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A decade-long study on pathological distinctions of resectable early versus late onset colorectal cancer and optimal screening age determination

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The incidence of Early-Onset Colorectal Cancer (EOCRC) is increasing. However, the prognosis of EOCRC compared to Late-Onset Colorectal Cancer (LOCRC), and the ideal age for initial colorectal cancer (CRC) screening are not clear. In this study, we identified the pathological differences between the groups and determined the optimal screening age for CRC patients. We included 10,172 patients diagnosed with CRC from January 2011 to December 2021 in this study. Survival differences were compared by plotting Kaplan–Meier survival curves and conducting landmark analysis. Additionally, the diagnostic age of CRC patients was analyzed using age cumulative curves. Compared to LOCRC patients, EOCRC patients had a higher proportion of deficient mismatch repair (dMMR) and more advanced TNM staging ($P < 0.05$). The five-year survival of EOCRC patients was significantly better than that of LOCRC patients ($P < 0.05$). Laparoscopic surgery improved the long-term survival of EOCRC patients. Proficient mismatch repair (pMMR) favored the long-term survival of EOCRC patients. The survival rate of EOCRC patients at TNM stages I and II was higher than that of LOCRC patients at the same stages ($P < 0.05$). The age cumulative curve showed a substantial increase in the number of CRC patients at 40 years. The long-term prognosis of EOCRC patients is better than that of LOCRC patients, especially among those with pMMR, stages I–II, and who undergo laparoscopic surgery. For people with a high risk of cancer, such as a family history of cancer and poor lifestyle habits, the starting age for CRC screening should be 40 years.

Keywords Early-onset colorectal cancer, Prognosis, Screening age, Surgical modalities, Microsatellite instability

Colorectal cancer (CRC) is a widespread health problem worldwide, with some of the highest incidence and mortality rates of all cancer types[1].The disease is frequently associated with advancing age, with median ages at diagnosis being 68 years for men and 72 years for women; compared to the median age of 63 years for other cancer types, CRC is generally diagnosed later[2]. In this study, we classified patients diagnosed before the age of 50 as having early-onset colorectal cancer (EOCRC), while those diagnosed after this threshold were categorized as late-onset colorectal cancer (LOCRC). Notably, although the incidence of LOCRC has declined over the past two decades, partly attributable to enhanced screening practices[3]. the incidence of EOCRC has exhibited a marked upward trend, This indicates that factors beyond genetics may be influential. such as Lynch Syndrome (LS), are recognized to elevate an individual's risk of developing CRC at a younger age[4]. However, these genetic conditions represent a relatively minor fraction of all CRC cases, with the majority of EOCRC instances being sporadic[4]. This phenomenon may be associated with adverse lifestyle factors including poor dietary habits, physical inactivity, and obesity[5–9].

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With the further understanding of EOCRC, its incidence is expected to continue to increase. Existing studies have shown that patients with EOCRC may face a greater disease burden than patients with LOCRC[10,11]. However, the exact cause of EOCRC remains unclear, and its cancer-related mortality is expected to increase in the next decade[12–14]. Although some studies, such as Liu et al.'s findings, pointed out that patients with early onset may have a higher overall survival rate (OS)[15,16], other studies, such as the study of Advanced People, showed that there was no significant difference in prognosis between patients with EOCRC and LOCRC[17]. In addition, the specific effects of different stages, surgical methods, and subgroups on OS in patients with EOCRC and LOCRC are not yet clear and require further research to determine. There is also no consensus on the optimal screening age for EOCRC patients. The American Cancer Society (ACS) recommends starting screening at age 45 for people at average risk[18,19], but in order to minimize costs, some researchers have recommended an earlier screening age of 40[20].

The study aims to investigate the differences in OS between sporadic EOCRC and LOCRC with respect to surgical approaches, clinical characteristics, and pathological features. We specifically excluded patients with LS and those who underwent non-surgical treatments to ensure that the focus of our study was on sporadic EOCRC. As LS is a genetic diseases with distinct pathogenic mechanisms and clinical features compared to sporadic CRC, its inclusion could introduce bias in our understanding of sporadic EOCRC. By excluding patients with LS, we are able to more accurately delineate the true clinical and pathological characteristics of sporadic EOCRC, thereby providing a more robust scientific foundation for future prevention and treatment strategies.

Results

Baseline characteristics of patients

During the study period, 10,172 patients were enrolled. Among them, 7709 patients met the inclusion criteria for a high-quality diagnosis of CRC. The preoperative characteristics of these patients were compared. The demographic and clinical features of the study population are shown in Table 1. The LOCRC group had a slightly higher proportion of males (59.0%) than the EOCRC group (57.8%). The EOCRC patients had a higher prevalence of dMMR (13.9%) than LOCRC patients (7.2%), according to the MMR status. The EOCRC patients had a higher proportion of stage II, III, and IV tumors than LOCRC patients, based on the TNM classification. The key laboratory parameters, including perineural invasion, vascular invasion, alkaline phosphatase, hemoglobin (HB), and platelet count (PLT), differed significantly between the LOCRC and EOCRC groups. These findings suggested that LOCRC and EOCRC patients have different baseline characteristics, which may affect the disease progression and treatment response.

