Surgery Improve the Prognosis of Colon Mucinous Adenocarcinoma with Liver Metastases: A SEER-Based Study

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Abstract

Background Mucinous adenocarcinoma (MAC) is the second common pathological type of colon carcinoma (CC). Colon cancer liver metastases (CLM) is common and lethal, complete resection for both of the primary tumor and metastases of CLM would be beneficial. However, there is still no consensus for the role of surgery in MAC of CC with liver metastases (M-CLM).

Methods Among 5816 patients who diagnosed with M-CLM or classical adenocarcinoma of CLM (A-CLM) from 2010 to 2013 in the Surveillance, Epidemiology, and End Results (SEER) database were retrieved. The clinicopathological features and overall survival (OS) and cancer-specific survival (CSS) data were compared and analyzed.

Results Total of 5816 M-CLM and A-CLM patients were enrolled in this study. Results showed M-CLM group had larger tumor size, more right colon location, high pT and pN stage compared with A-CLM group, as well as more female patients, more examined and positive lymph nodes and a higher proportion of surgery than A-CLM group. The OS and CSS of M-CLM patients accepted any surgery were significantly better than that didn't accept any surgery, but poorer than that of A-CLM patients. Meanwhile, the OS and CSS of M-CLM and A-CLM were comparable when they didn't receive any surgery. Moreover, partial colectomy provided the similar OS and CSS compared with hemicolectomy or greater for M-CLM, and surgery was an independent protective factor for long-term survival of M-CLM.

Conclusions M-CLM had distinct clinicopathological characteristics, surgery could improve the long-term survival and act as an independent protective prognostic factor for M-CLM, additionally, partial colectomy might be a better selection for M-CLM from this study.

Background

Colon carcinoma (CC) is one of the most common and lethal cancer in the world [1]. A large proportion of CC are dead due to metastasis, more than 20% of patients developed distant metastases at the time of diagnosis[2]. Although the mortality of whole CC is declining, the 5-year survival rate of metastatic CC (mCC) is still miserable and less than 10%[3]. Liver is the most frequent target organ for mCC, and liver metastasis (LM) occurs in up to 25% of stage IV patients [4]. Complete resection of primary tumor and metastatic lesion for some highly-selected resectable colon cancer liver metastasis (CLM) patients is advocated by guidelines and provides better survival than non-surgical treatment, but this part of patients are less than 20% [5–7].

Mucinous adenocarcinoma (MC) is the second most common pathological type after the classical adenocarcinoma (AC) in CC and accounts for 10–15% of all CC patients [8]. According to the WHO, MC is defined as more than 50% of the lesion is composed of extracellular mucin. The molecular characteristics of MC are relative high mutation of BRAF and KRAS, more microsatellite instability high (MSI-H) and CpG island methylator phenohype, and high expression of HATH1 and MUC2 compared with AC[9–11]. The pathogenesis for MC is rarely known, bacterial biofilms, inflammatory bowel diseases (IBD) and

radiotherapy are considered as potential risk factors[12, 13]. MC is frequently located in proximal colon and had shorter survival and poorer systemic treatment response compared with AC, thus is always suggested as a poor prognostic predictor for CC [9, 14–16]. Therefore, we should pay more attention in clinical management of MC patients.

To date, the prognosis of MC is still highly controversial, mainly because the treatment strategy deviation for metastatic disease [14, 17, 18]. Although MC has greater propensity for peritoneal dissemination than AC, liver is still the most common metastatic site and accounts for up to 50% of all metastases[19, 20]. Management of these MC CLM (M-CLM) patients has long been controversial. One of important reason is M-CLM is frequently accompanied metastases of other sites, thus a large proportion of M-CLM are traditionally considered unresectable unless emergency circumstances, and many studies suggest that incomplete resection is associated with high recurrence, poorer survival, as well as tumor growth and progression[10, 21–24]. However, the relatively poor response to chemotherapy of metastatic MC indicates that surgery may occupy a more important role in treatment of these patients although recurrence is high[14, 25, 26]. Thus, some study found MC patients with completed resection of primary lesion and M-CLM had poorer survival than AC CLM patients (A-CLM), but other study found surgery for UICC stage IV MC could provide comparable survival as AC patients[17, 18, 20]. Furthermore, there was still no research to study the role of surgery in M-CLM patients who couldn't perform radical resection. These situation and discrepancy evoke more attention to settle the role of surgery in treatment of M-CLM.

In this study, we have explored the prognosis of M-CLM patients who accepted surgery or not, to both or either of the primary and metastatic lesions. The purpose of this study was to clarify the value of surgery and the prognostic factors for M-CLM patients from the Surveillance, Epidemiology, and End Results program (SEER 18, 1975–2016 varying)(Nitsche et al., 2013;Vigano et al., 2014;Wang et al., 2019).

Materials And Methods

Data source

The current study relied on the SEER cancer registry, which is a publicly available and reliable database and could provide follow-up information regarding the vital survival status and death causes. We required cases from 18 SEER registries with the anonymous data and obtained permission to download the research data file from the SEER database, which did not require further informed patient consent.

Patients selection

We accessed the SEER database using the SEER program (www.seer.cancer.gov) and

Surveillance Research Program, National Cancer Institute SEER*Stat software (www.seer.cancer.gov/seerstat) version 8.3.6, and obtained patients diagnosed with CLM between 2010 and 2013. The study included CLM patients according to the following criteria: 1) the International Classification of Disease for Oncology, Third Edition (ICD-O-3) site codes: cecum, ascending colon,

hepatic flexure, transverse colon, splenic flexure, descending colon and sigmoid colon; 2) ICD-O-3 behavior codes: malignant; 3)diagnostic confirmation: positive histology; 4) ICD-O-3 histology codes: 8140/3: adenocarcinoma, NOS, 8480/3: mucinous adenocarcinoma; 5) American Joint Committee on Cancer (AJCC) 7th edition: M1a; 6) Vital status: alive, dead. The exclusion criteria were in the following: 1) surgery of primary site: blanks; 2) surgery of other regional site and distant site: blanks; 3) site-specific factor 1 (carcinoembryonic antigen, CEA): blanks; 4)age at diagnosis: unknown; 5): Total number of in situ/malignant tumors: unknown; 6) survival months: unknown.

