0.592-1.269, *P* = 0.461). The TNM stage III/IV, the approach of palliative surgery, rectal cancer, mucinous cancer and poorly differentiated tumor were independent factors for worse prognosis (Table 2).

As for the stage I and II disease, the 10-year overall survival and median survival time had not reached until the deadline in the younger group, which might be associated with the small sample of the study. There was no significant difference between the two groups (χ2 = 0.016, *P* = 0.899), (Figure 2A, Table 2). Fifty-one patients died of other diseases in the older group. In order to diminish the influence of the non-cancer death, the cases in the subgroup of stage I and II disease were analyzed; as a result, there was also no difference of cancer-related survival between the two groups (*χ2* = 0.356, *P* = 0.551), (Figure 2B). For stage III and IV disease, the outcome was worse in younger group than in older group (*χ2* = 5.101, *P* = 0.024), (Figure 3, Table 2). For the subgroup of radical surgery, in the older group, the median survival time had not reached until the deadline. There was significant difference between the two groups (*χ2* = 7.830, *P* = 0.005),( Figure 4A, Table 2). In the non-radical surgery subgroup, there was no significant difference between the two groups (*χ2* = 0.112，*P* = 0.737), (Figure 4A, Table 2).

**DISCUSSION**

A total of 1335 patients with colorectal cancer were analyzed retrospectively in this study, including 42 (3.1%) patients in younger group (aged ≤3 0 years). In other studies, the incidence rate was less than 1% and 3% if young patients with colorectal cancer were defined as those aged ≤ 30 years[17-19] and ≤ 40 years[4,15], respectively. The incidence rate in this study was higher than in other regions, with obvious regional difference. In this study, eastern China refers to Yangtze River delta region where people enjoy a similar lifestyle and economic status. Consequently, the epidemiological characteristics of colorectal cancer in this region are similar. Therefore, data from our center could represent the features of this tumor in eastern China. There might be constitution biases about the incidence rate of colorectal cancer in young patients because the data were collected retrospectively by a single medical center.

***Gender***

There was no no significant difference in gender ratio between the two groups. The percentage of female patients is becoming higher with the trend of younger in age in gastric cancer. This phenomenon was not seen in the colorectal cancer. Estrogen was considered to be related with the gastric cancer in younger patients[20]. It is not clear whether the estrogen was related to the occurrence of colorectal cancer in young people[21,22]. On the other hand, this study indicated that the female patients with colorectal cancer had better outcome than the male patients, but with no significant difference (OR = 0.969, *P* = 0.708) in survival as shown by the multivariate analysis.

***Tumor location***

In this study, the rectum and sigmoid were common sites of the tumor in both groups. The proportion of rectal cancer was higher in younger group (59.5%) than in older group (49.3%), but without significant difference (*P* = 0.191). Some reports indicated that the rate of rectal cancer in younger population was higher than in older ones[2]. That might be related to the epidemics of colorectal cancer that rectal cancer is more common than colonic cancer in China. Eating habit and lifestyle might contribute more to the occurrence of colorectal cancer than age.

***Pathological characteristics***

In this study, the mucinous tumor and signet ring cell cancer were more common in the younger group than in the older group. A majority of patients in younger group had poor histologic grade compared with the older group. The studies about gastric cancer also indicated that there were more poorly differentiated cancers in younger population than in the older population, especially the signet ring cell cancer[23]. It was not clear about the age impact on the occurrence of gastrointestinal cancer.

***Stage***

Compared with older population, the percentage of stage IV disease increased and the proportion of stage I decreased in younger group. As for the infiltration of tumor and nodal metastasis, the patients in younger group presented with more aggressive findings. Some studies found that 66.0% of the patients with colorectal cancer were diagnosed with stage III or IV disease, which was obviously lower (32.0%) in the older patients[24]. This may result from the poor differentiation and high aggressivon of tumors which were often diagnosed in younger patients with colorectal cancer. Besides, the younger patients with colorectal cancer often had delayed diagnosis, but the older ones would be diagnosed earlier through screening program.

***Overall survival***

The univariate analysis revealed that the patients in younger group had poorer survival than the older group. The impact of young age on the prognosis of colorectal cancer is not confirmed. Some studies showed that young patients with colorectal cancer had more mucinous cancer and signet ring cancer, poorer histologic grade, later stage and worse prognosis[2,7-9]. But results were contradictory from other studies which indicated that young age had no impact on the prognosis[10-15]. In our study, young colorectal cancer patients had worse prognosis, while the multivariate analysis indicated that age was not an independent factor for prognosis. Furthermore, the multivariate analysis also showed that the disease stage and approach of surgery were strongly related to the prognosis. Worse prognosis might result from stage III and IV disease and non-radical surgery. So stratified analysis with these two factors were carried out.

