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Role of Endoscopic Resection Versus Surgical Resection in Management of Malignant Colon Polyps: a National Cancer Database Analysis

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Abstract

Background Endoscopic resection (polypectomy) or surgery, are the main approaches in management of malignant colon polyps. There are very few large population-based studies comparing outcomes between the two.

Methods Using the National Cancer Database, we identified patients ≥ 18 years with the first diagnosis of T1N0M0 malignant polyp from 2004 to 2015. Patients with a positive resection margin were excluded. Outcomes were compared between those who had surgery versus those who had polypectomy. Overall survival was compared using Kaplan-Meier curves. Multivariate Cox proportional hazards analysis was performed to generate hazard ratios, adjusted for patient, demographic, and tumor factors.

Results A total of 31,062 patients met the inclusion criteria, out of which 2593 (8.3%) underwent polypectomy alone and 28,469 (91.7%) had surgery. Overall survival was significantly better in the surgical group compared with the polypectomy group. One-year and 5-year survival for surgery were 95.8% and 86.1% respectively compared with 94.2% and 80.6% for polypectomy ($p < .0001$). Hazard ratio for surgery after adjusting for various clinical-, demographic-, and tumor-level factors was 0.53 ($p < .0001$).

Conclusion Our study is the largest population-based analysis of patients with T1N0M0 malignant colon polyps. Overall survival was higher in patients who underwent surgery compared with polypectomy. This remained consistent even after adjusting for multiple patient and tumor factors between the two groups.

Keywords Colonic neoplasms · Adenocarcinoma · Colectomy · Endoscopic mucosal resection · Cohort studies

Introduction

Colon cancer remains the third most common cancer diagnosed in men and women in the USA. The American Cancer Society estimates that 101,420 cases of colon cancer will be diagnosed in 2019. However, the death rate from it has been consistently dropping over the last several decades. This is attributed to multiple factors. With advent of national colon cancer screening guidelines and widespread availability of screening modalities, adenomatous polyps are being found and removed prior to progression to cancer. Also, cancers are detected at an earlier stage when more effective or curative treatment is possible.[1]

Malignant polyp is a macroscopically benign appearing adenoma that harbors a focus of cancer with invasion beyond the muscularis mucosae into the submucosa. These account for approximately 2 to 5% of all polyps removed.[2] As the diagnosis is usually made on the basis of pathology, such polyps present a challenging scenario with respect to further management. The two main options are observation after the initial endoscopic resection/polypectomy (ER) or surgical

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resection/colectomy (SR). Completely resected polyps, with a clear margin (> 1–2 mm from the transected edge), well or moderate degree of tumor differentiation, and lack of lymphovascular invasion, favor adequate management through polypectomy alone. Positive resection margins, poor degree of tumor differentiation, lymphovascular invasion, presence of tumor budding, or deep submucosal invasion are associated with high risk of lymph node metastasis. Such lesions need follow-up colon resection.[3–7] These recommendations are consistent with the current NCCN guidelines but following these in usual clinical practice can be difficult. Sessile polyps, especially > 20 mm in size, are usually removed in piecemeal fashion, leading to fragmentation of the specimen and difficulty in assessing the degree of submucosal invasion.[7] There exists a high degree of interobserver variation among experienced gastrointestinal pathologists with regard to histological grade of differentiation and in the assessment of lymphovascular invasion.[8] Thus, a careful assessment of the pathology, and a prudent review of patient's surgical risk, is warranted in creating an optimal plan.

While polypectomy alone eludes the potential for morbidity associated with surgery, early local recurrence due to incomplete removal can pose a substantial risk.[9] Regional nodal metastasis can be seen in approximately 8 to 13% of localized T1 colon cancer cases.[6, 10, 11] Surgical approach can provide complete staging and decrease the risk of local recurrence. Although current laparoscopic approach is associated with improved postoperative recovery, risk of surgery in elderly patients with multiple co-morbidities may outweigh the potential benefits. There have been many small single institution case series comparing outcomes between endoscopic resection and surgery, but very few population-based studies have been performed.[12, 13] Only one population-based analysis has been published in an American cohort, by Cooper et al.[13] The study was limited to patients above the age of 65. Also, important prognostic information was lacking regarding tumor resection margins and presence or absence of lymphovascular invasion.