Outcome measures

For each patient, the survival outcomes were defined and analyzed: 1) overall survival (OS) was defined as the time from the date of diagnosis to death from any cause; 2) cancer-specific survival (CSS) was defined as the time from the date of diagnosis until cancer-associated death.

Statistical analysis

Patient characteristics were summarized in descriptive statistics, and we compared differences in baseline characteristics between the M-CLM groups and A-CLM groups. Continuous data were compared using the one-way ANOVA test, and categorical variables were compared using the chi-square test. The Kaplan-Meier curves were used to estimate OS and CSS, and the log-rank test was used to compare the differences among groups. The prognostic factors associated with OS and CSS were analyzed by univariate and multivariate Cox proportional regression model, and then hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated. All statistical analyses were performed with SPSS Statistical Package version 22.0 (SPSS Inc., Chicago, IL, USA), and $P < 0.05$ was considered to be statistical significant.

Results

The general demographic and clinicopathological characteristics of M-CLM

There are total of 7179 patients retrieved from SEER according to the inclusion and exclusion criteria. Then according to SEER Combined Metastasis at DX-liver (2010+) code, a total of 5816 CLM patients enrolled in this study from database of SEER 18 since 2010 to 2015, including 306 cases of M-CLM patients and 5510 cases of A-CLM patients. The demographic and clinicopathological characteristics of these patients were described in Table 1. Results showed that M-CLM patients had the general features of MC such as larger tumor size, more right colon location, high pT and pN stage than that of A-CLM patients ($P < 0.05$, respectively). In addition, the results also showed M-CLM group had more female patients, more examined and positive lymph nodes and a higher proportion of surgery than A-CLM group ($P < 0.05$, respectively). Other variables such as race, age, CEA level, primary tumor number and tumor differentiation were comparable between the two groups ($P > 0.05$, respectively). These results concluded

the primarily different characteristics of M-CLM from A-CLM, which mainly lie in the pathological status of primary lesion.

Table 1
The general demographic and clinicopathological features of mucinous colon adenocarcinoma liver metastasis (M-CLM) and classical colon adenocarcinoma liver metastasis (A-CLM) patients

Variables	A-CLM (5510)	M-CLM (306)	P value
Race			
White	4102(74.4%)	232(75.8%)	
Black	935(17.0%)	55(18.0%)	
Others	473(8.6%)	19(6.2%)	0.501
Age (years)			
≤ 60	2023(36.7%)	101(33.0%)	
60	3487(63.3%)	205(67.0%)	0.190
Sex			
Female	2439(44.3%)	153(50.0%)	
Male	3071(55.7%)	153(50.0%)	0.049
CEA			
Normal	593(10.8%)	33(10.8%)	
Elevated	3244(58.9%)	184(60.1%)	
Unknown	1673(30.4%)	89(29.1%)	0.890
Size (cm)			
≤ 5	2408(43.7%)	119(38.9%)	
5	1860(33.8%)	156(51.0%)	
Unknown	1242(22.5%)	39(10.1%)	< 0.001
Tumor number			
Solitary	4435(80.5%)	248(81.0%)	
Multiple	1075(19.5%)	58(19.0%)	0.811
Location			
Right colon	2403(43.6%)	181(59.2%)	
Transverse colon	486(8.8%)	34(11.1%)	
Left colon	2621(47.6%)	91(29.7%)	< 0.001
Differentiation			

Variables	A-CLM (5510)	M-CLM (306)	P value
Grade Ⅰ/Ⅱ	3634(66.0%)	188(61.4%)	
Grade Ⅲ/Ⅳ	1172(21.3%)	79(25.8%)	
Unknown	704(12.8%)	39(12.7%)	0.158
pT stage			
0–2	562(10.2%)	24(7.8%)	
3–4	3892(70.6%)	260(85.0%)	
Unknown	1054(19.1%)	22(7.2%)	< 0.001
pN stage			
N0	1668(30.3%)	62(20.3%)	
N+	3391(61.5%)	233(76.1%)	
Unknown	451(8.2%)	11(3.6%)	< 0.001
Examined lymph nodes	12.52 ± 11.43	16.26 ± 10.41	< 0.001
Positive lymph nodes	4.41 ± 5.04	5.37 ± 5.84	0.003
Surgery type			
No surgery	1627(29.5%)	34(11.1%)	
Any surgery	3876(70.3%)	272(88.9%)	
Unknown	7(0.2%)	0(0%)	< 0.001
Vital status			
Dead	4641(84.2%)	272(88.9%)	
Alive	869(15.8%)	34(11.1%)	0.028

The long-term survival of M-CLM

We then analyzed the potential survival difference between M-CLM and A-CLM patients and found more patients died in M-CLM group (88.9% vs. 84.2%, P = 0.028, Table 1), thus we further analyzed the difference via Kaplan- Meier curves and Log-rank tests. Results showed the follow-up of the whole study was 0–83 months and the median time was 17.0 months. The OS of M-CLM was comparable with that of A-CLM patients (22.59 ± 1.24 vs. 25.65 ± 0.36 months, P = 0.088, Fig. 1A), the CSS of M-CLM was also similar with that of A-CLM patients (24.33 ± 1.33 vs. 28.19 ± 0.39 months, P = 0.053, Fig. 1B), but the actual values of OS and CSS of M-CLM were lower than that of A-CLM though the difference was not statistically significant. These results indicated that survival of M-CLM is close to A-CLM.