The result of stratified analysis with stage indicated that younger patients had poor prognosis and the univariate analysis showed that the patients were presented with mainly stage III and IV disease. The reasons might be that young patients had more poorly differentiated tumor, and mucinous carcinoma and signet ring cell cancer, which were more aggressive in the same stage. As for the patients in stage I and II, age exerted no effect on the survival. In this study, there were more patients in older group who did not die of colorectal caner. In order to exclude the influence of the non-cancer special death, the cancer-related survival in stage I and II patients was analyzed. The result showed no significant difference in cancer-related survival in stage I and II tumor between the two groups. The study of Quah[25] considered that the patients in earlier stage had better survival in younger group than older group; the young patients were more tolerable to surgery and aggressive adjuvant chemotherapy and radiotherapy[26]. And the study of McMillan *et al*[27] indicated that in the older group, the non-special cancer factors were the major causes of death.

The stratified analysis with approach of surgery revealed that the patients had poorer prognosis in the younger group than in older group with radical surgery, but there was no significant difference between the two groups without radical surgery. In stratified analysis with stage, the patients of the two groups in stage I and II had similar prognosis. The tumors in stage I and II were often considered to be resectable. For the patients with resectable tumors in stage III and stage IV, younger age strongly contributed to poor survival. For the patients who received operation without adjuvant chemotherapy in the 1980s and 1990s, the value of the adjuvant therapy after operation should be highlighted for patients with resectable stage III or more advanced colorectal cancer[28].

The current study had some limitations. The clinical data did not include the signs and symptoms of the colorectal cancer patients. It was impossible to identify the alarming symptoms for the younger patients. Family histories were not described which were routinely detected in young population as the other studies[29]. The missing rate of the patients was 20% which might influence the result of survival. In China, there are several medical centers owning elaborate clinical data, but few centers carried out the systemic follow-up. The data of 10-year follow-up are rare.

In summary, compared with older patients, the younger ones had specific clinicopathologic characteristics that were worthy to be explored and managed differentially. Younger patients with colorectal cancer tended to be diagnosed at later stage. For younger patients who had poor survival, especially those in stage III and IV and treated with radical surgery, more aggressive adjuvant therapies are recommended.

**COMMENTS**

***Background***

The incidence rate of colorectal cancer has been increasing in recent years. The onset age of colorectal cancer is getting younger. Should the young colorectal cancer patients be treated as a heterogeneous group? It is important to explore the phenotype of young patients with colorectal cancer.

***Research frontiers***

Age is an independent prognostic factor for many cancers such as breast cancer, thyroid cancer and gastric cancer. The young patients have more triple negative breast cancers and worse prognosis. The lymph node-positive thyroid cancers are commonly diagnosed in the adolescent patients, who have satisfactory prognoses. The young patients with gastric cancer in early stage have better prognosis than the old ones, while their prognoses are worse in the advanced gastric cancer. It is unknown about the age impact on the prognosis of colorectal cancer. Some studies showed that young patients with colorectal cancer had more mucinous cancer and signet ring cancer, poorer histologic grade, later stage and worse prognosis. But results were contradictory in other studies which indicated that the young age had no impact on prognosis.

***Innovations and breakthroughs***

The authors described systematically for the first time the clinical characteristics and prognosis of young colorectal cancer patients in eastern China. The incidence rate of young colorectal cancer was higher than in other reports. Young colorectal cancer was characterized by poorer differentiation and advanced stage. Young colorectal cancer patients had worse prognosis, especially those in stage III and IV rather than stage I and II.

***Applications***

Relapse risk of postoperative stage II colonic cancer is a crucial factor for decision-making in postoperative treatment. This study showed that age was not an independent risk factor for stage II colorectal cancer. On the other hand, young colorectal cancer patients in stage III and IV had worse prognosis, more aggressive adjuvant therapy is recommended for these patients.

***Terminology***

Young colorectal cancer: Onset age of colorectal cancer was less than or equal to 30 years. Eastern China refers to Yangtze River delta region where people have similar lifestyle and economic conditions. Epidemiological characteristics of colorectal cancer in this region is also similar.

