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Clinicopathological features and prognosis analysis of proximal colonic mucinous adenocarcinoma

Fei Han[1], Yue Xu[2], Xiangyu Li[1], Zhaoxiang Song[1], Jinlin Xie[1] & Jianning Yao[1]✉

Mucinous adenocarcinoma (MAC) is a distinct subtype of colorectal cancer. Previous studies have confirmed the poor prognosis of rectal or left-sided colon MAC, while the prognosis and response to chemotherapy in proximal colon MAC remains controversial. The aim of this study was to investigate the clinicopathological characteristics, prognosis, response to chemotherapy, and risk prediction factors of proximal colon MAC. Patients with proximal colon MAC and non-mucinous adenocarcinoma (NMAC) were retrospectively analyzed in this study. The analyzed variables included gender, age, smoking, drinking, chemotherapy, metastasis, pathological stage, and tumor size. Overall survival (OS) was the primary outcome. Kaplan–Meier analysis was used to assess the impact of mucinous subtype and chemotherapy on OS. We conducted univariate and multivariate Cox regression analyses to determine prognosis factors for proximal colon MAC and NMAC. A total of 284 cases of proximal colon MAC and 1384 cases of NMAC were included in the study. Compared to NMAC, proximal colon MAC was diagnosed at a younger age. The proportion of synchronous and metachronous metastasis was also higher, as well as the pathological stage and tumor size. Proximal colon MAC had a worse prognosis than NMAC, especially in stage 3. Moreover, the prognosis of proximal colon NMAC improved after chemotherapy, while MAC showed no improvement in prognosis after chemotherapy. Advanced age, N1 and N2 stage were independent prognostic factors for adverse outcomes in MAC. For proximal colon adenocarcinoma, the independent predictors of adverse outcomes included mucinous subtype, order age, N1 and N2 stages, and pathological stage 4. Proximal colon MAC had a worse prognosis compared to NMAC. Chemotherapy did not improve the prognosis of proximal colon mucinous adenocarcinoma.

Keywords Proximal colon, Mucinous adenocarcinoma, Clinicopathological characteristics, Prognosis

Worldwide, colorectal cancer (CRC) ranks third among cancers diagnosed and second among cancer-related deaths[1–3]. It is also the second most common malignancy in males, second only to lung cancer, and the third most common in females, after breast and lung cancer[4]. It poses a significant burden on global health. The most common histological subtype of colorectal cancer is adenocarcinoma, accounting for over 90% of cases. Mucinous adenocarcinoma (MAC) is a unique subtype characterized by abundant extracellular mucin, constituting at least 50% of the tumor volume[5]. Statistics show that 10–20% of CRC patients belong to the mucinous subtype[6,7]. The incidence of MAC is lower in Asian colorectal cancer patients (4–5%)[8–10], while it is higher in Western countries[11–14].

MAC has been reported to have distinct clinical and pathological features compared tonon-mucinous adenocarcinoma (NMAC). MAC has a higher proportion of proximal colon tumors than NMAC (35.0% vs. 18.9% in China)[15]. MAC also exhibits a higher degree of microsatellite instability[16], a higher proportion of female and young patients[17–20], and some studies indicate a poorer prognosis for MAC[13,21–23]. Although previous studies have generally reported a poorer prognosis for MAC compared to NMAC, some researchers believe that this is due to the unfavorable prognosis of MAC in the rectum or left-sided colon[8,24–26]. And there is still controversy regarding the prognosis of proximal colon MAC. Some studies suggest that its prognosis is similar or even slightly better than that of proximal NMAC[26]. Therefore, we have narrowed the scope of our study to the more controversial and relatively less researched proximal colon, aiming to investigate the unique clinical and pathological characteristics and prognosis of proximal colon MAC compared to NMAC. Due to the rarity of this disease, there are currently no guidelines for treating colorectal MAC[27]. Patients with mucinous colorectal adenocarcinoma are currently

[1]Department of Gastroenterology, The First Affiliated Hospital of Zhengzhou University, No. 1 Jianshe East Road of Erqi District, Zhengzhou 450052, China. [2]Department of Pathology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, China. ✉email: rjyy@zzu.edu.cn

treated based on the standard guidelines for CRC, andthere is little information available about MAC treatment methods and prognoses. Current research has suggested that MAC may have impaired response to conventional chemotherapy[28,29]. Considering the unique histological characteristics of MAC, patients with colorectal MAC require personalized and precise treatment[30]. A comprehensive evaluation of the chemotherapy efficacy in MAC and predictive factors associated with overall survival (OS) not only helps identify patients at higher risk but also plays a vital role in reevaluating the effectiveness of existing treatment approaches and driving the exploration of personalized treatment options for MAC. Therefore, in order to further analyze and summarize the clinical and pathological characteristics of proximal colon mucinous adenocarcinoma, understand the prognosis of proximal colon mucinous adenocarcinoma, the impact of chemotherapy on prognosis, and independent predictive factors for adverse outcomes, a retrospective analysis of clinical data from patients admitted to our hospital with proximal colon cancer was conducted.