Hence, we conducted this study to evaluate outcomes of endoscopic resection alone compared with surgical resection in patients with malignant colon polyps (T1N0M0) utilizing the US-based National Cancer Database (NCDB).[14] We assessed clinical and pathologic factors associated with overall survival in these patients and, using multivariable analysis, assessed which factors predict high likelihood of endoscopic resection alone.

Materials and Methods

Data Source

The patient data was obtained from the National Cancer Database (NCDB) for this study. The NCDB is a nationwide oncology outcomes database, run jointly by the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society. It accounts for approximately 70% of all newly diagnosed cancer cases in the USA at the institutional level and now contains some 34 million records from hospital cancer registries across the country. The NCDB states that, "the data used in the study are derived from a de-identified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigator".[15]

The 2015 Participant User File (PUF) for colon cancer was used for this analysis. NCDB-PUF file is a Health Insurance Portability and Accountability Act (HIPPA)–compliant data file that contains de-identified patient level data that does not identify hospitals, health care providers, or patients. Each case is provided a unique case ID, and detailed information is provided on patient demographics, co-morbidities, and tumor characteristics including staging, treatment, and survival.[16] The information available is codified, and the NCDB-PUF Data Dictionary (Version: PUF 2015 – Containing cases diagnosed in 2004–2015) was used for data extraction.

This retrospective study was considered "exempt from IRB review" by the State University of New York, Upstate Medical University Institutional Review Board, under the exemption category no. 4 (protocol no. 1322624-1).

Patient Selection

From the dataset, we identified all patients more than or equal to 18 years of age, with invasive adenocarcinoma contained in a colon polyp, i.e., T1N0M0 colon cancer diagnosed between 2004 and 2015. Patients with rectal malignant polyps were not included in our study as treatment options beyond just polypectomy or surgery are available such as transanal endoscopic microscopic surgery (TEMS). To best represent the clinical situation of a patient found to have a malignant polyp without any clinically discernible metastatic spread, we included patients with pathologically determined tumor size and/or extension (pT1) and clinically determined absence of regional lymph node or distant metastasis (cN0, cM0). Cases were coded using the AJCC Cancer Staging Manual Edition in use during the year in which the case was diagnosed. NCDB designates sequence numbers that refer to the sequence of malignant and non-malignant tumors diagnosed in a patient to distinguish cases with multiple cancer diagnoses. Sequence number code 00 designates the patients with only one lifetime cancer diagnosis. Sequence number 01 indicates that the reported tumor is the first of multiple diagnoses. The NCDB has no mechanism by which to link separate case reports of the same patient. Therefore, we limited the analyses to patients with sequence numbers 00 and 01 to ensure that

any review of treatment or outcomes of the study cohort is not confounded by treatment administered for a prior cancer diagnosis. We then excluded all patients who had a positive margin of resection, if involvement of cancer at the margins could not be assessed or if the diagnosis was made at autopsy. All patients who had unknown or missing information for the above variables were also excluded. The patients were then grouped into those who had polypectomy/endoscopic resection (ER) and definitive surgery (SR).