Comparison of survival between EOCRC and LOCRC patients

After comparing the survival outcomes of patients with EOCRC and LOCRC, we found no significant difference in the survival rates between these two groups (Fig. 1A) ($P > 0.05$). For OS analysis, the 12-year follow-up was divided into intervals of five and seven years for landmark analysis. The EOCRC patients showed a significantly higher survival rate than the LOCRC patients after the fifth year (Fig. 1B) ($P < 0.05$). An examination of the changes in EOCRC patients over the past 12 years showed an increase in their proportion in the yearly diagnosed CRC population (Fig. 1C). A comprehensive analysis of the survival rates of CRC patients showed rates of 94.0%, 84.7%, and 78.4% at one, three, and five years, respectively (Supplementary Fig. 1A). The differences in the survival rates between rectal and colorectal cancer patients were not significant (Supplementary Fig. 1B) ($P > 0.05$). However, patients with left-sided colon cancer exhibited a more favorable prognosis than those with right-sided colon cancer (Supplementary Fig. 1C) ($P < 0.05$).

Impact of surgical modality on survival in patients with EOCRC and LOCRC

In this study, we examined the effect of open and laparoscopic surgeries on the survival outcomes of EOCRC and LOCRC patients. The results showed no significant differences in the survival rates between EOCRC and LOCRC patients who underwent either open or laparoscopic surgeries (Fig. 2A and B; $P > 0.05$). The results of the landmark analysis showed that the long-term survival differences in patients undergoing open surgery were not significant (Fig. 2C; $P > 0.05$). However, among patients who underwent laparoscopic surgery, EOCRC patients had a significantly higher survival rate than LOCRC patients after 5 years (Fig. 2D; $P < 0.05$). Additionally, laparoscopic surgery was associated with significantly greater survival of both EOCRC and LOCRC patients compared to open surgery (Supplementary Fig. 2A and B; $P < 0.05$).

Impact of the MMR status on the survival of patients with EOCRC and LOCRC

In this study, we analyzed 7672 patients with CRC who underwent MMR testing, including 6005 patients with LOCRC and 1667 patients with EOCRC. K-M survival curves were plotted and landmark analyses were conducted to compare the OS of dMMR patients in EOCRC and LOCRC groups. Our results showed that the difference in the 5-year survival rates between the EOCRC and LOCRC groups with either dMMR or pMMR was not significant (Fig. 3A and B; $P > 0.05$). The results of the landmark analysis showed comparable survival rates after five years between the EOCRC and LOCRC groups in dMMR patients (Fig. 3C; $P > 0.05$). Among pMMR patients, the survival rate after five years was significantly higher for the EOCRC group (Fig. 3D; $P < 0.05$). Additionally, the pMMR patients showed a significantly higher survival rate than the dMMR patients in the LOCRC and EOCRC groups (Supplementary Fig. 3A and B; $P < 0.05$). Subsequently, we analyzed the prognosis of dMMR patients at different stages, and the results showed that the prognosis of dMMR patients in TNM stages I and II was significantly better than that of patients in TNM stages III and IV (Supplementary Fig. 4A, B; $P < 0.05$).

Characteristic	Age		p-value[2]
	LO-CRC, N = 6034[a]	EO-CRC, N = 1675[a]	
Gender			0.368
Male	3561 (59.0%)	968 (57.8%)	
Female	2473 (41.0%)	707 (42.2%)	
Average age (year)	41.49	64.33	
MMR			< 0.001
dMMR	430 (7.2%)	232 (13.9%)	
pMMR	5575 (92.8%)	1435 (86.1%)	
Unknown	29	8	
TNM			< 0.001
I	1040 (19.1%)	216 (14.4%)	
II	1601 (29.4%)	455 (30.4%)	
III	1770 (32.5%)	502 (33.6%)	
IV	1042 (19.1%)	323 (21.6%)	
Unknown	581	179	
Fecal occult blood test			0.332
Positivity	4267 (70.7%)	1164 (69.5%)	
Negative	1767 (29.3%)	511 (30.5%)	
Preineural invasion			< 0.001
Positivity	4982 (82.6%)	1443 (86.1%)	
Negative	1052 (17.4%)	232 (13.9%)	
Vasculature invasion			< 0.001
Positivity	3249 (53.8%)	1039 (62.0%)	
Negative	2785 (46.2%)	636 (38.0%)	
Albumin (g/L)	40.7 ± 5.8	41.9 ± 5.9	< 0.001
Indirect bilirubin (μmol/L)	8.4 ± 5.7	8.3 ± 5.8	0.478
Alkaline phosphatase (U/L)	83 ± 50	78 ± 44	< 0.001
γ-Glutamyl Transferase (μ/L)	29 ± 60	30 ± 55	0.465
HB (g/L)	126 ± 23	124 ± 25	< 0.001
PLT (10^9)	217 ± 80	245 ± 96	< 0.001
APTT (s)	31 ± 8	32 ± 7	0.207
PT (s)	12.29 ± 1.41	12.37 ± 1.37	0.037

Table 1. EO-CRC and LO-CRC Patient demographics and baseline characteristics. HB, hemoglobin; HB, platelet; APTT, activated partial thromboplastin time; PT, prothrombin time. [a]n (%); Mean ± SD. [2]Pearson's Chi-squared test; Welch Two Sample t-test.

Impact of TNM staging on the survival of patients with EOCRC and LOCRC

As EOCRC patients are generally at an advanced TNM stage, they have received much attention from researchers. Therefore, in this study, we compared the overall survival of EOCRC and LOCRC patients at different TNM stages (I–IV) and found that EOCRC patients survived significantly longer than LOCRC patients at TNM stages I and II (Fig. 4A and B; $P < 0.05$). However, the difference in survival between the groups at TNM stages III and IV was not significant (Fig. 4C and D; $P > 0.05$).

