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Endoscopic treatment vs surgery for T1-stage colorectal cancer: a real-world retrospective cohort study

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Abstract

Endoscopic treatment is widely used for T1 colorectal cancer, yet there are limited studies that compare the survival outcomes of patients treated with endoscopy and surgery. This study utilized the data from the Surveillance, Epidemiology, and End Results database to evaluate the long-term survival of the two treatment regimens in America. The analysis of T1-stage colorectal cancer patients from 2000 to 2018 was assessed using Kaplan-Meier analyses and log-rank tests. Accounting for the imbalance in covariate distribution between the two groups, a propensity score matching method was employed, followed by a comparison of survival outcomes. Of the 4,834 patients included in this study, 4,116 underwent surgery, while 718 underwent endoscopic procedures. Overall survival did not significantly differ between the groups prior to the use of the propensity score matching method, but the surgery group's cancer-specific survival was noticeably higher (p = 0.0022). Following propensity score matching, there were no discernible variations in overall or cancer-specific survival. Subgroup analysis indicated that older patients, males, and those with higher histological grades had significantly better cancer-specific survival outcomes with surgery compared to endoscopic treatment. According to data from the American population, there was no variation in long-term survival rates for T1-stage colorectal cancer between the two groups.

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Introduction

Colorectal cancer (CRC) is a leading cancer worldwide, ranking third in both incidence and mortality in 2020[1]. Mortality rates increase significantly with disease progression^[2]. As CRC screening gains recognition for its role in preventing advanced-stage diagnoses and reducing mortality, early detection rates have shown consistent growth^[3]. The American Joint Committee on Cancer's TNM classification describes early CRC as invasive cancer that remains within the mucosal and submucosal layers of the colon (Tis or T1)[4]. Conventional surgical resection, whether open or laparoscopic-assisted, has long been considered as the standard treatment for CRC^[5]. However, minimally invasive options like endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are increasingly recognized as safe and effective alternatives^[6–8]. Compared to surgery, endoscopic treatment (ET) is associated with fewer complications, a lower mortality risk, reduced bleeding, and a shorter hospital stay^[9]. Moreover, ET usually requires curative en-bloc resection, which is mandatory and must be specifically considered as a quality parameter^[10]. To qualify as a successful curative resection, patients need to meet low-risk criteria, which include submucosal invasion of less than 1,000 µm, lack of poor differentiation, no lymphovascular infiltration, and no indication of tumor budding. If any of these criteria are not met, lymph node dissection is advised to reduce the risk of lymph node or distant metastases[11].

Understanding whether endoscopic treatment provides comparable outcomes to surgery for early CRC is essential. While most research on endoscopic treatment for early-stage colorectal cancer has been carried out in Asia, limited data are available from the USA. Consequently, further investigations into endoscopic resection outcomes in the American population are necessary. This study employed the the Surveillance, Epidemiology, and End Results

(SEER) database, which encompasses 34% of the US population, to examine the survival of T1 stage colorectal cancer patients who underwent either surgery or endoscopic treatment.

Materials and methods

Study population and data source

Retrospective cohort research was conducted utilizing the 'SEER Research Plus Data, 18 Registries, Nov 2020 Sub (2000-2018)' database (https://seer.cancer.gov). The eligibility requirements consisted of: (1) patients aged over 20 years, without limitations on gender or race; (2) individuals diagnosed with TisM0 or T1M0 colorectal adenocarcinoma (confined to the submucosa and without metastasis) through pathology, not involving the appendix and cecum; (3) only one primary tumor case and (4) those who received either endoscopic treatment (endoscopic mucosal resection, EMR; endoscopic submucosal dissection, ESD) or surgical intervention. Patients were dropped if they fulfilled any of the subsequent criteria: (1) non-adenocarcinoma histology, (2) metastatic cancer, (3) age below 20 years, (4) tumors identified solely through autopsy or death certificates, or (5) absent or unidentified information. The study applied the 7th edition of the American Joint Committee on Cancer (AJCC) TNM classification system. The collected data encompassed demographics (age, sex, race, and year of diagnosis), clinical and histological attributes(tumor size, lymph node metastases grade, TNM stage, and therapy type), survival duration, cancerspecific survival (CSS), and overall survival (OS). In the OS analysis, deaths from any cause were defined as events, while survivors were treated as censored. For the CSS analysis, only deaths due to CRC were considered events, with deaths from other causes or surviving patients regarded as censored. Patients with T1 stage CRC ('C18.0-C20.0 colon and rectum' ICD-O-3) were selected for the analysis.