***Peer review***

The study described the detailed clinicopathologic characteristics of 1335 cases of colorectal cancer in eastern China and analyzed the significance of prognosis by many statistical methods. The major goal of authors is to analyze the difference between younger patients (≤ 30 year-old) and older patients (> 30 year-old). The information enclosed in this manuscript is very plentiful and clear, and the authors applied many different statistical methods to perform the analysis. Although the results are not novel and methodology was orthodox, it is worth reporting the present results.

**REFERENCES**

1 **Edwards BK**, Ward E, Kohler BA, Eheman C, Zauber AG, Anderson RN, Jemal A, Schymura MJ, Lansdorp-Vogelaar I, Seeff LC, van Ballegooijen M, Goede SL, Ries LA. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. *Cancer* 2010; **116**: 544-573 [PMID: 19998273 DOI: 10.1002/cncr.24760]

2 **You YN**, Xing Y, Feig BW, Chang GJ, Cormier JN. Young-onset colorectal cancer: is it time to pay attention? *Arch Intern Med* 2012; **172**: 287-289 [PMID: 22157065 DOI: 10.1001/archinternmed.2011.602]

3 **Neufeld D**, Shpitz B, Bugaev N, Grankin M, Bernheim J, Klein E, Ziv Y. Young-age onset of colorectal cancer in Israel. *Tech Coloproctol* 2009; **13**: 201-204 [PMID: 19609485 DOI: 10.1007/s10151-009-0501-7]

4 **McMillan DC**, McArdle CS. The impact of young age on cancer-specific and non-cancer-related survival after surgery for colorectal cancer: 10-year follow-up. *Br J Cancer* 2009; **101**: 557-560 [PMID: 19672260 DOI: 10.1038/sj.bjc.6605222]

5 **Wu QJ**, Vogtmann E, Zhang W, Xie L, Yang WS, Tan YT, Gao J, Xiang YB. Cancer incidence among adolescents and young adults in urban Shanghai, 1973-2005. *PLoS One* 2012; **7**: e42607 [PMID: 22880052 DOI: 10.1371/journal.pone.0042607]

6 **Endreseth BH**, Romundstad P, Myrvold HE, Hestvik UE, Bjerkeset T, Wibe A. Rectal cancer in the young patient. *Dis Colon Rectum* 2006; **49**: 993-1001 [PMID: 16741599 DOI: 10.1007/s10350-006-0558-6]

7 **Chan KK**, Dassanayake B, Deen R, Wickramarachchi RE, Kumarage SK, Samita S, Deen KI. Young patients with colorectal cancer have poor survival in the first twenty months after operation and predictable survival in the medium and long-term: analysis of survival and prognostic markers. *World J Surg Oncol* 2010; **8**: 82 [PMID: 20840793 DOI: 10.1186/1477-7819-8-82]

8 **Kaplan MA**, Isikdogan A, Gumus M, Arslan UY, Geredeli C, Ozdemir N, Koca D, Dane F, Suner A, Elkiran ET, Kucukoner M, Seker M, Helvaci K, Guler T, Uncu D, Inal A, Yildiz R. Childhood, adolescents, and young adults (≤25 y) colorectal cancer: study of Anatolian Society of Medical Oncology. *J Pediatr Hematol Oncol* 2013; **35**: 83-89 [PMID: 23337551 DOI: 10.1097/MPH.0b013e31827e7f20]

9 **O'Connell JB**, Maggard MA, Liu JH, Etzioni DA, Livingston EH, Ko CY. Do young colon cancer patients have worse outcomes? *World J Surg* 2004; **28**: 558-562 [PMID: 15366745 DOI: 10.1007/s00268-004-7306-7]

10 **Yeo SA,** Chew MH, Koh PK, Tang CL. Young colorectal carcinoma patients do not have a poorer prognosis: a comparative review of 2,426 cases. *Tech Coloproctol* 2013; [Epub ahead of print] [PMID: 23460362 DOI: 10.1007/s10151-013-0977-z]

11 **Taggarshe D**, Rehil N, Sharma S, Flynn JC, Damadi A. Colorectal cancer: are the "young" being overlooked? *Am J Surg* 2013; **205**: 312-36; discussion 316 [PMID: 23414955 DOI: 10.1016/j.amjsurg.2012.10.016]