The long-term survival of M-CLM classified by surgery type

Because resection of both primary and metastatic lesions is an important option for survival advantage of CLM, we further explore the potential advantage of different surgery types via survival analyses. Results showed that the entire cohort who accepted the both of the resection had the best OS (41.15 ± 0.96 months, P < 0.001), followed by resection only to primary lesion (26.79 ± 0.47 months) or metastatic lesion (21.44 ± 4.22 months) which had similar OS (P = 0.388), and the patients who didn't perform any surgery had the poorest OS (13.08 ± 0.39 months, P < 0.001) (Fig. 1C). These results were also confirmed in CSS analysis (OS in turn: 43.51 ± 0.99, 29.38 ± 0.51, 22.27 ± 4.42 and 14.63 ± 0.45 months, Fig. 1D). Then, we classified and analyzed the effect of surgery to survival of M-CLM and A-CLM. Results showed M-CLM patients accepted any surgery (no matter both or only resection to primary and metastatic lesions) had significant better OS and CSS than that didn't accept any surgery (P < 0.001, respectively, Fig. 2A-B). The survival analyses in A-CLM group also drew the similar results (P < 0.001, respectively, Fig. 2C-D). These results concluded that surgery held an important position in treatment of M-CLM patients for a better survival, even though resection only to primary or metastatic lesions.

The survival difference of M-CLM and A-CLM stratified by surgery type

We previously found M-CLM had comparable OS and CSS with A-CLM (Fig. 1A-B), since surgery could obtain survival benefit, then we further analyzed the potential survival difference of M-CLM and A-CLM via stratification of surgery types. Results showed that M-CLM patients accepted any surgery had poorer OS (24.02 ± 1.34 vs. 30.84 ± 0.45months, P < 0.001, Fig. 3A) and CSS (25.74 ± 1.42 vs. 33.54 ± 0.48months, P < 0.001, Fig. 3B) than that of A-CLM patients. But the OS and CSS had no significant difference between M-CLM and A-CLM patients with none surgery (P = 0.394 and P = 0.404, respectively, Fig. 3C-D). Then we continued to explore the survival difference via stratification of surgery to primary or metastatic lesion. Results showed that in patients with surgery to primary lesion hierarchy, M-CLM had poorer OS and CSS than that of A-CLM patients (P < 0.001, respectively, Fig. 4A-B). The patients with surgery to metastatic lesion hierarchy also showed M-CLM had poorer OS and CSS than that of A-CLM patients (P = 0.044 and P = 0.011, respectively, Fig. 4C-D). These results concluded that although surgery provided survival advantage for entire CLM patients, M-CLM still had the relatively less benefit than A-CLM from surgery.

The effect of surgery option to primary lesion for survival of M-CLM

There are also controversial exist in surgery option selection to primary lesion for CLM to today, thus we further analyzed the surgery option for the survival of M-CLM. There are total of 272 (88.89%, 272/306) M-CLM patients accepted surgery in this study, and partial colectomy (26.10%, 71/272) and hemicolectomy or greater (72.06%, 196/272) were the most common options. Results showed that partial

colectomy had the similar OS compared with hemicolectomy or greater (24.63 ± 2.41 vs. 23.65 ± 1.60 months, P = 0.240), but better than no surgery (P < 0.001, respectively, Fig. 5A). The CSS analyses also showed the similar results (Fig. 5B). These results concluded that a more extensive surgery scope of primary lesion would not provide superior survival benefit for M-CLM.

The prognostic risk factors for survival of M-CLM

The survival for M-CLM is poor that we need to explore the potential prognostic risk factor for it. We analyzed the risk factors for OS and CSS of M-CLM by univariate and multivariate Cox proportional hazards regression models in this study. The univariate analyses results showed in Table 2 indicated black race (HR = 0.735, 95% CI: 0.543–0.996), pT3-4 stage (HR = 0.603, 95% CI: 0.392–0.929) and surgery to any or both lesions (Any HR = 0.506, 95% CI: 0.349–0.734; both HR = 0.314, 95% CI: 0.198–0.497) were associated with better OS of M-CLM (Table 2). The black race (HR = 0.691, 95% CI: 0.506–0.944), pT3-4 stage (HR = 0.570, 95% CI: 0.367–0.888) and surgery to any or both lesions (Any HR = 0.497, 95% CI: 0.337–0.735; both HR = 0.330, 95% CI: 0.205–0.531) were also associated with better CSS of M-CLM (Table 2). On the multivariate analysis demonstrated in Table 3, results showed only surgery type (Any HR = 0.478, 95% CI: 0.265–0.862; both HR = 0.316, 95% CI: 0.163–0.609) was independent prognostic factors for better OS; and black race (HR = 0.701, 95% CI: 0.499–0.986), pT3-4 stage (HR = 0.513, 95% CI: 0.306–0.860) and surgery type (Any HR = 0.497, 95% CI: 0.267–0.924; both HR = 0.350, 95% CI: 0.176–0.696) were also associated with better CSS of M-CLM (Table 3). These results concluded once again that the surgery was important for the better long-term survival of M-CLM, no matter surgery to primary lesion or metastatic lesion or both of them.

Table 2
Univariate analysis of factors associated with overall survival and cancer-specific survival of M-CLM

Variable	OS		CSS	
	HR(95%CI)	P	HR(95%CI)	P
Race				
White	1	0.064	1	0.025
Black	0.735(0.543–0.996)	0.047	0.691(0.506–0.944)	0.020
Others	0.562(0.317–0.999)	0.050	0.502(0.273–0.924)	0.027
Age (years)				
≤ 60	1		1	
60	1.128(0.876–1.453)	0.349	1.066(0.821–1.385)	0.629
Sex				
Female	1		1	
Male	0.886(0.698–1.124)	0.319	0.888(0.693–1.139)	0.350
CEA				
Normal	1	0.429	1	0.281
Elevated	1.195(0.800-1.784)	0.385	1.379(0.890–2.138)	0.151
Unknown	1.324(0.861–2.035)	0.202	1.456(0.911–2.328)	0.117
Size (cm)				
≤ 5	1	0.153	1	0.192
5	1.189(0.922–1.533)	0.182	1.157(0.888–1.508)	0.281
Unknown	1.455(0.964–2.197)	0.074	1.463 (0.955–2.241)	0.081
Tumor number				
Solitary	1		1	
Multiple	1.244(0.921–1.681)	0.155	1.073(0.772–1.492)	0.675