Methods

Study population

Clinical data from patients with proximal colon cancer who underwent surgery at the First Affiliated Hospital of Zhengzhou University from 2011 to 2021 were retrospectively analyzed. The patients were divided into 284 cases of proximal colon MAC and 1384 cases of proximal colon NMAC. All relevant data and examination results were obtained from the hospital's medical record system. Following are the inclusion criteria: (1) Diagnosis of MAC confirmed by pathological examination; (2) Patients who underwent surgical treatment. Below are the exclusion criteria: (1) Incomplete clinical data; (2) Unknown mucin proportion; (3) Multiple primary tumors in the colon or signet ring cell carcinoma; (4) Patients with lost or missing data during the follow-up period.

Study methods

A retrospective cohort study was conducted, collecting and analyzing clinical data of patients, including gender, age, smoking, drinking, chemotherapy status, T stage, N stage, synchronous and metachronous metastasis, pathologic stage, and tumor size. OS was defined as the time between surgery and death which was the primary outcome. Synchronous metastasis was defined as metastasis occurring within six months after surgery. As defined by the World Health Organization (WHO) classification of digestive system tumors 5th ed[31], mucinous adenocarcinoma was defined as a tumor with extracellular mucinous material comprising more than 50% of the tumor volume. Union for International Cancer Control (UICC) 8th edition classification of malignant tumors was used to determine the pathological stage[32].Clinical and pathological features of proximal colon MAC and NMAC were compared, and statistically significant differences were obtained for specific variables. The impact of mucinous subtype and chemotherapy on prognosis was explored using the Kaplan–Meier method. An analysis of prognostic risk factors was carried out using the Cox regression model. Variables with a p value < 0.05 in univariate analysis or those clinically believed to be closely related to patient prognosis were included in a multivariable Cox analysis to investigate independent prognostic factors for poor outcomes in MAC and NMAC. This study was approved by the Ethical Committee of Scientific Research and Clinical Trials of the First Affiliated Hospital of Zhengzhou University (2023-KY-0320z-001), and was conducted in accordance with the guidelines of the Declaration of Helsinki. This was a retrospective cohort study, and the requirement for informed consent from the study subjects was waived by the Ethical Committee of Scientific Research and Clinical Trials of the First Affiliated Hospital of Zhengzhou University.

Statistical analysis

Data was analyzed using SPSS version 26.0 statistical software and R version 4.2.2. Categorical data were presented as counts (n) and percentages (%), and the chi-square test was used to compare the two groups. Normally distributed continuous data were expressed as mean ± standard deviation and compared using the two-sample t-test. Skewed distributed continuous data were expressed as median (interquartile range) and compared using non-parametric tests (Mann–Whitney U test). Survival analysis was conducted using the Kaplan–Meier method, and log-rank tests were used to compare survival rates between groups. An analysis of prognostic risk factors was carried out using the Cox regression model, in which factors with a p value < 0.05 in univariate analysis were included in the multivariate analysis. Hazard ratios (HRs) were reported as point estimates with 95% confidence intervals (CIs). All tests were two-sided, and a p value less than 0.05 was considered statistically significant.

Results

Clinicopathological features

A total of proximal colon cancer patients who underwent surgical treatment at the First Affiliated Hospital of Zhengzhou University from January 2011 to December 2021 were included in the study, including 284 cases of MAC and 1384 cases of NMAC. The average follow-up time was 62.15 months. The median age (IQR) for MAC and NMAC was 56 (19.75) years and 60 (19) years, respectively. In the MAC group, 145 (51.1%) were male, while 776 (56.1%) were male in the NMAC group. Among the MAC patients, 206 received chemotherapy; among the NMAC patients, 991 received chemotherapy. Table 1 shows the clinical and pathological characteristics of the patients. Compared to NMAC, MAC patients were diagnosed at a younger age, had higher pathological T and N stages, a higher proportion of synchronous and metachronous distant metastasis, higher pathological staging, and larger tumor size.