Determining the optimal screening age

Between 2011 and 2023, our center treated 10,172 CRC patients who were 17–95 years old. These patients were categorized into four age groups: group 1 (< 30 years), group 2 (30–40 years), group 3 (40–50 years), and group 4 (> 50 years). As illustrated in Fig. 5A, the distribution was as follows: group 1 included 219 patients (2.15%), group 2 included 662 patients (6.51%), group 3 included 1810 patients (17.79%), and group 4 included 7481 patients (73.55%). We also conducted an age-proportional cumulative analysis to assess the age at initial diagnosis. The results showed an inflection point at 40 years, indicating a significant increase in the number of patients above this age (Fig. 5B).

Discussion

There are significant differences between EOCRC and LOCRC in epidemiology, clinical features, pathological features and therapeutic response. However, the comprehensive comparative study of EOCRC is not enough. in our study, We found that patients with EOCRC had a higher proportion of dMMR and earlier TNM stage than patients with LOCRC ($P < 0.05$). The 5-year survival rate of patients with EOCRC was significantly better than

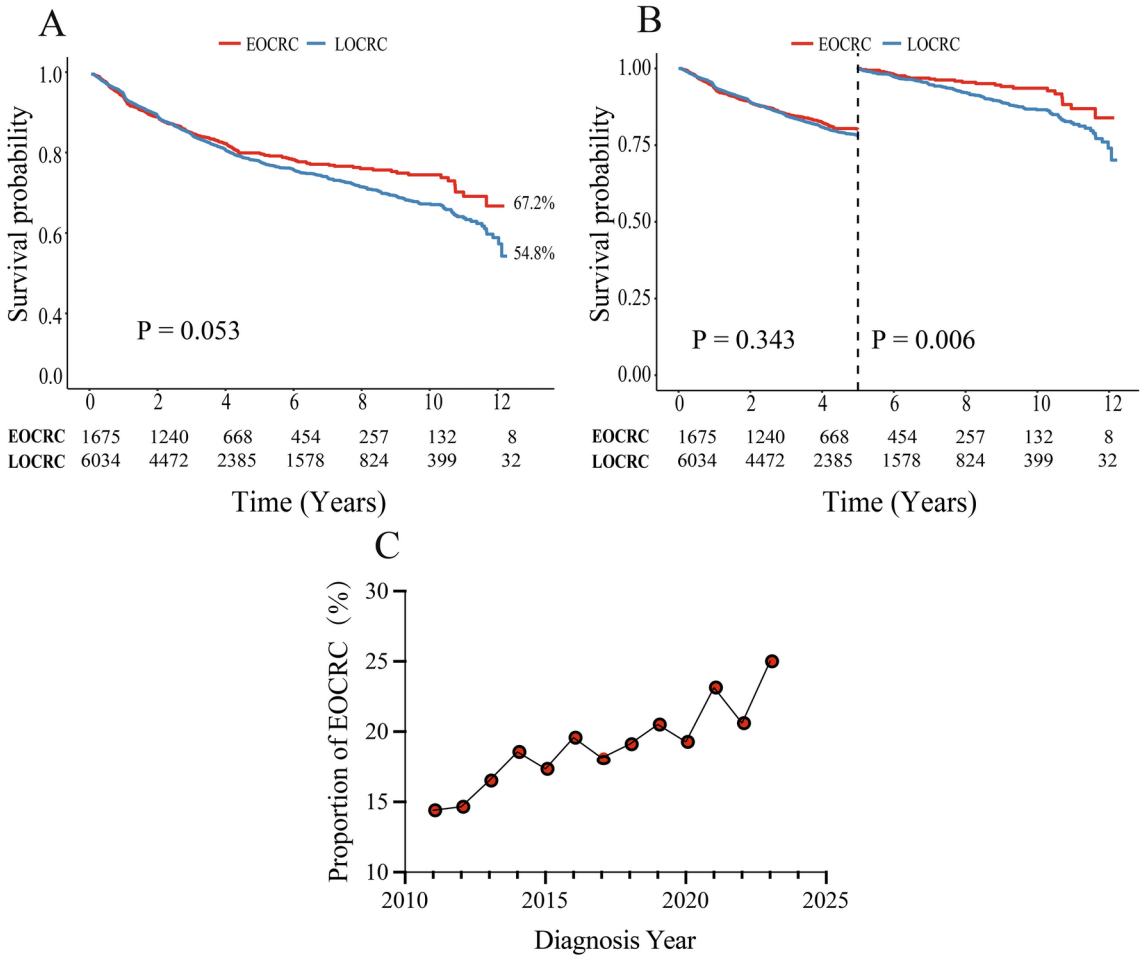

Fig. 1. Trend in the proportion of EOCRC patients in CRC patients (**A**). Kaplan–Meier estimates of survival probability in the EOCRC and LOCRC (**B**); landmark analysis distinguishes OS of EOCRC and LOCRC after 5 years of follow-up (**C**).

that of patients with LOCRC ($P < 0.05$). Laparoscopic surgery improves the long-term survival rate of patients with EOCRC. pMMR is beneficial for the long-term survival of patients with EOCRC. The survival rate of TNM stage I and II EOCRC patients was higher than that of LOCRC patients ($P < 0.05$). The age accumulation curve shows a significant increase in the number of CRC patients at age 40. Early screening for colorectal cancer is particularly important for people with long-term processed meat diets, obesity and other bad lifestyle habits.