Variables from NCDB included demographic characteristics such as age at diagnosis, race, gender, year of diagnosis, urban/rural status, insurance status, facility type, and location. Age was categorized dichotomously as less than, and more than or equal to 65. Race and Hispanic origin category were combined to form one variable, race/ethnicity with 5 classes based on presence or absence of Hispanic origin. If Hispanic origin was missing or absent and race was missing or absent, then race/ethnicity was coded as unknown/other. Year of initial tumor diagnosis was combined to form three categories each spanning 4 years. Charlson-Deyo score was recorded using either the ICD-9 or ICD-10 secondary diagnosis codes. Due to the small number of cases with a Charlson comorbidity score more than 3, this variable was truncated to 4 categories, 0, 1, 2, and ≥ 3.[17] The location of the facility reporting the case was recorded per US census division. Nine categories are recorded in the NCDB as follows: 1—New England (CT, MA, ME, NH,RI, VT); 2—Middle Atlantic (NJ, NY, PA); 3—South Atlantic (DC, DE, FL, GA, MD, NC, SC, VA, WV); 4—East North Central (IL, IN, MI, OH, WI); 5—East South Central (AL, KY, MS, TN); 6—West North Central (IA, KS, MN, MO, ND, NE, SD); 7—West South Central (AR, LA, OK, TX); 8—Mountain (AR, CO, ID, MT, NM, NV, UT, WY); and 9—Pacific (AK, CA, HI, OR, WA). For ease of analysis, 1 and 2 were combined to form North East, 4 and 6 formed North Central, 3 was renamed South East, 5 and 7 formed South Central, and 8 and 9 were recorded as West. Data were recorded for lymphovascular invasion and tumor grade. Patients diagnosed before 2010 did not have the data for lymphovascular invasion; therefore, these were noted as missing. The data for primary site of the tumor was recorded on the basis of the topography code for the site of origin, International Classification of Diseases for Oncology, third edition. It was combined to form two main categories, right colon (cecum, ascending colon, hepatic flexure, and transverse colon) and left colon (splenic flexure, descending, and sigmoid colon). Missing or not specified information was recorded as such. Clinical, demographic, and tumor characteristics are listed in Table 1.

Outcome Measures

Primary outcome measure was the overall survival. The patients were followed until death or last contact. Other outcomes of interest were length of inpatient hospital stay after the definitive treatment, unplanned readmission to the same hospital within 30 days of discharge for a cause related to the treatment, and 30- and 90-day mortality. Information regarding overall survival, 30- and 90-day mortality was not available for cases diagnosed in 2015 due to limited follow-up and, therefore, not included in the analyses.

Statistical Analysis

Descriptive characteristics between the two groups (ER vs SR) were compared using Wilcoxon rank sum test and chi-square analysis for continuous and categorical variables, respectively. Kaplan-Meier analysis was used to compare survival time between ER versus SR. To adjust for potential confounding factors and selection bias in the allocation of treatment, we performed multivariate Cox proportional hazard regression to generate adjusted hazard ratios with 95% confidence intervals. Patient- and tumor-level factors that affected overall survival were identified using the same model. Multivariable logistic regression was performed to generate odds ratios to identify factors that predicted the use of ER. Two-sided p values < 0.05 were considered statistically significant. All data analysis was conducted using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

There were a total of 832,638 patients diagnosed with colon cancer, from 2004 to 2015, in the dataset. All patients who were not pT1cN0cM0 ($n = 785{,}118$) had positive or indeterminate resection margins ($n = 1221$), had missing or unclear information for these variables ($n = 6194$), or had a history of prior cancer diagnosis ($n = 9043$) were excluded. Total patients included for analysis were 31,062 out of which 2593 (8.3%) underwent endoscopic resection alone and 28,469 (91.7%) had surgery. Table 1 shows clinical, demographic, and tumor factors grouped by treatment status.

Mean (SD) age among those who underwent polypectomy was 64.9 years (13.0) (median = 65.0 years) and 65.9 years (12.0) (median = 66.0 years) among those who underwent surgery. Men were more likely to undergo polypectomy compared with females (p 0.02). Non-Hispanic Blacks were more likely to undergo polypectomy compared with non-Hispanic Whites ($p < .0001$). Interestingly, patients above 65 were as likely to undergo polypectomy compared with patients younger than 65 (p 0.30). Patients with Charlson-Deyo score of 1 or 2 were less likely to undergo polypectomy compared with those with score of 0 ($p < .0001$, 0.02). Patients with any insurance were more likely to have definitive surgery compared with those without insurance. Tumors in the left colon were more likely to undergo polypectomy ($p < .0001$)