Survival analysis

The cohort of proximal colon MAC consisted of 284 patients, among whom 206 patients received chemotherapy. The NMAC cohort consisted of 1384 patients, with 991 patients receiving chemotherapy.When not considering

	MAC N = 284 (17.0%)	NMAC N = 1384 (83.0%)	*p* value
Gender			
Female	139 (48.9%)	608 (43.9%)	0.122
Male	145 (51.1%)	776 (56.1%)	
Age (years), median (i.q.r.)	56 (19.75)	60 (19.00)	**< 0.001**
Smoke			
No	233 (82.0%)	1138 (82.2%)	0.941
Yes	51 (18.0%)	246 (17.8%)	
Drink			
No	255 (89.8%)	1246 (90.0%)	0.902
Yes	29 (10.2%)	138 (10.0%)	
Adjuvant chemotherapy			
No	78 (27.5%)	393 (28.4%)	0.660
5-Fu	10 (3.5%)	63 (4.6%)	
5-FU + oxaliplatin	157 (55.3%)	733 (53.0%)	
5-FU + irinotecan	14 (4.9%)	51 (3.7%)	
Unknown	25 (8.8%)	144 (10.4%)	
Metachronous metastases			
No	237 (83.5%)	1306 (94.4%)	**< 0.001**
Yes	47 (16.5%)	78 (5.6%)	
T stage			
T1	0 (0.0%)	19 (1.4%)	**< 0.001**
T2	24 (8.5%)	171 (12.4%)	
T3	65 (22.9%)	433 (31.3%)	
T4	195 (68.7%)	761 (55.0%)	
N stage			
N0	169 (59.5%)	885 (63.9%)	**0.002**
N1	54 (19.0%)	314 (22.7%)	
N2	61 (21.5%)	185 (13.4%)	
Synchronous metastases			
No	230 (81.0%)	1216 (87.9%)	**0.002**
Yes	54 (19.0%)	168 (12.1%)	
Pathologic stage			
I	15 (5.3%)	157 (11.3%)	**0.001**
II	133 (46.8%)	673 (48.6%)	
III	82 (28.9%)	386 (27.9%)	
IV	54 (19.0%)	168 (12.1%)	
Size (cm), median (i.q.r.)	6.25 (3.5)	5 (3)	**< 0.001**

Table 1. Clinicopathological characteristics of patients with proximal colon mucinous and nonmucinous adenocarcinomas. Values are presented as frequency (corresponding percentage) or median (IQR). Bolded *p* values are statistically significant values. *MAC* mucinous adenocarcinoma, *NMAC* non-mucinous adenocarcinoma, *5-FU*5 fluorouracil, *IQR* interquartile range.

tumor pathological staging, MAC of the proximal colon had a worse prognosis compared to NMAC (5 years OS: 77.9% vs. 88.0%, $p < 0.001$) (Fig. 1A). However, when considering pathological staging, only stage 3 MAC showed a significantly worse prognosis compared to NMAC (5 years OS: 66.9% vs. 87.2%, $p < 0.001$) (Fig. 1B). When considering the chemotherapy factor, the prognosis of NMAC of the proximal colon improved (5 years OS: 84.8% vs. 89.3%, $p = 0.004$) (Fig. 2A), primarily observed in stage 2 and stage 3 patients (89.0% vs. 96.0%, $p = 0.001$ and 76.7% vs. 90.2%, $p < 0.001$) (Fig. 2B). In contrast, MAC patients did not show a better survival rate after receiving adjuvant chemotherapy (Fig. 3A,B). Setting significance level at 0.05, power anaylsis showed that using the sample size (n = 1668) to detect the survival difference between the MAC and NMAC groups was reliable, with a power of 0.99.

Univariate and multivariate Cox analysis of the prognostic factors

Univariate Cox analysis showed that adverse prognostic factors for survival in proximal colon MAC patients were older age, N1 and N2 stage, pathologic stage 4 and smaller tumor size (Table 2). Incorporating these factors into the multivariable Cox regression analysis revealed that advanced age ($P < 0.001$, HR = 1.037), N1 stage ($P = 0.029$, HR = 3.752) and N2 stage ($P < 0.001$, HR = 7.823) were independent predictive factors for poor outcomes in MAC. For NMAC, the independent prognostic factors for poor outcomes were advanced age ($P < 0.001$,