We performed landmark analysis of patients with EOCRC and LOCRC to explore their survival. The results of the analysis showed that at 5 years, the survival rate of patients with EOCRC was not significantly different from that of patients with LOCRC. This is consistent with other research findings[21]. Although patients with EOCRC are often at a later stage of the disease when diagnosed, thanks to continuous advances in colorectal cancer treatment technology, these patients can achieve survival rates similar to those of patients with LOCRC through aggressive treatment. In clinical treatment, we also noticed that younger patients tend to respond more positively to treatment. This may have something to do with their youth advantage, which is that they are more able to withstand the side effects that may occur during treatment, or it may have something to do with the differences in biological characteristics of younger patients. after the first five years, however, LOCRC patients had significantly lower survival rates than EOCRC patients. This trend may be related to the fact that LOCRC patients are more likely to be concomitant with multiple diseases, such as cardiovascular disease and diabetes, which may impair their tolerance to treatment and affect their prognosis[22]. At the same time, as older patients age, their physiological function may gradually decline, which may also negatively affect their treatment response and recovery ability. These findings provide us with valuable insights that will help us better understand survival in patients with different stages of colorectal cancer and guide us to make more targeted decisions in future treatment strategies.

In this study, we conducted a comprehensive analysis of the clinical characteristics of patients with EOCRC and LOCRC. The findings indicated a significant advantage in the nutritional status among EOCRC patients. Compared to their LOCRC, EOCRC patients were more likely to receive an integrated approach involving genetic testing, targeted therapy, radiation therapy, and chemotherapy[23]. Notably, despite undergoing more intensive treatment regimens, EOCRC patients maintained a health-related quality of life (HRQOL) similar to

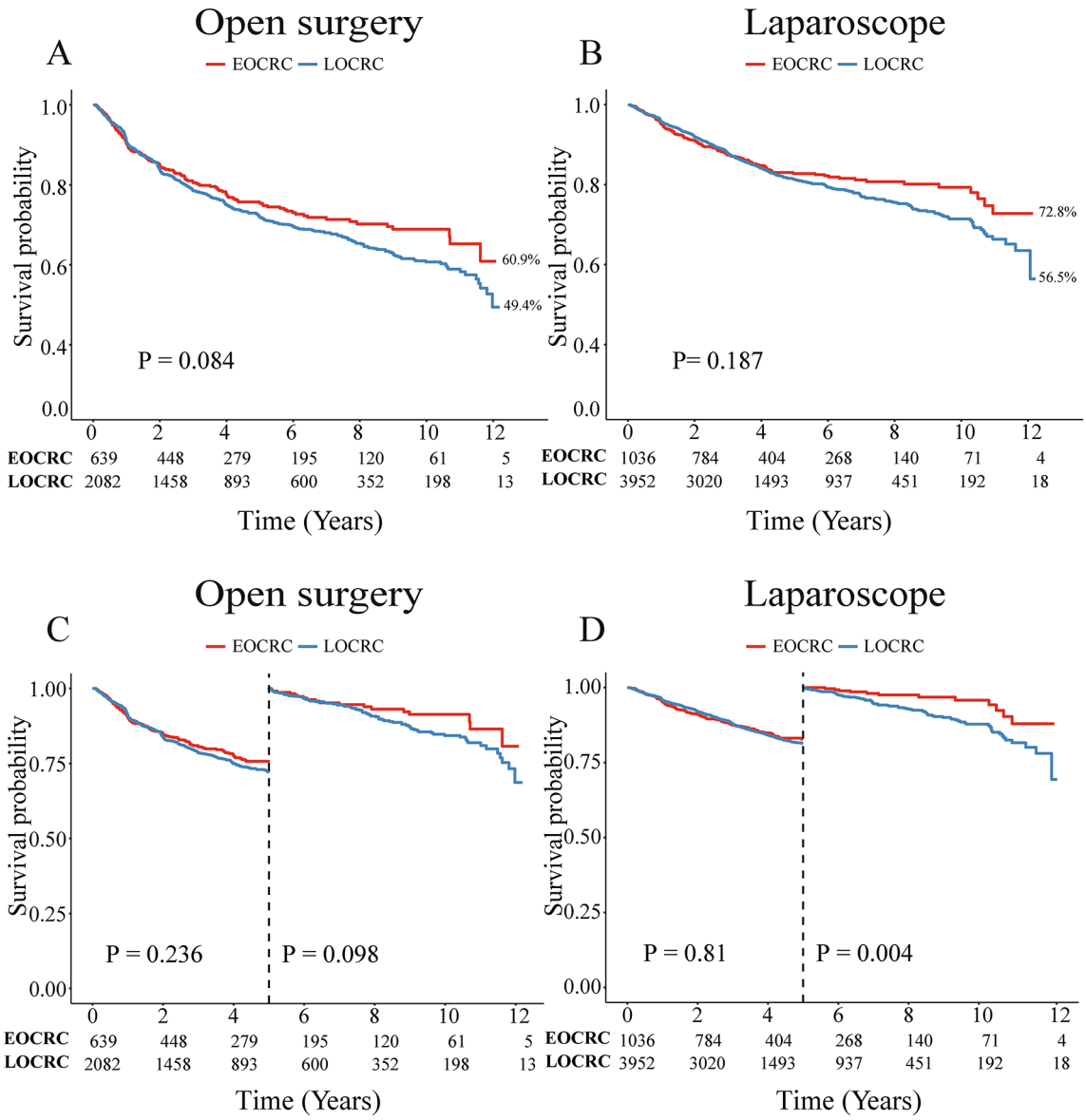

Fig. 2. Kaplan–Meier estimates of survival probabilities for EOCRC and LOCRC are shown in open surgery (**A**) and laparoscopic surgery (**B**). Landmark analysis shows survival of EOCRC and LOCRC after 5 years during Open surgery (**C**) and laparoscopic surgery (**D**).

that of LOCRC patients, suggesting better tolerance in terms of nutrition and physical function[24]. Additional baseline analyses revealed that EOCRC patients had superior albumin levels and coagulation function indicators compared to those with LOCRC. Moreover, EOCRC patients demonstrated slightly enhanced liver function and overall physical performance[17].