12 **O'Connell JB**, Maggard MA, Liu JH, Etzioni DA, Ko CY. Are survival rates different for young and older patients with rectal cancer? *Dis Colon Rectum* 2004; **47**: 2064-2069 [PMID: 15657655 DOI: 10.1007/s10350-004-0738-1]

13 **Chung YF**, Eu KW, Machin D, Ho JM, Nyam DC, Leong AF, Ho YH, Seow-Choen F. Young age is not a poor prognostic marker in colorectal cancer. *Br J Surg* 1998; **85**: 1255-1259 [PMID: 9752871 DOI: 10.1046/j.1365-2168.1998.00805.x]

14 **Li M**, Li JY, Zhao AL, Gu J. Do young patients with colorectal cancer have a poorer prognosis than old patients? *J Surg Res* 2011; **167**: 231-236 [PMID: 21316708 DOI: 10.1016/j.jss.2010.10.040]

15 **Enblad G**, Enblad P, Adami HO, Glimelius B, Krusemo U, Påhlman L. Relationship between age and survival in cancer of the colon and rectum with special reference to patients less than 40 years of age. *Br J Surg* 1990; **77**: 611-616 [PMID: 2383722 DOI: 10.1002/bjs.1800770605]

16 **Ueno H**, Mochizuki H, Akagi Y, Kusumi T, Yamada K, Ikegami M, Kawachi H, Kameoka S, Ohkura Y, Masaki T, Kushima R, Takahashi K, Ajioka Y, Hase K, Ochiai A, Wada R, Iwaya K, Shimazaki H, Nakamura T, Sugihara K. Optimal colorectal cancer staging criteria in TNM classification. *J Clin Oncol* 2012; **30**: 1519-1526 [PMID: 22430272 DOI: 10.1200/JCO.2011.39.4692]

17 **Al-Barrak J**, Gill S. Presentation and outcomes of patients aged 30 years and younger with colorectal cancer: a 20-year retrospective review. *Med Oncol* 2011; **28**: 1058-1061 [PMID: 20680521 DOI: 10.1007/s12032-010-9639-4]

18 **Rodriguez-Bigas MA**, Mahoney MC, Weber TK, Petrelli NJ. Colorectal cancer in patients aged 30 years or younger. *Surg Oncol* 1996; **5**: 189-194 [PMID: 9067568 DOI: 10.1016/S0960-7404(96)80043-0]

19 **Kam MH**, Eu KW, Barben CP, Seow-Choen F. Colorectal cancer in the young: a 12-year review of patients 30 years or less. *Colorectal Dis* 2004; **6**: 191-194 [PMID: 15109385 DOI: 10.1111/j.1463-1318.2004.00596.x]

20 **Kim JH**, Boo YJ, Park JM, Park SS, Kim SJ, Kim CS, Mok YJ. Incidence and long-term outcome of young patients with gastric carcinoma according to sex: does hormonal status affect prognosis? *Arch Surg* 2008; **143**: 1062-107; discussion 1067 [PMID: 19015464 DOI: 10.1001/archsurg.143.11.1062]

21 **Koo JH**, Jalaludin B, Wong SK, Kneebone A, Connor SJ, Leong RW. Improved survival in young women with colorectal cancer. *Am J Gastroenterol* 2008; **103**: 1488-1495 [PMID: 18510616 DOI: 10.1111/j.1572-0241.2007.01779.x]

22 **Olofinlade O**, Adeonigbagbe O, Gualtieri N, Freiman H, Ogedegbe O, Robilotti J. Colorectal carcinoma in young females. *South Med J* 2004; **97**: 231-235 [PMID: 15043328 DOI: 10.1097/01.SMJ.0000072360.33202.F2]

23 **Park JC**, Lee YC, Kim JH, Kim YJ, Lee SK, Hyung WJ, Noh SH, Kim CB. Clinicopathological aspects and prognostic value with respect to age: an analysis of 3,362 consecutive gastric cancer patients. *J Surg Oncol* 2009; **99**: 395-401 [PMID: 19347884 DOI: 10.1002/jso.21281]

24 **O'Connell JB**, Maggard MA, Livingston EH, Yo CK. Colorectal cancer in the young. *Am J Surg* 2004; **187**: 343-348 [PMID: 15006562 DOI: 10.1016/j.amjsurg.2003.12.020]

25 **Quah HM**, Joseph R, Schrag D, Shia J, Guillem JG, Paty PB, Temple LK, Wong WD, Weiser MR. Young age influences treatment but not outcome of colon cancer. *Ann Surg Oncol* 2007; **14**: 2759-2765 [PMID: 17593332 DOI: 10.1245/s10434-007-9465-x]