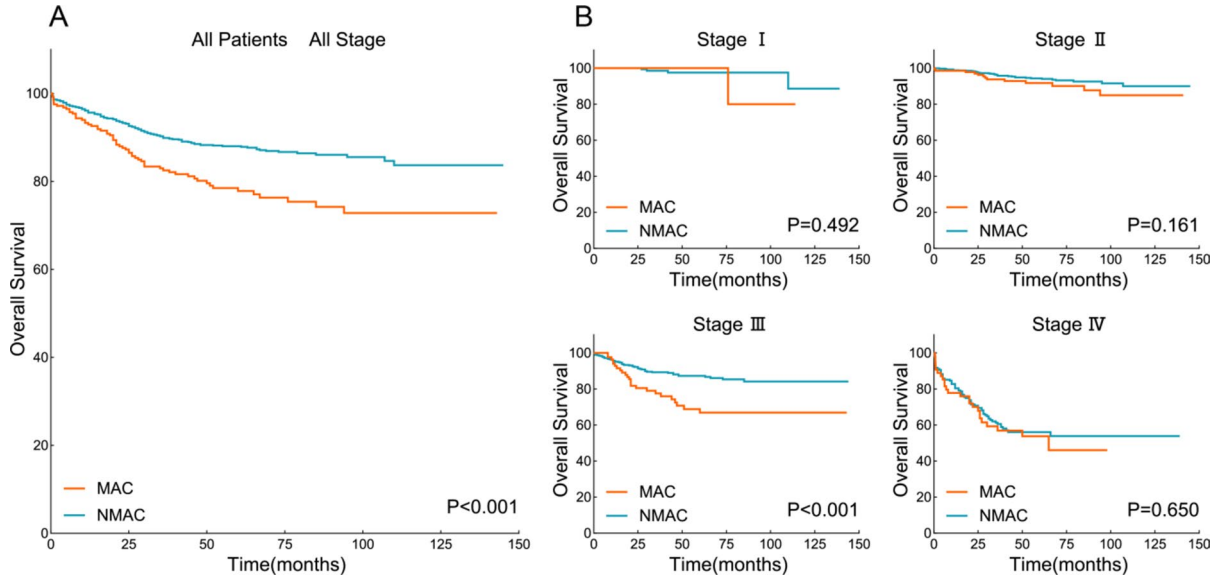

Figure 1. Kaplan–Meier curves stratified by mucus components for proximal colon adenocarcinoma. (**A**) All stages; (**B**) according to pathologic stages.

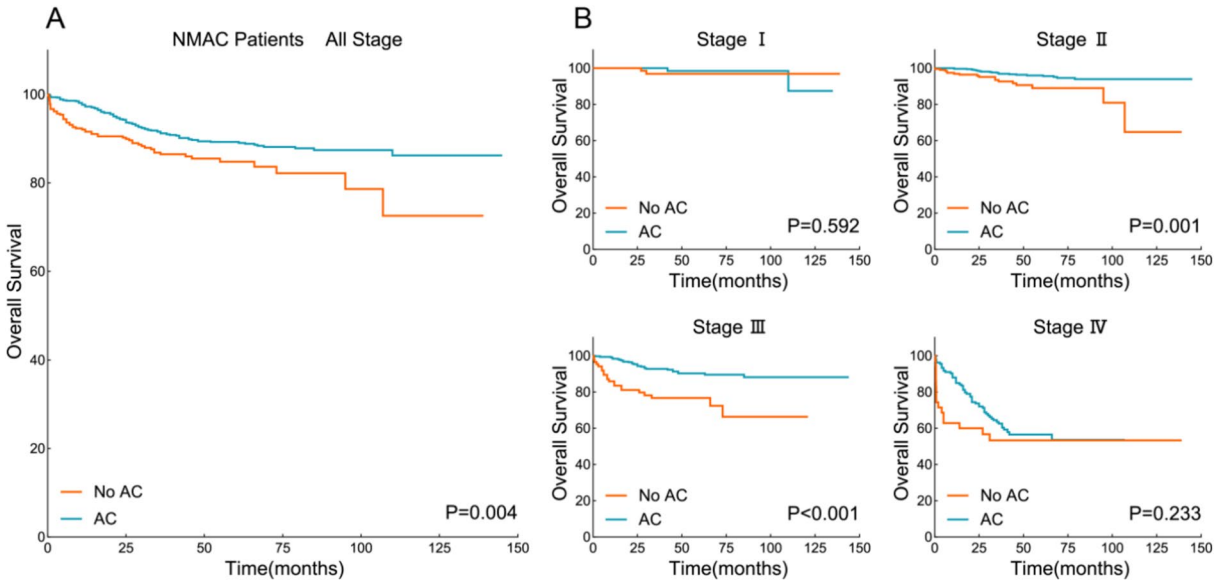

Figure 2. Kaplan–Meier curves stratified by adjuvant chemotherapy for proximal colon nonmucinous adenocarcinoma. (**A**) All stages; (**B**) according to pathologic stages.