LS is a hereditary condition resulting from germline mutations, characterized by early onset and familial traits, which leads to a significantly more favorable prognosis compared to other CRC patients. To elucidate the distinctions between EOCRC and LOCRC, this study excluded Lynch patients based on their family history in conjunction with genetic testing results. The findings revealed that sporadic EOCRC exhibited a higher ratio of dMMR, as well as increased frequencies of perineural and vascular invasion. These findings align with those reported by Gabriel et al.[25–27], who observed an escalation in the aggressiveness of EOCRC in correlation with advancing tumor stage. In concordance, a study following the exclusion of LS, determined that the prevalence of dMMR among EOCRC patients reached 29.4%[28]. This prevalence is notably higher than that observed in the general CRC population. Furthermore, other studies have similarly reported that the proportion of dMMR in sporadic EOCRC ranges from approximately 10% to 15%[29,30]. It is noteworthy that microsatellite stable and chromosomally stable tumors are predominantly subdiploid, contrasting with the increased frequency of dMMR observed in EOCRC as opposed to LOCRC. This suggests that EOCRC possesses distinct epigenetic features[31]. This is consistent with our findings and reinforce the molecular distinctiveness of EOCRC, particularly with respect to the elevated prevalence of dMMR. These results underscore the significance of molecular markers

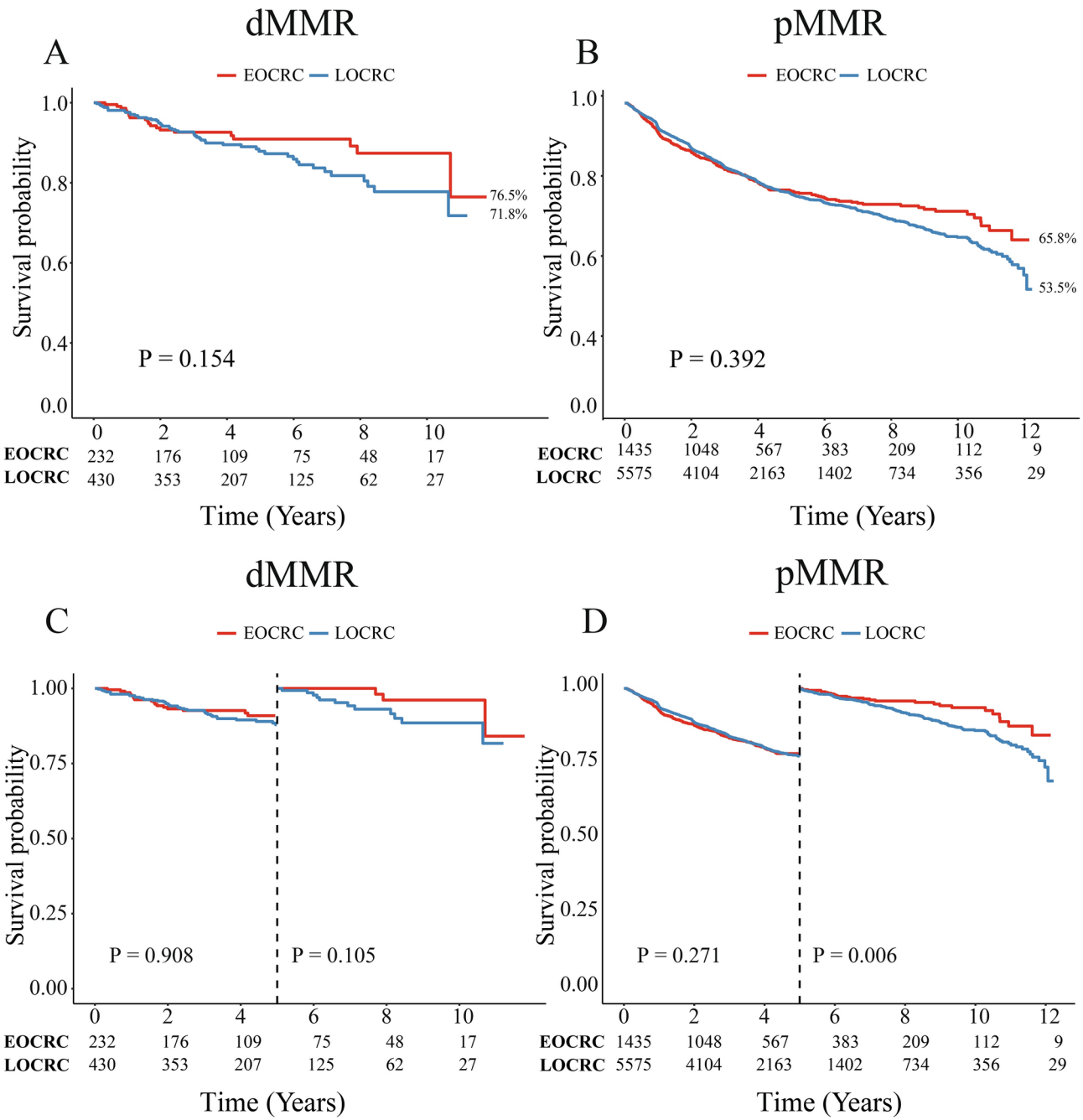

Fig. 3. Kaplan–Meier estimates of survival probabilities for EOCRC and LOCRC are shown in dMMR (**A**) and pMMR (**B**). Landmark analysis showed survival rates for EOCRC and LOCRC after 5 years in dMMR (**C**) and pMMR (**D**).

in the clinical management of EOCRC and offer a fresh avenue for research aimed at unraveling the molecular underpinnings of EOCRC and the development of targeted therapeutic strategies.