They were divided into two groups based on treatment: endoscopic treatment (ET) and surgery. Figure 1 shows the study population selection flowchart.

This study adhered to the ethical norms established by institutional and national research committees in accordance with the principles of the 1964 Helsinki Declaration and its subsequent revisions or similar standards. The SEER Program offers anonymised data derived from population-based cancer registries. The SEER database comprises public-use data. Hence, no further approval or local ethical declaration was necessary for this work.

Statistical analysis

The research utilized SEER* Stat software (version 8.3.9) for data extraction. Analytical procedures were conducted using two primary statistical platforms: SPSS (version 25.0, Chicago, IL, USA) and R software (version 3.5.1, available at www.R-project.org). Propensity score matching was implemented to address potential baseline clinicopathological variations. The matching protocol employed a 1:1 ratio between surgical and endocrine therapy groups, with a match tolerance of 0.01. Categorical variables were assessed via the R \times C Chi-squared test. Survival analysis was performed via the Kaplan–Meier method, with intergroup comparisons assessed by the log–rank test. Variables demonstrating a p-value below 0.1 in univariate analysis were further examined through a multivariate Cox proportional hazards model to ascertain independent

prognostic factors. The overall survival (OS) and cancer–specific survival (CSS) rates for 3–year and 5–year intervals were assessed. Statistical significance was determined using two–sided tests, setting a threshold of p < 0.05.

Additionally, subgroup analyses were conducted using Cox regression models stratified by age, sex, tumor grade, tumor location, and tumor size to explore potential heterogeneity in outcomes.

Results

Baseline characteristics of T1 stage CRC patients

This study included 4,834 colorectal cancer (CRC) patients who met the inclusion criteria, among whom 4,116 (85.15%) underwent surgical intervention, while 718 (14.85%) had endoscopic treatment (ET). Figure 1 depicts the complete procedure of patient selection. In both treatment groups, the bulk of patients were between 60 and 79 years old. There were notable variations between the two groups with regard to tumor size, histological grade, lymph node metastasis (LNM), tumor site, overall stage, and T stage (p < 0.001) (Table 1).

A decreasing trend in the proportion of patients undergoing endoscopic treatment for T1 stage CRC was observed, with rates declining from 16.0% in 2000–2004 to 5.0% in 2011–2018 (p < 0.001) (Fig. 2). Furthermore, a binary multivariable logistic regression

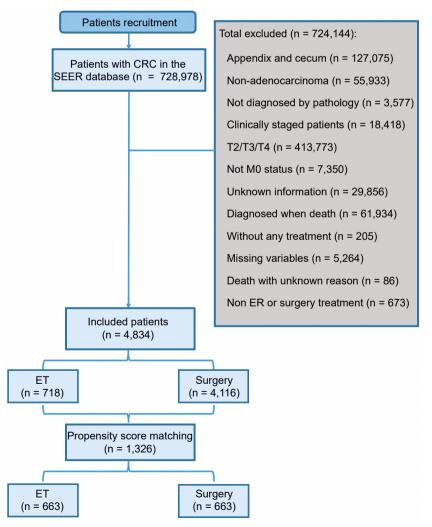


Fig. 1 Flow diagram of eligible patients diagnosed with T1 stage CRC.

Table 1. Baseline characteristics of patients treated with surgery and ET for T1 stage colorectal cancer before PSM.