HR = 1.041), N2 stage ($P < 0.001$, HR = 2.882), and pathological stage IV ($P < 0.001$, HR = 14.416). Additionally, adjuvant chemotherapy ($P = 0.028$, HR = 0.674) was identified as an independent protective factor for NMAC (Table 3). When conducting the Cox regression analysis on proximal colon adenocarcinoma, after adjusting for factors such as pathological stage and age, the mucinous subtype was found to be an independent prognostic factor for poor outcomes ($P < 0.001$, HR = 1.888) (Table 4).

Discussion

MAC is a distinct pathological subtype first described by Parham in 1923[33]. Studies have shown that MAC and NMAC exhibit significantly different clinical and pathological characteristics. Previous research has indicated that MAC is more common in women and younger patients[17,34,35]. Our data showed that MAC patients were younger than NMAC patients, and this difference was statistically significant, in line with previous research. Compared to previous studies, there was one significant difference: our data showed that although the proportion of female patients was higher in the MAC group compared to NMAC, the difference was not significant. Similar to previous research[9,10], MAC was more prone to lymph node metastasis and distant metastasis, both synchronous and metachronous, and correspondingly, had a higher pathological stage, consistent with MAC's more aggressive biological behaviour.

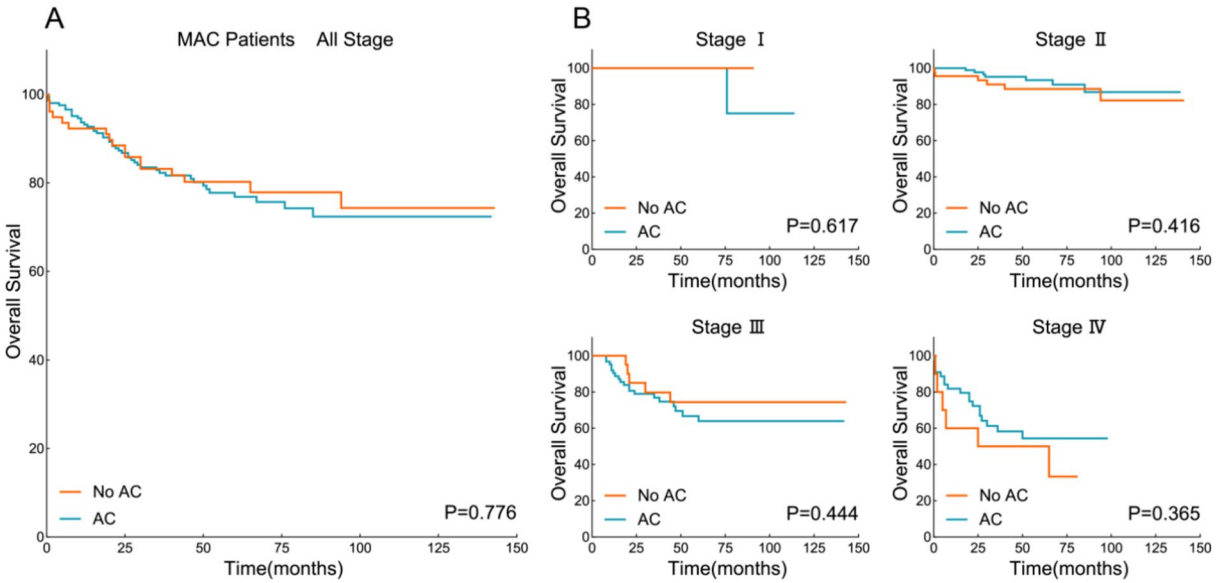

Figure 3. Kaplan–Meier curves stratified by adjuvant chemotherapy for proximal colon mucinous adenocarcinoma. (**A**) All stages; (**B**) according to pathologic stages.