In this study, the proportion of male patients was slightly higher. This disparity may be associated with variations in the intestinal microbiome, specifically, lower levels of probiotic bacteria and higher levels of oncogenic bacteria in men, which may increase their risk of developing CRC[32]. The incidence of CRC is correlated with androgen levels[33,34], and mutations in the KRAS oncogene in male patients may increase the expression of the KDM5D gene on the Y-chromosome[35]. Other factors like smoking, alcohol consumption, and dietary habits may also contribute to this gender disparity. These findings highlighted the need to further investigate gender-specific factors related to the development of CRC.

We conducted a comparative analysis of rectal and colon cancers and found that the OS rates were similar in both groups. The patients with left-sided CRC exhibited better OS compared to those with right-sided CRC. Although the difference in OS between the early-stage EOCRC and LOCRC patients was not significant, EOCRC

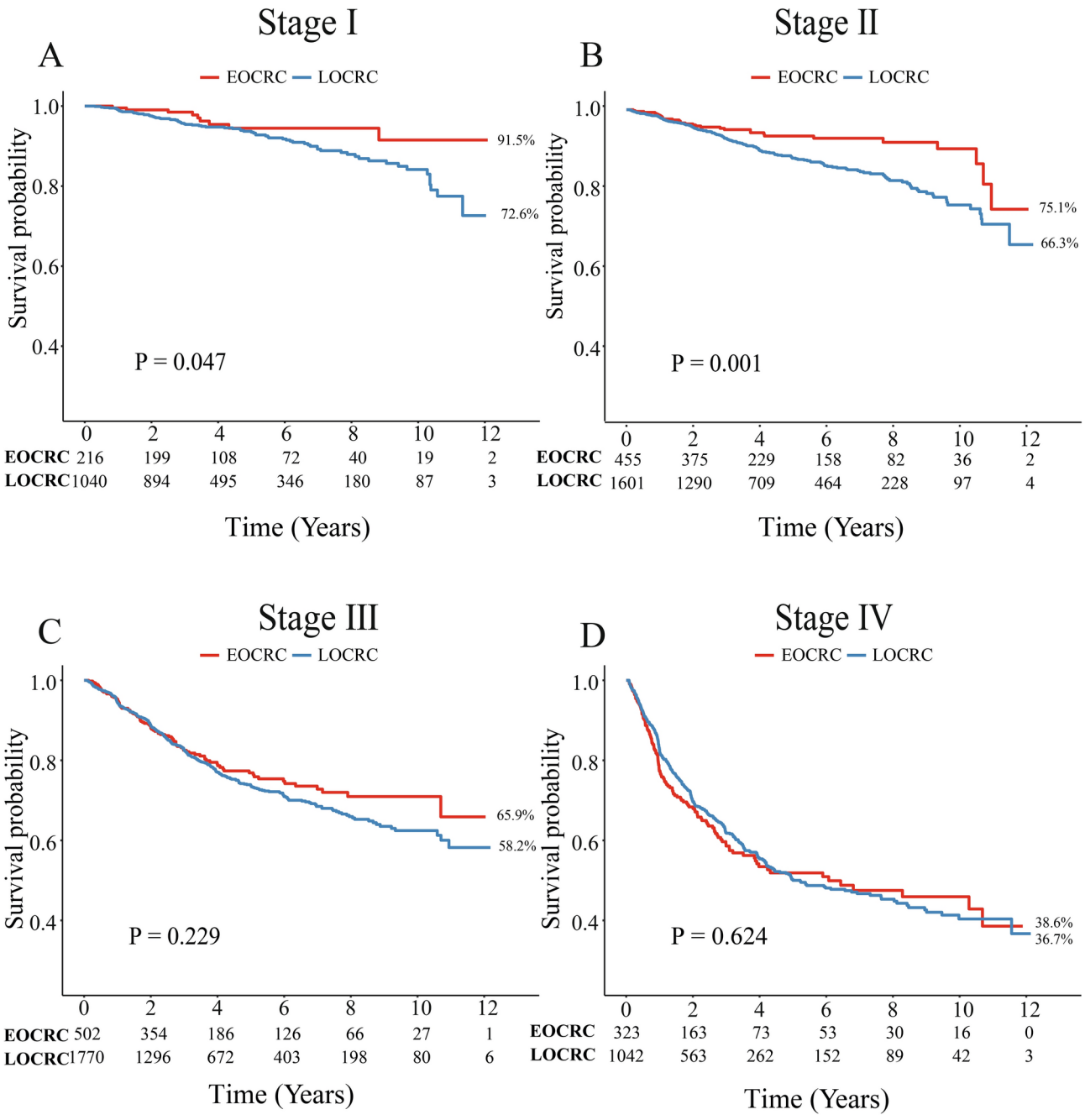

Fig. 4. Kaplan–Meier estimates of the survival probability of EOCRC and LOCRC are shown in TNM stage I (**A**), stage II (**B**), stage III (**C**), and stage IV (**D**).

patients showed a significantly higher survival rate after five years. This trend occurred probably because EOCRC patients had a higher chance of completing the treatment regimen and receiving more intensive treatment. In the last decade, the number of EOCRC cases increased considerably, imposing a greater disease burden on the younger patient group.