Table 1 Patient characteristics by treatment status

	Treatment status							
	Missing		ER		SR		Total	
	N	%	*N*	%	*N*	%	*N*	%
Clinical and demographic factors								
Age (dichotomous)								
< 65	156	47.3	1293	49.9	12,487	43.9	13,936	44.4
≥ 65	174	52.7	1300	50.1	15,982	56.1	17,456	55.6
Race/ethnicity								
Non-Hispanic White	254	77.0	1925	74.2	22,350	78.5	24,529	78.1
Non-Hispanic Black	39	11.8	378	14.6	3480	12.2	3897	12.4
Non-Hispanic NA/API	12	3.6	105	4.0	1028	3.6	1145	3.6
Hispanic/Latino	15	4.5	135	5.2	1251	4.4	1401	4.5
Other/unknown	10	3.0	50	1.9	360	1.3	420	1.3
Gender								
Male	167	50.6	1451	56.0	14,386	50.5	16,004	51.0
Female	163	49.4	1142	44.0	14,083	49.5	15,388	49.0
Charlson-Deyo score								
0	241	73.0	1948	75.1	19,626	68.9	21,815	69.5
1	76	23.0	441	17.0	6304	22.1	6821	21.7
2	9	2.7	122	4.7	1758	6.2	1889	6.0
≥ 3	4	1.2	82	3.2	781	2.7	867	2.8
Year of diagnosis								
2004–2007	71	21.5	428	16.5	3918	13.8	4417	14.1
2008–2011	111	33.6	849	32.7	10,694	37.6	11,654	37.1
2012–2015	148	44.8	1316	50.8	13,857	48.7	15,321	48.8
Urban/status—2013								
Missing	16	4.8	60	2.3	743	2.6	819	2.6
Metro counties	261	79.1	2209	85.2	23,783	83.5	26,253	83.6
Urban counties	51	15.5	295	11.4	3467	12.2	3813	12.1
Rural counties	2	0.6	29	1.1	476	1.7	507	1.6
Insurance status								
Not insured	9	2.7	82	3.2	406	1.4	497	1.6
Private insurance	129	39.1	1055	40.7	11,666	41.0	12,850	40.9
Medicaid	15	4.5	137	5.3	1033	3.6	1185	3.8
Medicare	163	49.4	1239	47.8	14,790	52.0	16,192	51.6
Other government	5	1.5	31	1.2	254	0.9	290	0.9
Insurance status unknown	9	2.7	49	1.9	320	1.1	378	1.2
Facility type								
Missing	9	2.7	55	2.1	441	1.5	505	1.6
Community cancer program	61	18.5	453	17.5	3570	12.5	4084	13.0
Comprehensive community cancer program	139	42.1	1112	42.9	13,847	48.6	15,098	48.1
Academic/research program	99	30.0	712	27.5	7583	26.6	8394	26.7
Integrated network cancer program	22	6.7	261	10.1	3028	10.6	3311	10.5
Facility location								
Missing	9	2.7	55	2.1	441	1.5	505	1.6
Northeast	88	26.7	698	26.9	6342	22.3	7128	22.7
Southeast	54	16.4	432	16.7	5850	20.5	6336	20.2
North Central	112	33.9	766	29.5	7744	27.2	8622	27.5

Table 1 (continued)

	Treatment status							
	Missing		ER		SR		Total	
	N	%	*N*	%	*N*	%	*N*	%
South Central	43	13.0	307	11.8	4059	14.3	4409	14.0
West	24	7.3	335	12.9	4033	14.2	4392	14.0
Tumor factors								
Lymphovascular invasion								
Missing	127	38.5	727	28.0	8051	28.3	8905	28.4
Not present	146	44.2	1318	50.8	16,304	57.3	17,768	56.6
Present	10	3.0	71	2.7	1605	5.6	1686	5.4
Not applicable	.	.	1	0.0	7	0.0	8	0.0
Unknown	47	14.2	476	18.4	2502	8.8	3025	9.6
Primary tumor site								
Right colon	63	19.1	506	19.5	15,000	52.7	15,569	49.6
Left colon	238	72.1	1974	76.1	12,797	45.0	15,009	47.8
Missing	14	4.2	6	0.2	286	1.0	306	1.0
Colon, NOS	15	4.5	107	4.1	386	1.4	508	1.6
Grade								
Well differentiated	87	26.4	652	25.1	6174	21.7	6913	22.0
Moderately differentiated, moderately well differentiated, intermediate differentiation	165	50.0	1313	50.6	17,628	61.9	19,106	60.9
Poorly differentiated	10	3.0	79	3.0	1609	5.7	1698	5.4
Undifferentiated, anaplastic	2	0.6	12	0.5	207	0.7	221	0.7
Cell type not determined, not stated or not applicable, unknown primaries, high grade dysplasia	66	20.0	537	20.7	2851	10.0	3454	11.0