Variable (MAC)	Univariate			Multivariate		
	HR	95%CI	*p* value	HR	95% CI	*p* value
Gender						
Female	1					
Male	0.635	0.383–1.053	0.078			
Age	1.025	1.006–1.044	**0.010**	1.037	1.018–1.056	**< 0.001**
Smoke						
No	1					
Yes	0.724	0.357–1.469	0.372			
Drink						
No	1					
Yes	0.841	0.395–2.130	0.918			
Chemotherapy						
No	1					
Yes	1.084	0.620–1.896	0.777			
T stage						
T2	1					
T3	4.005	0.913–17.578	0.066			
T4	3.033	0.736–12.502	0.125			
N stage						
N0	1			1		
N1	2.812	1.398–5.656	**0.004**	3.752	1.144–12.299	**0.029**
N2	6.378	3.547–11.469	**< 0.001**	7.823	2.605–23.494	**< 0.001**
TNM stage						
I	1			1		
II	1.477	0.193–11.290	0.707	0.973	0.126–7.540	0.979
III	5.021	0.679–37.127	0.114	0.600	0.061–5.929	0.662
IV	10.298	1.391–76.244	**0.022**	2.655	0.295–23.877	0.384
Size	0.901	0.820–0.991	**0.032**	0.935	0.847–1.033	0.186

Table 2. Univariate and multivariate Cox regression analysis of OS in patients with proximal colon mucinousadenocarcinoma. Bolded *p* values are statistically significant values. *MAC* mucinous adenocarcinoma, *HR* hazard ratio, *CI* confdence interval.

Variable (NMAC)	Univariate			Multivariate		
	HR	95%CI	*p* value	HR	95%CI	*p* value
Gender						
Female	1					
Male	0.765	0.561–1.041	0.089			
Age	1.043	1.029–1.057	**< 0.001**	1.041	1.027–1.056	**< 0.001**
Smoke						
No	1					
Yes	0.744	0.479–1.157	0.190			
Drink						
No	1					
Yes	0.704	0.391–1.268	0.242			
Chemotherapy						
No	1			1		
Yes	0.625	0.451–0.866	**0.005**	0.674	0.475–0.958	**0.028**
T stage						
T1	1					
T2	0.268	0.054–1.331	0.107			
T3	0.771	0.186–3.201	0.720			
T4	1.192	0.294–4.829	0.806			
N stage						
N0	1			1		
N1	2.675	1.842–3.884	**< 0.001**	1.753	0.973–3.156	0.062
N2	4.752	3.259–6.928	**< 0.001**	2.882	1.611–5.154	**< 0.001**
TNM stage						
I	1			1		
II	2.229	0.795–6.244	0.127	2.267	0.806–6.375	0.121
III	5.240	1.891–14.521	**0.001**	2.511	0.779–8.088	0.123
IV	22.540	8.223–61.785	**< 0.001**	14.416	4.808–43.227	**< 0.001**
Size	0.942	0.881–1.008	0.083			

Table 3. Univariate and multivariate Cox regression analysis of OS in patients with proximal colon nonmucinousadenocarcinoma. Bolded *p* values are statistically significant values. *NMAC* non-mucinous adenocarcinoma, *HR* hazard ratio, *CI* confdence interval.

Many studies have compared the survival outcomes of MAC with NMAC. However, the prognostic significance of the mucinous colorectal cancer subtype remains controversial. In some studies, the survival rate of patients with mucinous and non-mucinous subtypes was similar[35–37]. In a population-based study, after multivariate analysis and propensity score matching, mucinous histology had no negative impact on survival rates[36]. Similarly, in a study based on national cancer registries, Ott et al.[35] reported no significant differences in survival rates for stage I, II, and III colon cancer. However, some studies suggest that MAC often has a worse prognosis than NMAC[38,39]. A study based on the SEER database showed that after adjusting for tumour pathological staging, the prognosis of stage II, III, and IV MAC was worse compared to the corresponding pathological stages of NMAC[39]. However, Hugen et al.[34] suggested that the adverse prognosis of MAC was limited to rectal cancer and did not apply to colon cancer. Catalano et al. [40] argued that the poor prognosis of rectal MAC drives the controversy regarding the prognosis of colorectal MAC. Meanwhile, colon MAC and NMAC do not differ significantly. Therefore, most studies confirm the poor prognosis of rectal MAC, while the prognosis of colon MAC remains highly debated, and few studies consider the subgroups of proximal colon MAC and NMAC (Supplementary Information 1).