Variable	OS		CSS	
	HR(95%CI)	P	HR(95%CI)	P
Location				
Right colon	1	0.996	1	0.939
Transverse colon	1.003(0.675–1.492)	0.987	1.038(0.687–1.567)	0.859
Left colon	0.989(0.759–1.290)	0.937	1.049(0.797–1.380)	0.734
Differentiation				
Grade /	1	0.528	1	0.547
Grade /	1.000(0.754–1.326)	0.998	1.013(0.755–1.358)	0.933
Unknown	1.221(0.855–1.745)	0.271	1.229(0.847–1.783)	0.278
pT stage				
0–2	1	0.004	1	0.002
3–4	0.603(0.392–0.929)	0.022	0.570(0.367–0.888)	0.013
Unknown	1.104(0.610–1.997)	0.745	1.105(0.602–2.028)	0.747
pN stage				
N0	1	0.117	1	0.192
N+	0.844(0.629–1.134)	0.261	0.892(0.652–1.219)	0.473
Unknown	1.502(0.787–2.867)	0.217	1.570(0.796–3.097)	0.193
Surgery type				
No surgery	1	< 0.001	1	< 0.001
Surgery to primary or metastatic lesion	0.506(0.349–0.734)	< 0.001	0.497(0.337–0.735)	< 0.001
Both	0.314(0.198–0.497)	< 0.001	0.330(0.205–0.531)	< 0.001
Others	1.080(0.259–4.509)	0.916	1.201(0.286–5.037)	0.802

Table 3
Multivariate analysis of factors associated with OS and CSS of M-CLM

Variable	OS		CSS	
	HR(95%CI)	P	HR(95%CI)	P
Race				
White		NS	1	0.008
Black			0.701(0.499–0.986)	0.041
Others			0.362(0.183–0.715)	0.003
Surgery type				
No surgery	1	0.004	1	0.017
Surgery to primary or metastatic lesion	0.478(0.265–0.862)	0.014	0.497(0.267–0.924)	0.027
Both	0.316(0.163–0.609)	0.001	0.350(0.176–0.696)	0.003
Others	1.080(0.182–4.159)	0.862	0.864(0.177–4.218)	0.856
pT stage				
0–2		NS	1	0.039
3–4			0.513(0.306–0.860)	0.011
Unknown			0.785(0.365–1.688)	0.535

Abbreviations: NS: no significant difference.

Discussion

Surgery for colon cancer with liver metastasis is a critical and controversial issue and continues to this day. Though most researchers believe that completed resection of both of primary and metastatic lesions would provide a survival advantage than systemic therapy, the mainly dispute is whether palliative resection of part of lesions is benefit for patients, especially resection only to primary colon cancer or liver metastasis[27]. What's more, systemic chemotherapy, molecular targeted therapy, immunotherapy, portal vein or hepatic artery embolization and radiofrequency ablation play a gradually more important role in mCC treatment, which might provide a potentially longer survival and downstaging of tumor[5, 23, 27, 28]. This situation causes that surgery occupies a gradual weakening trend in CLM treatment, and many studies support the view that surgery would bring more trauma, stress and immunosuppression for CLM

patients and probably prompt tumor growth, recurrence and wouldn't bring survival benefit [24, 29–33]. However, there are also some studies stated clearly that resection primary colon cancer or liver metastasis associated with improved survival, and suggested a more aggressive method for the incurable diseases[23, 34–36].

This dilemma is amplifying in M-CLM, because MC is always characterized by peritoneal implant and metastases at multiple sites which increase difficulty of completed resection[18, 20, 37]. What's more, most studies consider MC histology is an adverse prognostic for survival, as well as in M-CLM, which aggravate the concern of surgery[10, 15, 17]. However, the relatively low response to systemic therapy of MC compared with AC draws a dilemma in treatment of M-CLM, which evokes the rethinking of surgery in M-CLM[15, 37]. In this study, we found M-CLM also had general features as MC that such as more right colon location, larger tumor size and advanced pT and pN stage compared with A-CLM, but the long-term survival of overall M-CLM and A-CLM were comparable. These overturn the traditional knowledge of MC had poorer survival than AC, especially diagnosed at a high stage (III/IV)[14, 38]. However, our findings were consistent with some recent studies that survival of overall MC was poorer than AC, but stage IV MC had similar survival as AC[17, 39]. These findings indicated that though M-CLM had specific clinicopathological features, the long-term survival is comparable with A-CLM.

Another important finding of the present study was no matter surgery to both primary and metastatic lesions or only to any of the lesions of CLM patients, the survival were better than that of no surgery. This conclusion was also verified by stratification of M-CLM and A-CLM, and confirmed the importance of surgery for survival benefit of M-CLM, which was also supported by some former studies[34, 36]. We also explored the potential independent risk factors for survival of M-CLM by univariate and multivariate analyses. Results also showed surgery played a dominated role for favor OS and CSS, no matter surgery to both primary and metastatic lesions or any of the lesions. These results once again highlighted the importance of surgery for better prognosis of M-CLM. However, we further found M-CLM had the poorer OS and CSS than A-CLM in hierarchy of patients accepted any surgery. This finding was different from studies about surgery to stage IV MC[17, 40], but similar with a recent study from Italy that M-CLM associated with worse OS and disease-free survival[18]. One potential explanation for the discrepancy is the studies of stage IV MC didn't stratify the sub-classification of M-CLM, since M-CLM always accompanied other sites and/or peritoneal metastasis which would deteriorate the prognosis[15, 18, 37]. Another possible reason is that adjuvant chemotherapy is an important option for postoperative treatment for M-CLM though this study didn't include the information. However, M-CLM always resistant to systemic chemotherapy which might also lead to relatively poor survival after surgery[15, 41].