Furthermore, our study aimed to investigate the impact of various surgical modalities on patient survival; thus, we excluded individuals who received non-surgical interventions. Our data indicated that the proportion of patients undergoing non-surgical treatment was less than 5% in the initial cohort. To maintain consistency in baseline characteristics and facilitate a more accurate comparison between EOCRC and LOCRC, we excluded patients from both groups who had received non-surgical treatments. The findings revealed that the effect of surgical modalities on the survival of EOCRC and LOCRC patients was low. However, by comparing the groups based on surgical approach, we found that patients who underwent laparoscopic surgery showed a significantly higher survival rate than those who underwent open surgery, which matched the findings of other studies[36]. No significant difference was observed in OS between pMMR and dMMR patients in the EOCRC and LOCRC

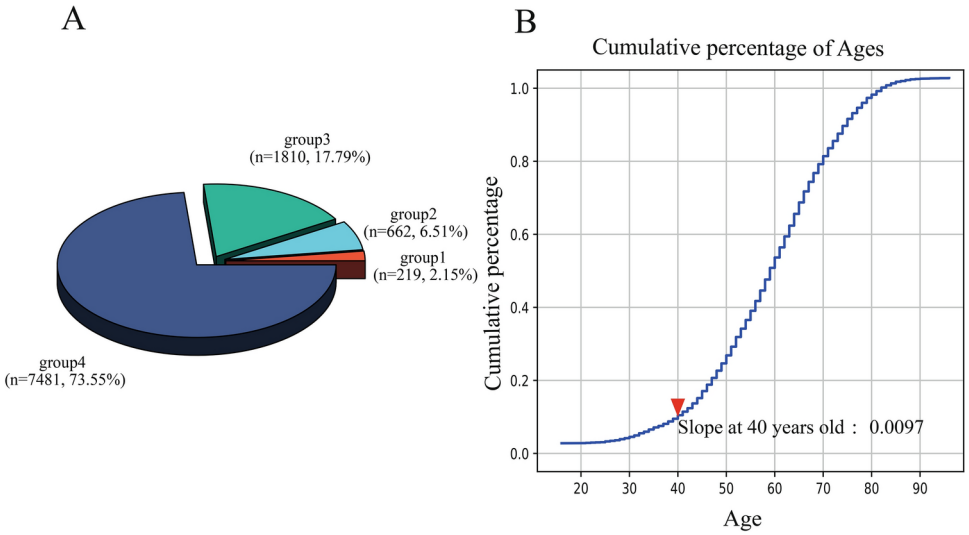

Fig. 5. The pie chart shows the percentage of patients with CRC by age group (**A**); the cumulative age proportion curve shows the age of the inflection point when the number of patients with CRC increases dramatically (**B**); Group1 is for CRC patients under 30 years old; Group2 is for CRC patients aged 30–40; Group3 is for CRC patients aged 40–50; and Group4 is for CRC patients over 50.

groups, although long-term survival was better for pMMR patients in the EOCRC group than in the LOCRC group. This difference in survival was not found among dMMR patients, probably because their sample size was smaller. The dMMR patients had higher OS than the pMMR patients. Some studies have found a significant prevalence of dMMR in EOCRC patients, with a longer five-year disease-free survival rate in the dMMR group than in the pMMR group[37,38]. These findings highlighted the need for further research on the effect of the MMR expression status in EOCRC patients.

We also found that EOCRC patients generally presented with more advanced TNM stages at diagnosis compared to LOCRC patients. The incidence of advanced disease might be higher because patients with EOCRC are generally diagnosed after the onset of symptoms, resulting in a higher incidence of late detection[39], as shown by O'Sullivan et al.[40]. In contrast, because of regular screening practices, LOCRC patients are diagnosed at earlier stages. For TNM stages I and II, the survival rate of EOCRC patients was considerably higher than that of LOCRC patients. However, in stages III and IV, the differences in the survival rate were not significant. These observations emphasized the need for early screening in younger populations to enhance survival by diagnosing diseases at lower TNM stages. Current medical guidelines suggest that screening for colorectal cancer should begin at age 50; however, this approach overlooks younger at-risk demographics. In this study, we analyzed nearly 12 years of colorectal cancer data, encompassing 10,172 cases. The incidence rate of colorectal cancer in individuals under 30 years was relatively low at 1.93% but increased sharply after the age of 40, and reached 15.93% in the 40–50-year-old age group. Correspondingly, the age-proportional cumulative curve showed a significant increase in the number of patients who were 40 years old, marking a critical inflection point.