Variables		Surgery (n = 4,116)	ET (n = 718)	<i>p</i> -value
Age (years)	20-59	970 (83.8)	188 (16.2)	0.175
,	60-79	2,374 (86.0)	388 (14.0)	
	≥ 80	772 (84.5)	142 (15.5)	
Marital status	Unmarried	1,532 (84.8)	274 (15.2)	0.646
	Married	2,584 (85.3)	444 (14.7)	
Sex	Male	2,089 (84.8)	373 (15.2)	0.571
	Female	2,027 (85.5)	345 (14.5)	
Race	Non-API	3,840 (85.0)	675 (15.5)	0.515
	API	276 (86.5)	43 (13.5)	
Tumor size	≤ 3 cm	2,413 (81.2)	557 (18.8)	< 0.001
	> 3 cm	1,703 (91.4)	161 (8.6)	
Histological	Grade I	984 (81.4)	225 (18.6)	< 0.001
grade	Grade II	2,813 (86.3)	446 (13.7)	
	Grade III–IV	319 (87.2)	47 (12.8)	
LNM	Negative	3,888 (84.4)	716 (15.6)	< 0.001
	Positive	288 (99.1)	2 (0.9)	
Tumor location	Colon	2,927 (90.4)	311 (9.6)	< 0.001
	Rectum	1,189 (74.5)	407 (25.5)	
Stage	0	269 (72.9)	100 (27.1)	< 0.001
	1	3,407 (85.0)	602 (15.0)	
	2	217 (93.9)	14 (6.1)	
	3	223 (99.1)	2 (0.9)	
T stage	Tis	277 (73.5)	100 (26.5)	< 0.001
	T1	3,839 (86.1)	618 (13.9)	

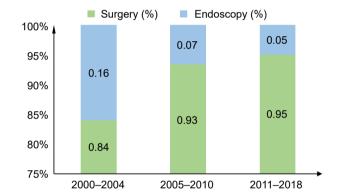


Fig. 2 Proportion of different treatments between 2000-2018.

analysis indicated that tumors located in the colon, higher histological grade, and greater tumor size were strongly linked to a higher chance of receiving surgical therapy (Supplementary Table S1).

OS and CSS comparison between ET and surgery groups

In this study, 437 patients (60.86%) in the ET group and 2,451 (59.55%) in the surgical group passed away. Among them, 114 patients (15.88%) who underwent ET and 469 patients (11.39%) who underwent surgical treatment were confirmed to have died from colorectal cancer (CRC).

Overall survival (OS) was comparable across the two groups. The median OS for the ET group was 141.0 months, with a 5-year OS rate of 73.3% (n = 191), while the surgery group exhibited a median OS of 146.0 months and a corresponding 5-year OS rate of 76.4% (n = 947) (p = 0.88) (Fig. 3a). However, the 5-year cancer-specific survival (CSS) rates were markedly inferior in the ET group relative to the surgical group, at 90.6% (n = 61) vs 92.9% (n = 262) (p = 0.0022) (Fig. 3b).

Multivariable cox regression

No significant difference in mortality risk was observed between the ET and surgical groups after adjusting for other variables, including OS (HR) and CSS (HR). Older age (60-79 years HR: 3.363, 95% CI 2.963–3.816, p < 0.001; ≥ 80 years HR: 9.797, 95% CI 8.513–11.273, p < 0.001), male (HR: 1.302, 95% CI 1.205–1.407, p < 0.001), married patients (HR: 0.780, 95% CI 0.720-0.846, p < 0.001), greater tumor size (HR: 1.101, 95% CI 1.021-1.188), T stage (HR: 0.123, 95% CI 0.039-0.385) and higher stage (stage 1: HR: 7.463, 95% CI 2.362-23.580; stage 2: HR: 7.942, 95% CI 2.443-25.822; stage 3: HR: 32.986, 95% CI 2.877-387.235) exhibited a strong correlation with OS, while older age (60–79 years HR: 1.857, 95% CI 1.477–2.335, p < 0.001; ≥ 80 years HR: 3.757, 95% CI 2.866–4.926, p < 0.001), male (HR: 1.270, 95% CI 1.069–1.508, p = 0.007), married patients (HR: 0.751, 95% CI 0.628-0.897, p = 0.002), larger tumor size (HR: 1.362, 95% CI 1.153–1.610, p < 0.001), higher histological grade (Grade III–IV HR: 1.627, 95% CI 1.193–2.219, p = 0.002), tumor location in rectum (HR:1.238, 95% CI 1.041–1.473, p = 0.016) and endoscopic treatment (HR: 1.474, 95% CI 1.184-1.834) constituted independent risk factors for CSS (Table 2).

Propensity score matching

To minimize potential biases, propensity score matching (PSM) at a 1:1 ratio with a caliper of 0.001 was implemented, yielding two well-balanced cohorts of 663 patients each in the endoscopic therapy (ET) and surgical groups. Post-PSM, no notable discrepancies were detected between the two groups regarding the baseline characteristics (p > 0.05) (Table 3).