Surgery type of primary lesion is also a most debated issue for M-CLM, the most often types are partial colectomy and hemicolectomy or greater. Some surgeons tend to choose the partial colectomy cause M-CLM is a terminal stage and surgery couldn't improve survival even bring poor prognosis[29–31]. However, others thought extended resection such as hemicolectomy or greater would provide a probability for subsequent curable resection or sensitivity for systemic chemotherapy, which might prolong survival[32, 35, 36]. In the present study, we found partial colectomy provided a similar OS and

CSS as hemicolectomy or greater, this finding strengthened the concept of minimizing the trauma for advanced cancer. There are some potential speculation for this, it is most likely that the extended resection would have broken immune system and homeostasis, and sometimes even promoted tumor growth and metastasis[24]. Thus, a more appropriate surgery option should be selected carefully when an operation decision is made for M-CLM.

This study has found the important role of surgery for better survival of M-CLM. However, there were also some limitation in the study. First and foremost, we couldn't obtain the pre- and/or post-operative systemic therapy information which would weaken the scientific and academic rigour. Secondly, this study couldn't recognize which patients received primary and metastatic lesions resection synchronously or subsequently. Third, because our study enrolled patients with pathological confirmation and detailed staging information in the SEER database, which would exclude many metastatic disease patients without pathological diagnosis. Thus, more excellent designed retrospective and prospective multi-center studies are needed in the future to overcome these weaknesses.

Despite these limitations, this study concluded M-CLM had distinct clinicopathological characteristics from A-CLM, and highlighted surgery could improve the long-term survival and was the independent favorable prognostic factor for survival even though surgery to any lesion of M-CLM, in addition, partial colectomy might be a better selection for M-CLM from this study. In conclusion, our study updated the understanding of surgery for MAC of metastatic colon carcinoma.

List Of Abbreviations

mucinous adenocarcinoma (MAC); colon carcinoma (CC); colon cancer liver metastases (CLM); MAC of CC with liver metastases (M-CLM); End Results (SEER); overall survival (OS); cancer-specific survival (CSS); adenocarcinoma (AC); bowel diseases (IBD); carcinoembryonic antigen (CEA); hazard ratios (HRs); confidence intervals (CIs);

Declarations

Ethics approval and consent to participate

The data obtained permission to download the research data file from the SEER database, which did not require further informed ethics approval and consent to participate.

Consent for publication

Not applicable.

Availability of data and material

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

JH, GDC, KF, SX conceived the study and wrote the manuscript. JH, GDC, HL, RT, YWZ, QLH, KF, XDP and SX conducted the experiments and contributed to the analysis of data. KF, XDP and SX revised the manuscript.. All authors read and approved the final manuscript.