Zaborowski et al., emphasized the need for earlier screening and risk assessment for CRC, particularly for individuals at high risk[41,42]. Studies have shown that the prevalence of young-onset adenoma is around 9%, and the prevalence increases with age. The risk for metachronous advanced neoplasia after diagnosis is around 6%[43], with a majority being disseminated cases of EOCRC. The U.S. Multi-Society Task Force (MSTF) on CRC recommends screening all relatives ($\geq$40 years old) of CRC patients diagnosed before 60 years[44]. The 2023 CSCO guidelines suggested regular CRC screening from 50 years of age for those at average risk. Only about 20% of individuals diagnosed with CRC before 50 years carry a cancer-related genetic mutation[45]. After implementing standardized screening guidelines in the United States in 2000, the incidence and mortality of CRC decreased. This decrease is particularly noticeable among those who are 65 years old and older and undergo regular screening. In contrast, an approximate annual increase of 2% was found in the incidence of proximal, distal colon, and rectal cancers in individuals under 50. This increase was most pronounced in the 20–29-year-old age group[46]. A recent large-scale screening study in China involving nearly 100,000 residents suggested initiating screening for CRC at over 40 years of age[47].

Considering that some individuals may have additional risk factors, initiating CRC screening at 50 years may lead to more advanced disease stages and poorer prognosis. Because of the prevalent sedentary lifestyle and unhealthy diet, earlier screening for specific populations is advisable. We recommend that CRC screening should start at age 40 in the Chinese population, particularly for groups with a higher incidence of the disease or other risk factors. Lowering the screening age can reduce the tumor burden on EOCRC patients, which can decrease the incidence and mortality rates.

This study provided insights into the differences between EOCRC and LOCRC patients. However, it had certain limitations. First, as it was a retrospective cohort study, the partial lack of baseline patient information may have affected the precision of our interpretations. Second, as this was a single-center study, our findings

may not fully represent other populations and cannot be used to analyze CRC incidence trends among patients over 40, based on demographic data. Additionally, the analysis of EOCRC patient subgroups was limited due to incomplete MMR testing and a relatively small sample size. Despite these limitations, our study provided important insights into the clinical characteristics of EOCRC patients and their differences from LOCRC patients, corroborated by other relevant studies. Our findings highlighted the importance of early screening of EOCRC patients to lower their TNM stage and improve survival outcomes.

Conclusions

The long-term survival rate of EOCRC patients was higher than that of LOCRC patients, especially for those with pMMR, TNM stages I–II, and who underwent laparoscopic surgery. Due to the substantial increase in CRC cases starting at age 40, we recommend starting CRC screening for high-risk groups in China at and above this age. This approach can decrease CRC related mortality and enhance the prognosis for younger patients, thus facilitating early diagnosis and treatment.

Materials and methods

General information

Between January 2011 and December 2021, 10,172 patients diagnosed with CRC were admitted to Xijing Hospital and treated. Among them, 7709 patients were regularly followed up, including 1675 cases of EOCRC and 6034 cases of LOCRC. Information on clinical variables such as age, gender, albumin, globulin, direct and indirect bilirubin, alkaline phosphatase, γ-glutamyl transferase, alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), carbohydrate antigen 19–9 (CA199), carbohydrate antigen 125 (CA125), fecal occult blood test, hemoglobin (HB), platelet count (PLT), activated partial thromboplastin time (APTT), prothrombin time (PT), mismatch repair (MMR), S-100, CD34, and TNM stage was collected. Peripheral venous blood was collected from the patients at 6:00 a.m. before treatment. Serum levels of tumor biomarkers (CEA, CA199) were measured using a Cobas 8000 analyzer. The inclusion criteria were as follows: (1) pathological diagnosis of CRC, (2) complete follow-up information, and (3) surgical resection of CRC. The exclusion criteria were as follows: (1) multiple primary tumors; (2) Rule out known genetic syndromes, such as Lynch syndrome, through family history and genetic test results.; (3) less than one month of follow-up; (4) incomplete visit information, (5) other malignant diseases, (6) colorectal invasion by malignant tumors from other organs, and (7) recurrent CRC.

This study was approved by the Medical Ethics Committee of XiJing Hospital (No. KY20232232-F-1) in 2023. The study was approved by the ChiCTR platform (https://www.chictr.org.cn/showproj.html?proj=206034, registration number: ChiCTR2300075253).The study was retrospective, in which oral informed consent was obtained during telephone follow-up with patients. The study protocol was approved by the ethics committee. The study were performed in accordance with the relevant guidelines and regulations.

Observation indicators and evaluation criteria

All CRC patients were followed up until November 2023 after surgery. Follow-up appointments were scheduled every three months in the first year and every 6 months thereafter. Outpatient reviews were the primary method of follow-up, with telephone consultations performed if required. The study endpoint was OS. The pathological tissues obtained through surgery were stained with hematoxylin and eosin (H&E), and the pathologist made the pathological diagnosis. The clinical and pathological characteristics of the patients were evaluated, and the clinicopathological differences between EOCRC and LOCRC were compared and analyzed. Additionally, survival analysis was conducted to compare the five-year and 10-year survival rates of the two groups.

Statistical analysis

Statistical analyses were conducted using the R software (version 4.2.2). Data distribution was assessed by conducting a normality test, and appropriate descriptive statistics were used for variables that followed a normal/non-normal distribution. Survival curves were generated and compared using the Kaplan–Meier (K–M) method and the log-rank test. Segmented survival curves were plotted using Landmark analysis with a five-year cutoff point. The statistical analyses were conducted and plots were constructed using R-related software packages, including survival, survminer, ggplot2, and ggforce. All differences were considered to be statistically significant at $P < 0.05$ (two-tailed).

Data availability

Access of data and corresponding codes could be provided upon reasonable request with the consent of the corresponding authors.

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Author contributions
JL, XC and PY designed the study. JS , TH and LQ contributed to the conception of the study and completed the manuscript together. JZ, YQ and SL contributed significantly to statistical analysis and manuscript preparation. All authors contributed to the article and approved the submitted version.

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