Following PSM, no substantial difference was observed in the 5-year overall survival rate and median OS between ET and surgery group (5-year OS rate: 73.3% (n = 176) vs 78.0% (n = 143), median OS: 142.0 months vs 153.0 months; p = 0.540) (Fig. 3c). Meanwhile, The 5-year CSS rates were 91.3% (n = 52) in ET group and 92.9% (n = 43) in surgery group (p = 0.14) (Fig. 3d).

In the PSM Cox regression model, the ET group exhibited no significant differences in overall survival (HR: 1.074, 95% CI 0.934-1.235, p = 0.316) and cancer-specific survival (HR: 1.273, 95%) CI 0.947–1.710, p = 0.110) when compared to the surgical group. Following matching, the multivariable analysis revealed that advanced age (60–79 years HR: 3.677, 95% CI 2.892–4.675, p < 0.001; ≥ 80 years HR: 11.638, 95% CI 8.883 –11.248, p < 0.001), male (HR: 1.257, 95% CI 1.079–1.465, p = 0.003) and married patients (HR: 0.762, 95% CI 0.650-0.894, p = 0.001) were significantly correlated with OS (Table 4, Fig. 4a), while older age (60-79 years HR: 1.898, 95% CI 1.269–2.838, p = 0.002; ≥80 years HR: 4.286, 95% CI 2.625-6.999, p < 0.001), male (HR: 1.480, 95% CI 1.072-2.044, p = 0.017), Asian Pacific Islander (API) (HR: 2.004, 95% CI 1.126–3.569, p = 0.018) and higher histological grade (Grade II HR:1.560, 95% CI 1.070-2.275, p = 0.021; Grade III-IV HR: 2.170, 95% CI 1.143-4.120, p = 0.018) were independent risk factors of CSS (Table 4, Fig. 4b).

Subgroup analysis

Subgroup analysis revealed that among older patients (aged 60–79 years), male patients, and those with higher histological grades, the cancer-specific survival (CSS) rates were significantly greater in the surgery group compared to the endoscopic treatment (ET) group (p = 0.0063, 0.018, and 0.00036, respectively; Fig. 5). However, no significant differences in overall survival (OS) rates were observed between the two groups (Supplementary Fig. S1).

For other subgroups, including tumor size, disease stage, and tumor location, no statistically significant differences were

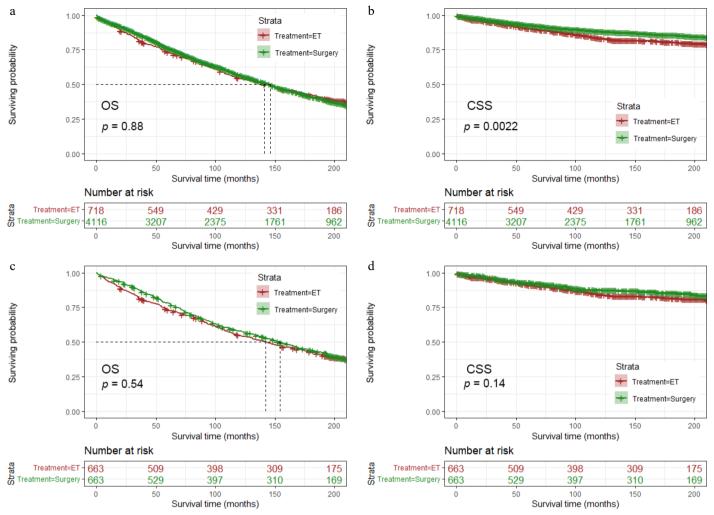


Fig. 3 Kaplan–Meier curves of overall and cancer-specific survival according to treatment methods (a), (b) before PSM, and (c), (d) after PSM.

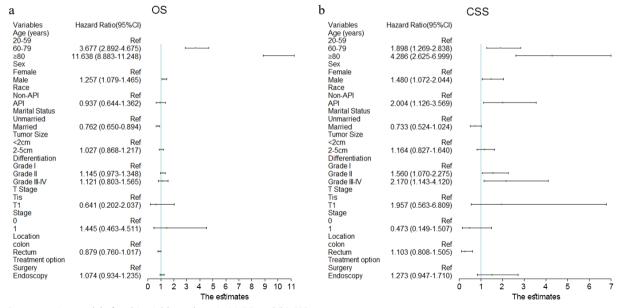


Fig. 4 Cox regression model of multivariable analyses in (a) OS, and (b) CSS.

identified between the ET and surgery groups in terms of both OS and CSS rates.