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Figures

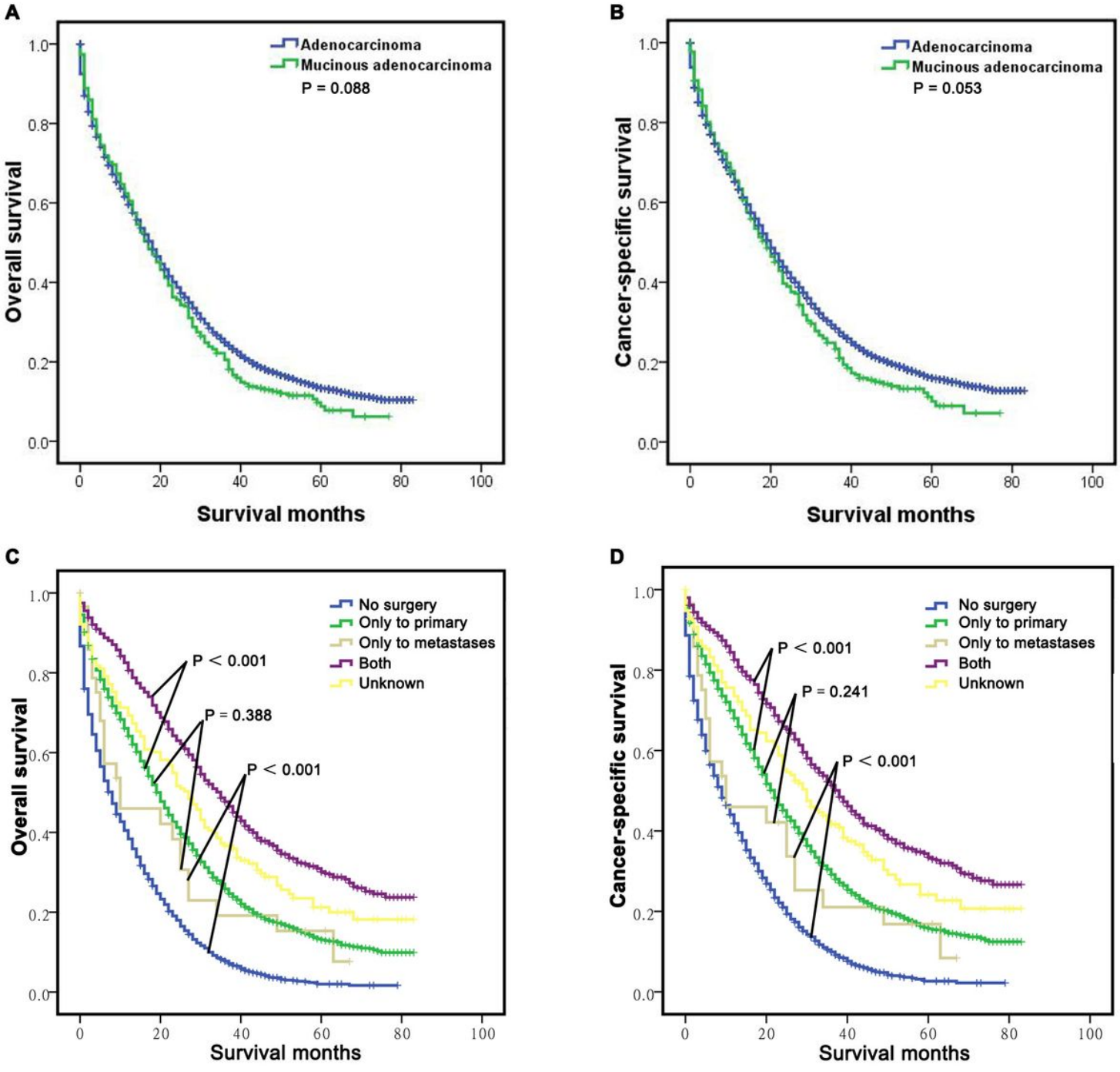

Figure 1

Long-term survival of CLM. A-B: The survival curves showed that the overall M-CLM group had similar overall survival (OS) (A) and cancer-specific survival (CSS) (B) with the A-CLM group; C-D: The survival

curves showed that the CLM group who accepted the resection both to primary lesion and metastatic lesion had the best OS (C) and CSS (D), followed by the resection only to primary lesion or metastatic lesion which had similar OS and CSS, and the patients who didn't receive any surgery had the poorest OS and CSS.

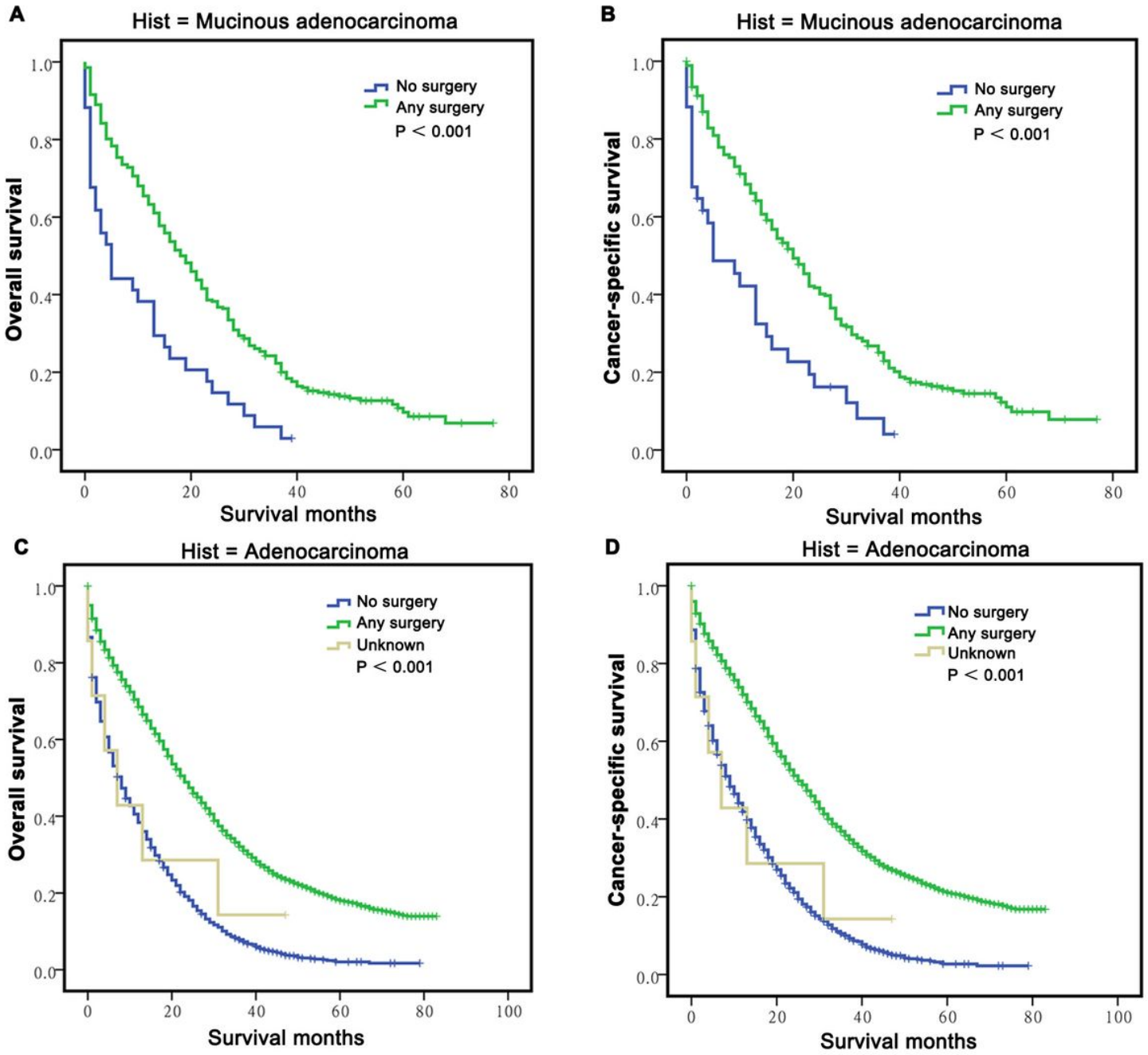

Figure 2

Long-term survival of CLM grouped by surgery and stratified by histology. A-B: The survival curves showed that the M-CLM patients who received any surgery had better OS (A) and CSS (B) than those didn't accept any surgery; C-D: The survival curves showed A-CLM patients who received any surgery also had better OS (C) and CSS (D) than those didn't accept any surgery.