ER, endoscopic resection; *SR*, surgical resection; *NH*, non-Hispanic; *NA/API*, Native American/Asian Pacific Islanders

compared with right colon. Other tumor factors such as presence of lymphovascular invasion or poor degree of differentiation were associated with a higher chance of surgery ($p < .0001$). Facilities in the North East were more likely to perform polypectomy. A slight increase in trend was noted as cases diagnosed between 2012 and 2015 had higher odds of polypectomy compared with those diagnosed earlier (p 0.01). Table 2 shows multivariate analysis of factors associated with polypectomy (ER).

75.4% of the patients who underwent polypectomy were alive at last contact compared with 81.8% of those who had surgery. Median (interquartile range) follow-up for ER was 3.5 years (2.0, 5.3) and 3.9 years for SR (2.3, 5.7) ($p < .0001$). Figure 1 shows the Kaplan-Meier analysis comparing overall survival between ER versus SR. The unadjusted hazard ratio (HR) for mortality for SR compared with ER was 0.66 (95% confidence interval (CI) = 0.576, 0.757; $p < .0001$). Figure 2 shows 1- and 5-year survival estimates based on contingency table analysis. At 1 year, mortality for ER was 5.8% versus 4.2% for SR; relative risk (RR) for ER/mortality = 1.37 (95% CI = 1.15, 1.64). At 5 years, the patients who had ER had a mortality of 19.4% compared with 13.9% for SR; RR for ER/mortality = 1.39 (95% CI = 1.28, 1.53).

Table 3 shows multivariate Cox proportional hazards model. Adjusted HR for mortality for SR compared with ER was 0.53 ($p < .0001$). Factors that were independently associated with improved survival included female gender, Native American/Asian Pacific Islander race, age less than 65 years, Charlson score of 0, and absence of lymphovascular invasion ($p < .0001$). The primary site of the tumor did not have any effect on survival (p 0.47). Survival was comparable between well, moderate, and poor degree of differentiation but worse if the tumor was undifferentiated (p 0.04). Also, facilities in the South East had worse survival compared with facilities in the North East and facilities in the West had slightly improved overall survival (p 0.03).

Patients who underwent SR had longer length of stay in the hospital compared with ER (5.8 days vs 1.7 days; $p < .0001$) as well as higher chance of unplanned readmission to the hospital within 30 days as a result of the surgery for the cancer (4.6% vs 2.3%; RR for ER = 0.50 (95% CI = 0.38, 0.64)). Thirty-day mortality was higher in patients who had SR compared with ER (1.5% vs 0.55%; RR for ER = 0.37 (95% CI = 0.21, 0.65)), but there was no significant difference in 90-day mortality (SR 2.49% vs ER 2.29%; RR for ER = 0.92 (95% CI = 0.69, 1.22)).

Table 2 Multivariate analysis of characteristics that predict endoscopic resection