Discussion

With the advancement of endoscopic screening methods, endo-

Table 2. Univariate and multivariate analyses of OS and CSS in patients with T1 stage colorectal cancer treated with surgery and endoscopy before propensity score matching.

Univariate analysis				Multivariate analysis					
Variables		CSS		OS		CSS		OS	
		HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value
Age (years)	20-59	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	60–79	1.818 (1.448–2.283)	< 0.001	3.409 (3.004–3.867)	< 0.001	1.857 (1.477–2.335)	< 0.001	3.363 (2.963–3.816)	< 0.001
	≥ 80	3.818 (2.934–4.968)	< 0.001	10.286 (8.963–11.805)	< 0.001	3.757 (2.866–4.926)	< 0.001	9.797 (8.513–11.273)	< 0.001
Sex	Female	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	Male	1.075 (0.914–1.265)	0.384	1.073 (0.998–1.155)	0.058	1.270 (1.069–1.508)	0.007	1.302 (1.205–1.407)	< 0.001
Race	Non-API	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	API	1.181 (0.874–1.596)	0.278	0.774 (0.658-0.910)	0.002	1.327 (0.980-1.796)	0.068	0.918 (0.780-1.080)	0.302
Marital status	Unmarried	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	Married	0.685 (0.581-0.807)	< 0.001	0.660 (0.612-0.710)	< 0.001	0.751 (0.628-0.897)	0.002	0.780 (0.720-0.846)	< 0.001
Tumor size	≤ 3 cm	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	> 3 cm	1.404 (1.193-1.652)	< 0.001	1.182 (1.097-1.273)	< 0.001	1.362 (1.153-1.610)	< 0.001	1.101 (1.021-1.188)	0.013
Histological	Grade I	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
grade	Grade II	1.177 (0.962-1.439)	0.113	1.025 (0.941-1.117)	0.569	1.156 (0.942-1.418)	0.166	1.014 (0.930-1.106)	0.753
	Grade III–IV	1.725 (1.270-2.343)	< 0.001	1.097 (0.942-1.276)	0.234	1.627 (1.193-2.219)	0.002	1.085 (0.931-1.265)	0.295
LNM	Negative	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	Positive	1.864 (1.383-2.511)	< 0.001	1.004 (0.841-1.198)	0.966	0.595 (0.053-6.709)	0.674	0.248 (0.059-1.047)	0.058
T stage	Tis	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	T1	0.726 (0.552-0.954)	0.022	0.836 (0.733-0.953)	0.007	0.165 (0.023-1.194)	0.074	0.123 (0.039-0.385)	< 0.001
Stage	0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	1	0.732 (0.552-0.970)	0.030	0.858 (0.750-0.980)	0.024	4.779 (0.646-35.344)	0.125	7.463 (2.362-23.580)	0.001
	2	0.669 (0.377-1.189)	0.171	0.825 (0.621-1.095)	0.183	4.965 (0.630-39.152)	0.128	7.942 (2.443-25.822)	0.001
	3	1.359 (0.915-2.019)	0.129	0.849 (0.683-1.055)	0.140	16.551 (0.252-1087.739)	0.189	32.986 (2.877-387.235)	0.005
Location	Colon	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	Rectum	1.246 (1.056-1.472)	0.009	0.851 (0.787-0.921)	< 0.001	1.238 (1.041-1.473)	0.016	0.934 (0.861-1.014)	0.101
Treatment	Surgery	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
option	ET	1.375 (1.120–1.687)	0.002	0.992 (0.896–1.098)	0.878	1.474 (1.184–1.834)	0.001	1.080 (0.970-1.203)	0.159

 $CI, confidence\ interval; CSS, cancer-specific\ survival; OS, overall\ survival; HR, hazard\ ratio; API, Asian\ Pacific\ Islander.$

Table 3. Baseline characteristics of patients treated with surgery and ET for T1 stage colorectal cancer after PSM.