26 **Pedrazzani C**, Cerullo G, De Marco G, Marrelli D, Neri A, De Stefano A, Pinto E, Roviello F. Impact of age-related comorbidity on results of colorectal cancer surgery. *World J Gastroenterol* 2009; **15**: 5706-5711 [PMID: 19960568 DOI: 10.3748/wjg.15.5706]

27 **McMillan DC**, Hole DJ, McArdle CS. The impact of old age on cancer-specific and non-cancer-related survival following elective potentially curative surgery for Dukes A/B colorectal cancer. *Br J Cancer* 2008; **99**: 1046-1049 [PMID: 18797465 DOI: 10.1038/sj.bjc.6604669]

28 **Lin JT**, Wang WS, Yen CC, Liu JH, Yang MH, Chao TC, Chen PM, Chiou TJ. Outcome of colorectal carcinoma in patients under 40 years of age. *J Gastroenterol Hepatol* 2005; **20**: 900-905 [PMID: 15946138 DOI: 10.1111/j.1440-1746.2005.03893.x]

29 **Boardman LA**, Morlan BW, Rabe KG, Petersen GM, Lindor NM, Nigon SK, Goldberg J, Gallinger S. Colorectal cancer risks in relatives of young-onset cases: is risk the same across all first-degree relatives? *Clin Gastroenterol Hepatol* 2007; **5**: 1195-1198 [PMID: 17702662 DOI: 10.1016/j.cgh.2007.06.001]

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**Figure 1 Overall survival of patients in younger group (≤ 30 years) and older group (> 30 years).** The younger group had worse prognosis than the older group (*P* = 0.000).

**Figure 2 Overall survival of younger patients (≤ 30 years) and older patients (> 30 years) in stage I and II tumor subgroup.** A: Overall survival was totally similar between two groups (*P* = 0.899); B: Cancer-related survival was similar between two groups (*P* = 0.551).

**Figure 3 Overall survival of younger patients (≤ 30 years) and older patients (>30 years) in stage III and IV tumor subgroup.** The younger group had worse prognosis than the older group (*P* = 0.024).

**Figure 4 Overall survival of younger patients (≤30 years) and older patients (>30 years) based on approach of surgery.** A: The younger group had worse prognosis than the older group (*P* = 0.005) undergoing radical surgery. B: There was no difference between two groups (*P* = 0.737) treated with non-radical surgery.

**Table 1** Clinical and pathologic characteristics of colorectal cancer in younger group and older group *n* (%)

|  |  |  |  |
| --- | --- | --- | --- |
| Variables | Younger group (*n* = 42)  (≤ 30 yrs) | Older group (*n* = 1293)  (> 30 yrs) | *P* value |
| Gender |  |  | NS |
| Male | 24 (57.1) | 738 (57.1) |  |
| Female | 18 (42.9) | 555 (42.9) |  |
| Location of tumor |  |  |  |
| Cecum | 1 (2.4) | 69 (5.3) |  |
| Ascending colon | 1 (2.4) | 154 (11.9) |  |
| Hepatic flexure | 1 (2.4) | 86 (6.7) |  |
| Transverse colon | 2 (4.8) | 52 (4.0) |  |
| Splenic flexure | 1 (2.4) | 29 (2.2) |  |
| Descending colon | 6 (14.3) | 49 (3.8) |  |
| Sigmoid | 5 (11.9) | 201 (15.5) |  |
| Rectosigmoid junction | 0 | 16 (1.2) |  |
| Rectum | 25 (59.5) | 637 (49.3) | 0.1911 |
| Histology |  |  |  |
| Mucinous cancer | 14 (33.3) | 179 (13.8) | 0.0002 |
| Signet ring cell cancer | 3 (7.1) | 22 (1.7) | 0.0103 |
| Papillary adenocarcinoma | 5 (11.9) | 237 (18.3) |  |
| Tubular adenocarcinoma | 17 (40.5) | 732 (56.6) |  |
| Undifferentiated adenocarcinoma | 1 (2.4) | 6 (0.5) |  |
| Adenosquamous cancer | 0 | 2 (0.2) |  |
| Adenocarcinoma (unclassified) | 2 (4.8) | 115 (8.9) |  |
| Differentiation |  |  | 0.000 |
| Well | 2 (9.5) | 276 (21.3) |  |
| Moderate | 14 (33.3) | 630 (48.7) |  |
| Poor | 25 (28.6) | 203 (15.7) |  |
| Undifferentiated | 1 (2.4) | 184 (14.2) |  |
| Stage T |  |  | 0.264 |
| Tis | 0 | 17 (1.3) |  |
| T1 | 1 (2.4) | 41 (3.2) |  |
| T 2 | 4 (9.5) | 232 (17.9) |  |
| T 3 | 16 (38.1) | 526 (40.7) |  |
| T 4 | 21 (50.0) | 477 (36.9) |  |
| Number of lymph node metastasis |  |  | 0.001 |
| 0 | 11 (26.2) | 669 (51.7) |  |
| 1-3 | 10 (23.8) | 337 (26.1) |  |
| >4 | 15 (35.7) | 184 (14.2) |  |
|  |  |  |  |
| Nx | 6 (14.3) | 103 (8.0) |  |
| Distant metastasis |  |  | 0.021 |
| M0 | 30 (71.4) | 1094 (84.6) |  |
| M1 | 12 (28.6) | 99 (15.4) |  |
| AJCC stage |  |  | 0.001 |
| 0 | 0 | 17 (1.3) |  |
| I | 1 (2.4) | 221 (17.1) | 0.0084 |
| II | 9 (21.4) | 427 (33.0) |  |
| III | 19 (45.2) | 428 (33.1) |  |
| IV | 13 (31.0) | 200 (15.5) | 0.0075 |
| Approach of surgery |  |  | 0.028 |
| Radical surgery | 28 (66.7) | 1084 (83.8) |  |
| Palliate surgery | 10 (23.8) | 151 (11.7) |  |
| Unsectable | 4 (9.5) | 58 (4.5) |  |