Our study focused on the proximal colon, where interval colorectal cancer is more likely to occur[41,42]. The results revealed that MAC in the proximal colon has a worse prognosis compared to NMAC, particularly among patients in stage 3 of the disease.Actually, patients with stage 1 colon cancer generally have a better prognosis, and the NCCN guidelines do not recommend chemotherapy for stage 1 colon cancer patients[43]. The prognosis for stage 4 patients is generally poor regardless of whether chemotherapy is administered. However, for stage 3 colon cancer patients, although their prognosis is worse compared to stage 1 and 2 patients, they often experience improved survival benefits through adjuvant chemotherapy and curative surgery[44–46]. The results of our survival analysis mainly demonstrate that, among stage 3 proximal colon cancer patients, MAC has a worse prognosis compared to NMAC, and NMAC patients in stage 3 show a significant improvement in survival after adjuvant chemotherapy, while MAC patients in stage 3 exhibit poor response to chemotherapy. This finding raises questions about the effectiveness of current treatment approaches for MAC and suggests that when formulating treatment plans, the mucinous subtype should be considered as an important factor. Further exploration of

Variable	Univariate			Multivariate		
	HR	95% CI	*p* value	HR	95%CI	*p* value
Histology						
Nonmucinous	1			1		
Mucinous	1.880	1.402–2.520	<**0.001**	1.888	1.395–2.554	<**0.001**
Gender						
Female	1			1		
Male	0.716	0.551–0.931	**0.013**	1.045	0.797–1.371	0.749
Age	1.035	1.024–1.046	<**0.001**	1.040	1.029–1.052	<**0.001**
Smoke						
No	1					
Yes	0.742	0.510–1.079	0.119			
Drink						
No	1					
Yes	0.763	0.471–1.235	0.271			
Chemotherapy						
No	1			1		
Yes	0.709	0.536–0.939	**0.016**	0.806	0.596–1.091	0.163
T stage						
T1	1					
T2	0.309	0.066–1.458	0.138			
T3	0.958	0.233–3.936	0.953			
T4	1.310	0.324–5.288	0.705			
N stage						
N0	1			1		
N1	2.673	1.924–3.713	<**0.001**	2.193	1.292–3.722	**0.004**
N2	5.384	3.936–7.364	<**0.001**	3.886	2.336–6.466	<**0.001**
TNM stage						
I	1			1		
II	2.181	0.870–5.463	0.096	1.886	0.750–4.748	0.178
III	5.694	2.301–14.090	<**0.001**	1.782	0.629–5.050	0.277
IV	20.552	8.354–50.563	<**0.001**	9.441	3.528–25.271	<**0.001**
Size	0.950	0.900–1.002	0.057			

Table 4. Univariate and multivariate Cox regression analysis of OS in patients with proximal colonadenocarcinoma. Bolded *p* values are statistically significant values. *HR* hazard ratio, *CI* confdence interval.

treatment strategies that are more suitable for mucinous adenocarcinoma is needed to achieve more personalized and targeted treatment. Proximal colon mucinous adenocarcinoma has a poorer prognosis and shows a poor response to adjuvant chemotherapy, which may be related to its unique clinical and pathological characteristics and genetic features. Previous analyses have also shown that although MAC patients are relatively younger, they have a higher tendency for lymphatic spread, local and distant metastasis, indicating a more aggressive biological behaviour. One hypothesis for the higher incidence of lymph node and peritoneal metastasis in MAC is that under the pressure of abundant extracellular mucus, cancer cells are more prone to dissemination and metastasis, leading to a higher occurrence of synchronous and metachronous metastasis compared to NMAC[47]. Additionally, increasing evidence suggests that MAC and NMAC have distinct molecular characteristics. A high CpG island methylation phenotype and MSI-Hare associated with MAC. In addition, RAF/RAS/MAPKand PI3K/AKT mutations are also frequent in MAC[48]. Its molecular features also promote tumour growth and invasion[49–51], contributing to the poor prognosis of colorectal cancer patients[52]. Furthermore, studies have found an association between MAC and overexpression of the MUC2 gene[53], which encodes mucin. The mucin layer formed by MUC2 overexpression may protect MAC from anti-tumor immune factors and promote MAC development[30,54]. Some articles have mentioned that both proximal colon cancer and the mucinous subtype are associated with higher levels of microsatellite instability[51,55]. Patients with microsatellite instability have been found to exhibit resistance to 5-fluorouracil (5-FU)-based chemotherapy[56–58]. Additionally, studies have shown overexpression of genes associated with oxaliplatin resistance in MAC, such as GSTP1, ATP7B, and SRPK1, which may provide a molecular explanation for the poorer efficacy of adjuvant chemotherapy in MAC[6,59,60].