Variables		Surgery (n = 663) n (%)	Endoscopy (n = 663) n (%)	<i>p</i> -value
Age (years)	20-59	170 (50)	170 (50)	0.991
	60-79	367 (49.9)	369 (50.1)	
	≥ 80	126 (50.4)	124 (49.6)	
Marital status	Unmarried	248 (49.8)	250 (50.2)	0.955
	Married	415 (50.1)	413 (49.9)	
Sex	Male	341 (49.8)	344 (50.2)	0.912
	Female	322 (50.2)	319 (49.8)	
Race	Non-API	632 (50.0)	633 (50.0)	1.000
	API	31 (50.8)	30 (49.2)	
Tumor size	≤ 3 cm	511 (50.0)	511 (50.0)	1.000
	> 3 cm	152 (50.0)	152 (50.0)	
Histological	Grade I	198 (50.0)	198 (50.0)	1.000
grade	Grade II	430 (50.1)	429 (49.9)	
	Grade III-IV	35 (49.3)	36 (50.7)	
LNM	Negative	662 (50.0)	662 (50.0)	1.000
	Positive	1 (50.0)	1 (50.0)	
Location	Colon	301 (50)	301 (50)	1.000
	Rectum	362 (50)	362 (50)	
Stage	0	69 (49.6)	70 (50.4)	0.988
	1	583 (50.1)	581 (49.9)	
	2	10 (47.6)	11 (52.4)	
	3	1 (50)	1 (50)	
T stage	Tis	69 (49.6)	70 (50.4)	1.000
	T1	594 (50)	593 (50.0)	

scopic treatments have become a well-established option for early colorectal cancer (CRC), leading to a higher rate of complete resections^[12]. Numerous studies have assessed the effectiveness and

safety of endoscopic resection for early CR^[13,14]. However, there is limited research directly comparing endoscopic resection with surgical treatment for early-stage CRC, particularly among Western populations. In this study, overall survival (OS) and cancer-specific survival (CSS) were evaluated in patients undergoing endoscopic resection vs surgical treatment. To ensure a more accurate comparison, the following approaches were applied: (1) a propensity score matching (PSM) algorithm to minimize confounding factors, including tumor size, histological grade, lymph node metastasis (LNM), stage, and tumor location; (2) competing risk regression as an alternative to Cox regression, accounting for competing survival outcomes, such as tumor-specific mortality and mortality from other causes.

Surgical resection remains the primary treatment modality for early-stage gastrointestinal cancers due to its advantages in achieving complete tumor removal and lymph node dissection[15]. However, it is often associated with significant postoperative morbidity and mortality rates^[16]. In contrast, endoscopic treatment (ET) offers a minimally invasive alternative with lower complication rates, reduced mortality, and better preservation of organ function, thereby enhancing the quality of life. The primary indications for ET include mucosal (Tis) and superficial submucosal (T1a) cancers without lymph node involvement in CRC^[17]. Despite the advancements in endoscopic techniques, a declining trend in the use of ET for T1-stage colorectal cancer (CRC) was observed from 2000 to 2018, while surgical treatment rates remained higher. This may be attributed to certain limitations of ET, which can hinder its widespread adoption in Western populations. Endoscopic procedures may pose a higher risk of intraoperative complications, including bleeding and perforation, and may result in positive margins due to the challenges in accurately defining tumor boundaries^[18].

 Table 4.
 Univariate and multivariate analyses of OS and CSS in patients with T1 stage colorectal cancer treated with surgery and ET after PSM.