1Rectum *vs* other sites of tumor; 2Mucinous cancer *vs* other histological types; 3Signet ring cell cancer *vs* other histological types; 4 Stage I *vs* other stages; 5 Stage IV *vs* other stages. Tis : Tumor *in situ*. NS: Non-significance.

**Table 2** **Multivariate analysis (Cox proportional hazard model) of prognostic factors for 1335 patients with colorectal cancer**

|  |  |  |  |
| --- | --- | --- | --- |
| Variables | OR | 95.0%CI | *P* value |
| Stage(III+IV/I+II) | 2.196 | 1.827-2.639 | 0.000 |
| Approach of surgery(Non-radical/ Radical) | 4.496 | 3.718-5.437 | 0.000 |
| Age(> 30 yr/≤3 0 yr) | 0.866 | 0.592-1.269 | 0.461 |
| Gender (male/female) | 0.997 | 0.852-1.167 | 0.970 |
| Tumor local (rectum /colon) | 1.270 | 1.084-1.488 | 0.003 |
| Differentiation (moderate+well /low ) | 0.802 | 0.650-0.990 | 0.041 |
| Histology (others/mucinous) | 0.791 | 0.632-0.990 | 0.041 |

**Table 3** **Survival of subgroup patients by stratified analysis with stage and approach of surgery**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Age (yr) | *n* | 5-year OS | 10-year OS | Median survival time(mo, 95%CI) |
| Total1 | ≤ 30 | 42 | 33.9% | 26.1% | 29.0 (18.0-40.0) |
| * 30 | 1293 | 60.1% | 52.2% | 140.0 (111.6-168.4) |
| Stage I and II | ≤ 30 | 10 | 68.6% | /4 | /4 |
| * 30 | 665 | 78.6% | 69.8% | 264.0 (203.5-324.5) |
| Stage III and IV2 | ≤ 30 | 32 | 24.6% | 14.8% | 22 (2.6-41.4) |
| < 30 | 628 | 40.4% | 33.3% | 35 (27.9-42.1) |
| Radical surgery3 | ≤ 30 | 28 | 44.3% | 34.2% | 40.0 (10.1-69.9) |
| * 30 | 1082 | 69.6% | 60.5% | /5 |
| Non-radical surgery | ≤ 30 | 14 | 14.3% | 0% | 6 (2.3-9.7) |
| > 30 | 211 | 11.8% | 0% | 11 (9.2-12.8) |

1*χ2* = 14.146, *P* = 0.000; 2*χ2* = 5.101, *P* = 0.024; 3*χ2* = 7.830, *P* = 0.005; 4The sample was too small to analyze. 5The median survival time was not reached.