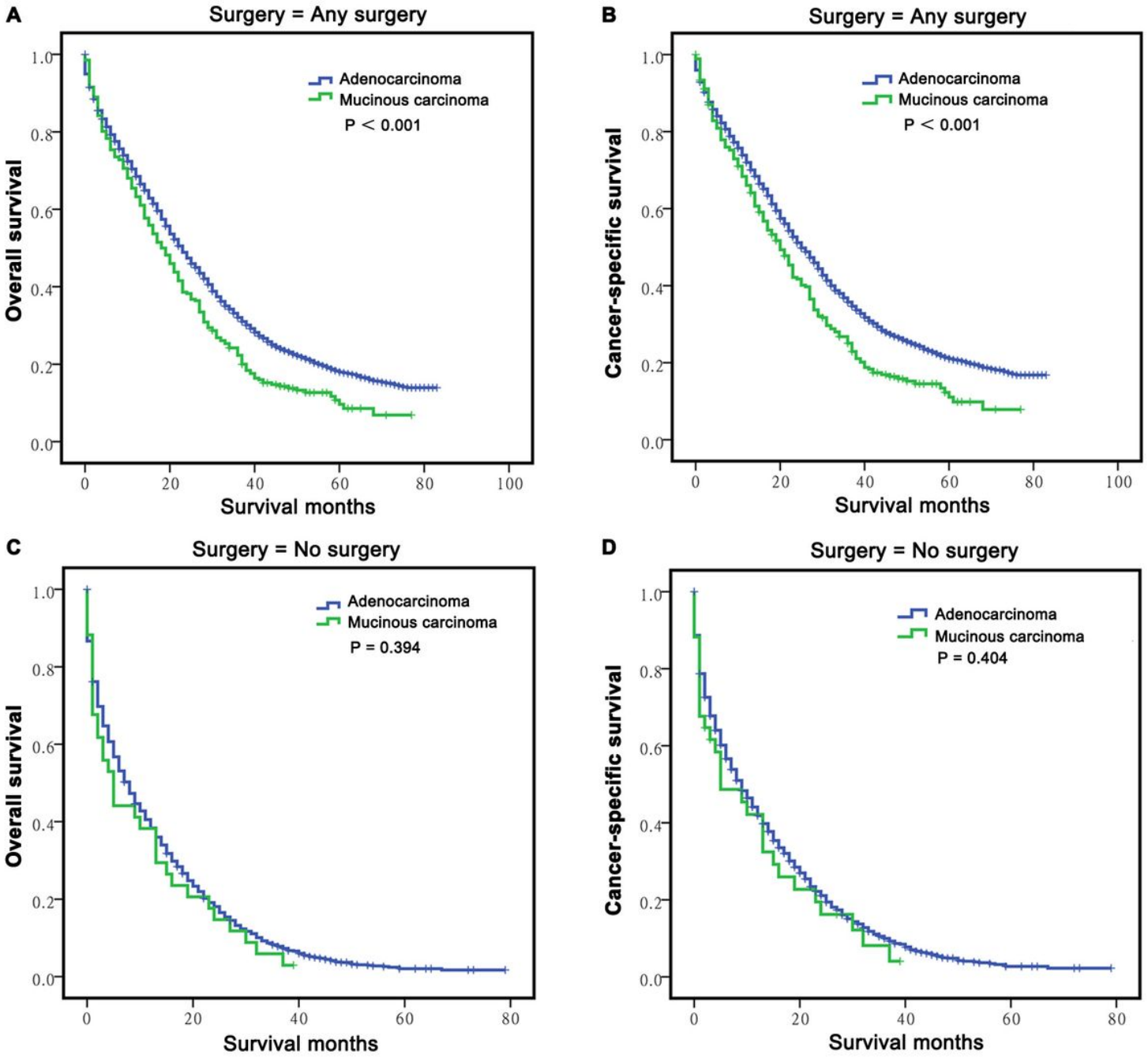

Figure 3

The stratified analysis for long-term survival of CLM according to surgery type. A-B: The survival curves showed that the M-CLM group received any surgery had poorer OS (A) and CSS (B) than the A-CLM group; C-D: the survival curves showed M-CLM and A-CLM groups had similar OS (C) and CSS (D) when didn't perform any surgery.