Univariat Variables CSS		e analysis		Multivariate analysis					
		CSS		OS		CSS		OS	
		HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value
Age (years)	20-59	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
,	60-79	1.811 (1.216-2.699)	0.003	3.698 (2.912-4.696)	< 0.001	1.898 (1.269-2.838)	0.002	3.677 (2.892-4.675)	< 0.001
	≥ 80	4.070 (2.557-6.476)	< 0.001	12.375 (9.527-16.075)	< 0.001	4.286 (2.625-6.999)	< 0.001	11.638 (8.883-11.248)	< 0.001
Sex	Female	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	Male	1.120 (0.834-1.505)	0.452	0.915 (0.975-1.051)	0.209	1.480 (1.072-2.044)	0.017	1.257 (1.079-1.465)	0.003
Race	Non-API	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	API	1.531 (0.870-2.692)	0.139	0.720 (0.497-1.043)	0.083	2.004 (1.126-3.569)	0.018	0.937 (0.644-1.362)	0.733
Marital status	Unmarried	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	Married	0.667 (0.495-0.899)	0.008	0.599 (0.486-0.644)	< 0.001	0.733 (0.524-1.024)	0.068	0.762 (0.650-0.894)	0.001
Tumor size	≤ 3 cm	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	> 3 cm	1.242 (0.890-1.733)	0.203	1.042 (0.883-1.229)	0.627	1.164 (0.827-1.640)	0.384	1.027 (0.868-1.217)	0.754
Histological	Grade I	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
grade	Grade II	1.534 (1.067-2.204)	0.021	1.043 (0.893-1.218)	0.598	1.560 (1.070-2.275)	0.021	1.145 (0.973-1.348)	0.102
	Grade III–IV	2.042 (1.088-3.834)	0.026	1.084 (0.780-1.506)	0.632	2.170 (1.143-4.120)	0.018	1.121 (0.803-1.565)	0.503
Nodal status	Negative	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	Positive	NA	NA	0.050 (0.001-44.849)	0.387	NA	NA	NA	NA
T stage	Tis	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	T1	1.083 (0.657-1.786)	0.754	0.910 (0.729-1.136)	0.403	1.957 (0.563-6.809)	0.291	0.641 (0.202-2.037)	0.451
Stage	0	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	1	1.077 (0.653-1.776)	0.773	0.916 (0.734-1.143)	0.436	0.473 (0.149-1.507)	0.205	1.445 (0.463-4.511)	0.526
	2	1.937 (0.565-6.641)	0.293	0.472 (0.149-1.494)	0.201	NA	NA	NA	NA
	3	NA	NA	NA	NA	NA	NA	NA	NA
Location	Colon	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
	Rectum	1.150 (0.853-1.550)	0.360	0.860 (0.748-0.989)	0.034	1.103 (0.808-1.505)	0.536	0.879 (0.760-1.017)	0.082
Treatment	Surgery	Ref	1.0	Ref	1.0	Ref	1.0	Ref	1.0
option	ET	1.246 (0.927–1.673)	0.145	1.044 (0.908–1.201)	0.541	1.273 (0.947–1.710)	0.110	1.074 (0.934–1.235)	0.316

CI, confidence interval; CSS, cancer-specific survival; OS, overall survival; HR, hazard ratio; API, Asian Pacific Islander.

A major concern with endoscopic resection of early-stage CRC is the potential for lymph node (LN) metastasis^[19]. Studies have reported that approximately 10% of submucosal colon cancers are associated with LN metastasis^[20]. According to the guidelines established by the Japanese Society for Cancer of the Colon and Rectum (JSCCR), for CRC cases treated with endoscopic resection, surveillance is recommended in instances where the tumor is a differentiated adenocarcinoma with submucosal invasion of less than 1,000 µm, no vascular invasion, low-grade tumor budding (grade 1), and negative horizontal margins. Conversely, submucosal cancers not meeting these criteria should be considered for additional surgical intervention with lymph node dissection^[21].

This study demonstrated that the OS and CSS rates in the endoscopic treatment and surgical resection groups were comparable among Western populations, aligning with findings from prior studies conducted in Asian countries^[22–24]. Although initial comparisons before PSM indicated a higher CSS rate in the surgery group, this result may have been influenced by confounding factors due to differences in pathological characteristics between the two groups. After adjusting for these confounding variables, no statistically significant differences in CSS were observed. While previous studies have established the safety and efficacy of ET, with long-term survival outcomes comparable to those of surgical resection, ET remains unsuitable in certain cases. Notably, the subgroup analysis revealed significantly lower CSS rates in the ET group, particularly among older patients, male patients, and those with higher histological grades. These findings suggest that early-stage colorectal cancer (CRC) patients exhibiting these characteristics may benefit more from surgical resection to achieve improved survival outcomes.