Given the rarity of MAC and the controversy surrounding its prognosis, current treatment approaches for MAC do not differentiate between mucinous and non-mucinous colon adenocarcinomas. Most treatment guidelines follow recommendations for colorectal adenocarcinoma, and there are still no specific guidelines for

managing this disease[27]. The treatment of MAC patients may need to be adjusted, according to some researchers[30]. Our survival analysis of MAC and NMAC patients with and without adjuvant chemotherapy supports this viewpoint. Therefore, a comprehensive evaluation of predictive factors related to OS in MAC can help identify patients at higher risk and improve personalized management for MAC patients. Through univariate and multivariate Cox regression analysis of the MAC and NMAC groups, it was demonstrated that advanced age, N1 and N2 staging are independent predictive factors for poor prognosis in MAC patients. In NMAC patients, advanced age, absence of adjuvant chemotherapy, N2 staging, as well as pathological stage 4 were identified as independent predictive factors for adverse prognosis. Unlike MAC, NMAC showed significant improvement in prognosis with chemotherapy after adjusting for age and pathological staging. This further suggests that chemotherapy has limited efficacy in treating the mucinous subtype of proximal colon cancer, and we should differentiate the treatment approach for this subgroup of patients from NMAC patients. In the overall analysis of proximal colon cancer, mucinous subtype, older age, N1 and N2 staging, and pathological stage 4 remained as independent risk factors. This further demonstrates that, even after adjusting for other confounding factors, MAC of the proximal colon still has a worse prognosis than NMAC.

This study was based on the colon cancer cohort from the First Affiliated Hospital of Zhengzhou University. In our study, we not only included MAC patients but also included NMAC patients as a reference. The current research on the prognosis of mucinous subtype in colorectal cancer is controversial, possibly due to the lack of cancer site-specificity in most studies and the failure to differentiate between colon and rectal cancer subgroups. There are also suggestions by some scholars that the poor prognosis of the mucinous subtype exists only in rectal cancer[34]. Furthermore, studies have shown that proximal colon cancer has different molecular mechanisms and distinct biological behaviour[61–63], is more likely to develop interval colon cancer after colonoscopy[41], and has significant differences from the distal colon based on embryonic origin[64]. Therefore, this study focused on the proximal colon. In contrast to most other studies, we included patients with pathological stage 4. Research has indicated that 23–36% of stage IV patients survive 5–10 years after surgery, and surgery and adjuvant chemotherapy have curative intent (including resection of metastatic lesions)[65]. Therefore, we included stage 4 patients in our study, which may provide a better understanding of the real-world population of proximal colon MAC patients treated at our hospital.

This study has several limitations. Firstly, due to the significant amount of missing information in some samples, essential factors such as perineural invasion, vascular invasion, and differentiation grade were not included in the analysis. Patients with unknown mucin proportions were excluded from the analysis, which could introduce selection bias. The limitations of this study also include being a single-centre and retrospective study. The acquisition of survival data relied on telephone follow-up, which may be subject to recall bias. In the future, more extensive analyses, including large-scale and multicenter studies, are necessary to investigate further the characteristics and prognosis of proximal colon mucinous adenocarcinoma.

Conclusions

In summary, this study analyzed the clinic pathological features and prognosis of proximal colon mucinous adenocarcinoma, revealing that patients with MAC in the proximal colon were younger, had higher pathological stages, were more prone to metastasis, and had poorer prognosis than patients with NMAC. Furthermore, chemotherapy did not enhance the prognosis of patients with proximal colon mucinous adenocarcinoma, regardless of the pathological stage. Older age and lymph node metastasis were identified as independent prognostic factors for adverse outcomes in proximal colon mucinous adenocarcinoma. As a result of this analysis, adjuvant chemotherapy is recommended in stage 2 and stage 3 non-mucinous adenocarcinomas of the proximal colon, while questioning its benefits for proximal colon mucinous adenocarcinoma. This suggests exploring more appropriate treatment approaches for targeted management of proximal colon mucinous adenocarcinoma.

Data availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions

F.H. collected and analyzed data and wrote the main manuscript text. Y.X. provided study materials and patients and revised the manuscript. Y.L., X.S. and L.X. collected data and provided methodological guidance. N.Y. revised the manuscript for important intellectual content and provided financial support. All authors read and approved the final manuscript.

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Competing interests

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Additional information

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Correspondence and requests for materials should be addressed to J.Y.