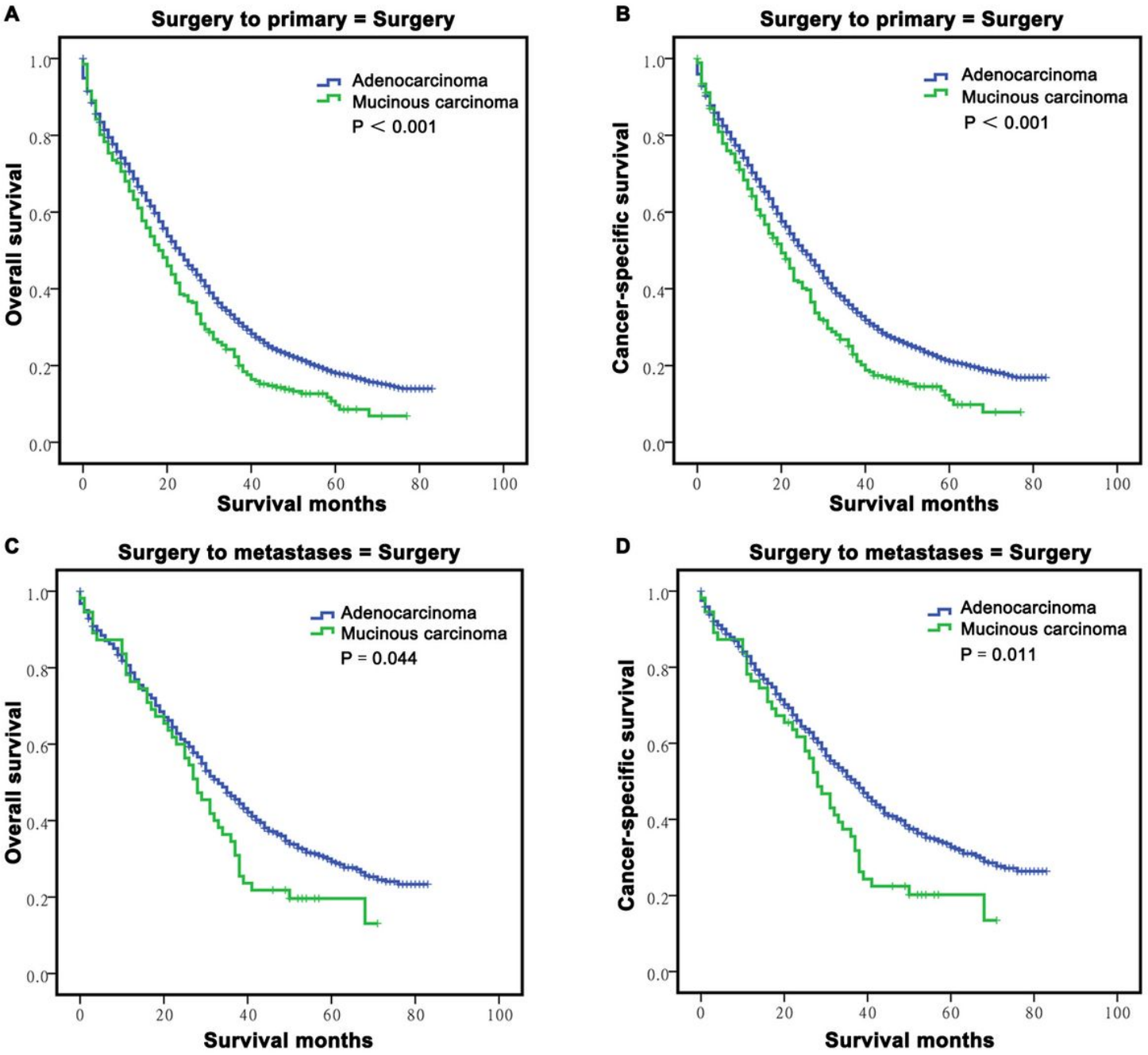

Figure 4

The stratified analysis for long-term survival of CLM according to resection of tumor lesions. A-B: The survival curves showed that the M-CLM group had poorer OS (A) and CSS (B) than the A-CLM group in patients with surgery to primary lesion; C-D: The survival curves showed that the M-CLM group had poorer OS (C) and CSS (D) than the A-CLM group in patients with surgery to metastatic lesion.

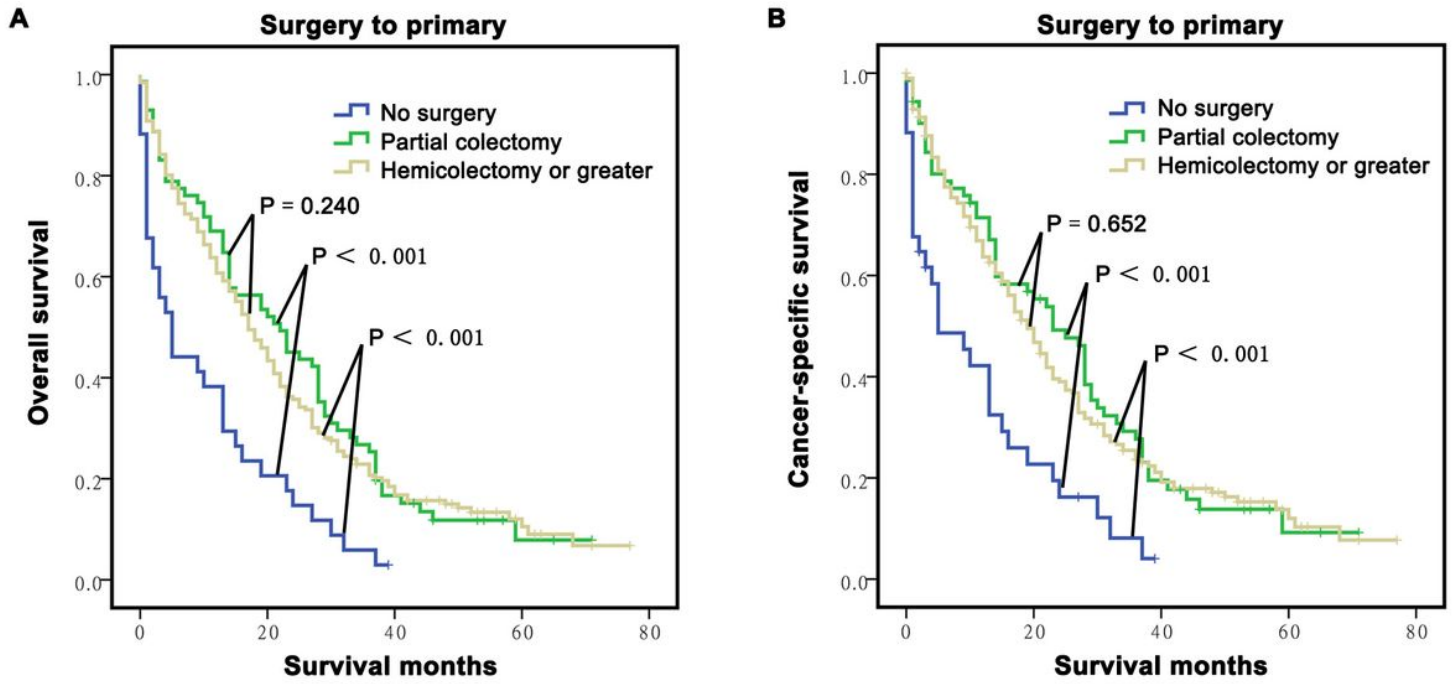

Figure 5

Long-term survival of M-CLM according to surgery type of primary lesion resection. A: The survival curves showed that the M-CLM patients who accepted partial colectomy had the similar OS compared with those group who accepted hemicolectomy or greater, but better than those didn't accept surgery. B: The CSS analysis also showed the similar results.