This research possesses multiple limitations. Initially, as a retrospective analysis, the selection of subjects is based on historical data rather than random assignment, which may result in samples that are not representative of the actual target population. It is inherently susceptible to selection bias. There were notable imbalances between the two groups in key factors, including tumor size, histological grade, lymph node metastasis, tumor location, and stage. While propensity score matching was implemented to mitigate selection bias, the possibility of residual biases remains, which could have influenced the findings. Second, the absence of certain critical parameters in the dataset, including information on procedurerelated complications, tumor resection margins, management of recurrence, detailed depth of infiltration, and details regarding the type of endoscopic (EMR or ESD) or surgical approach (open or laparoscopic), may have impacted the accuracy of this analysis. At the same time, it cannot be ignored that the pathological evaluation after conventional endoscopic surgery (including ESD and EMR) will list the depth of invasion of the lesion in the submucosal layer in more detail (such as T1a and T1b). Unfortunately, the seer database fails to provide such information. Lastly, given the generally high 5year survival rates for early-stage colorectal cancer, identifying substantial disparities in survival outcomes between the ET and surgical cohorts may have proven difficult. A 10-year survival analysis would provide a more comprehensive evaluation of long-term outcomes. However, the limited follow-up duration within the SEER database restricted the study's ability to assess 10-year survival rates. Despite these limitations, the study is notable for being the first to conduct a direct comparison of long-term survival outcomes between ET and surgical treatment. Additionally, as a populationbased study with substantial sample size and extended follow-up duration, the results offer valuable insights and contribute to the existing body of evidence in this field.

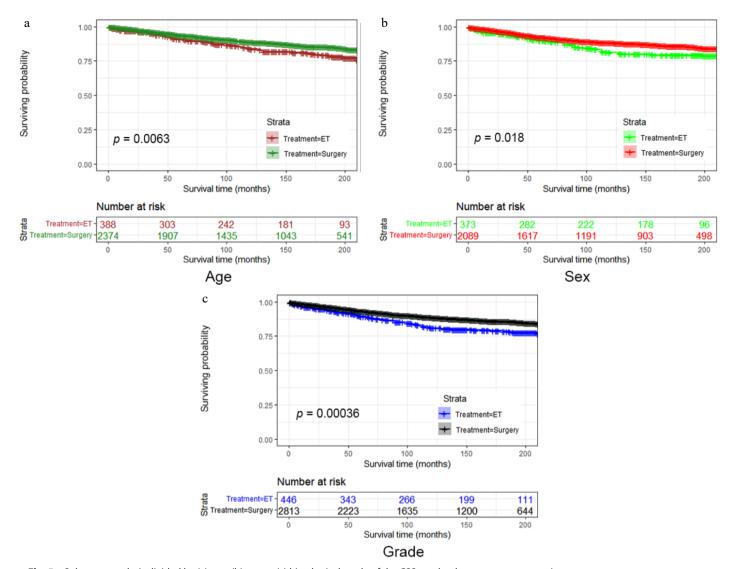


Fig. 5 Subgroup analysis divided by (a) age, (b) sex, or (c) histological grade of the CSS rate by the two treatment options.

Conclusions

In conclusion, this study demonstrated no significant difference in long-term survival between the endoscopic treatment (ET) and surgery groups for T1-stage colorectal cancer. Consequently, endoscopic resection could be a suitable alternative for patients ineligible for surgery due to comorbidities or other considerations. However, surgical resection may be a more appropriate choice for older individuals and those with tumors of higher histological grade. Given the limitations of this study, further prospective multicenter investigations are recommended to corroborate these findings and furnish more substantial data.

Ethical statements

This study utilized public-accessible data from the Surveillance, Epidemiology, and End Results (SEER) database provided by the National Cancer Institute (NCI). Approval from an institutional review board and informed consent were unnecessary for the current investigation due to the public availability of SEER research data and the de-identification of all patient information. Therefore, no ethics committee approval was required for this study.

Author contributions

The authors confirm contribution to the paper as follows: conceptualization, project administration: Zhou X, Zhang G; methodology: Su W, Chen H; formal analysis, writing - original draft: Su W, Chen H, Hu D; investigation, writing - review and editing: Su W, Chen H, Hu D, Li X, Si X, Ye B; supervision: Zhou X, Ye B. All authors reviewed the results and approved the final version of the manuscript.

Data availability

Data is included in the manuscript or additional information files. The datasets utilized and examined in this investigation are obtainable from the relevant author upon a reasonable request.

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Conflict of interest

The authors declare that they have no conflict of interest.

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