Characteristic	Odds ratio	95% confidence interval		*p* value
Sex-female (male = reference)	0.886	0.800	0.981	0.0196
Race/ethnicity (non-Hispanic White = reference)				
Hispanic/Latino	0.978	0.774	1.237	0.8537
Non-Hispanic Black	1.540	1.330	1.784	< 0.0001
Non-Hispanic NA/API	0.932	0.721	1.205	0.5931
Other/unknown	1.241	0.829	1.858	0.2946
Age ≥ 65 years (< 65 years = reference)	0.924	0.794	1.076	0.3078
Charlson-Deyo score (0 = reference)				
1	0.692	0.604	0.793	< 0.0001
2	0.768	0.606	0.974	0.0295
≥ 3	1.298	0.983	1.713	0.0658
Urban/rural status (metro counties = reference)				
Rural counties	0.531	0.316	0.893	0.0170
Urban counties	0.968	0.826	1.133	0.6839
Insurance status (no insurance = reference)				
Unknown	0.794	0.476	1.323	0.3753
Medicaid	0.616	0.430	0.883	0.0083
Medicare	0.564	0.409	0.779	0.0005
Other government	0.613	0.355	1.057	0.0783
Private insurance	0.435	0.322	0.589	< 0.0001
Facility type (community cancer program = reference)				
Academic/research program	0.762	0.649	0.895	0.0009
Comprehensive community cancer program	0.688	0.593	0.797	< 0.0001
Integrated network cancer program	0.736	0.601	0.899	0.0028
Facility location (northeast = reference)				
Northcentral	0.860	0.748	0.990	0.0356
Southcentral	0.711	0.597	0.846	0.0001
Southeast	0.646	0.549	0.760	< 0.0001
West	0.875	0.737	1.038	0.1264
Lymph vascular invasion (not present = reference)				
Not applicable	2.665	0.299	23.778	0.3801
Present	0.528	0.409	0.682	< 0.0001
Unknown	1.844	1.626	2.091	< 0.0001
Tumor grade (well differentiated = reference)				
Cell type not determined	1.450	1.235	1.703	< 0.0001
Moderately differentiated	0.720	0.635	0.816	< 0.0001
Poorly differentiated	0.455	0.334	0.619	< 0.0001
Undifferentiated, anaplastic	0.696	0.360	1.345	0.2814
Primary site (right colon = reference)				
Colon, NOS	7.564	5.573	10.268	< 0.0001
Left colon	4.412	3.899	4.993	< 0.0001
Missing	0.573	0.211	1.554	0.2738
Year of diagnosis—2012–2015 (2008–2011 = reference)	1.163	1.042	1.299	0.0072

NA/API, Native American/Asian Pacific Islanders; *NOS*, not otherwise specified

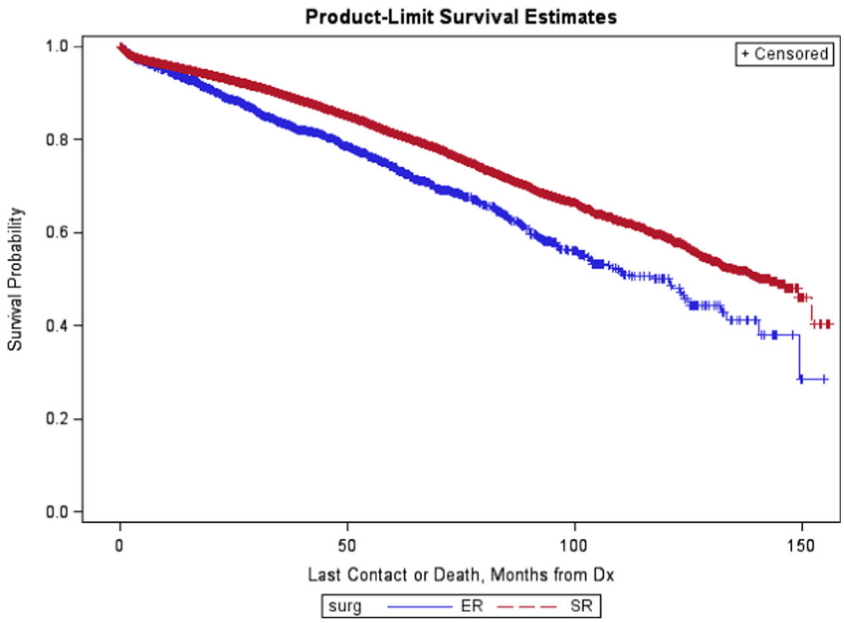

Fig. 1 Kaplan-Meier analysis comparing overall survival between ER versus SR. Dx, diagnosis; ER, endoscopic resection; SR, surgical resection

Discussion

This large retrospective population-based cohort study demonstrated a survival benefit with surgical resection compared with polypectomy alone in patients with malignant colon polyps.

As a randomized controlled trial comparing the two approaches does not exist, current guidelines are based on case series.[18] Factors that favor polypectomy alone include completely resected polyps, with a clear margin (> 1–2 mm from the transected edge), well or moderate degree of tumor differentiation, and lack of lymphovascular invasion.[3–7] These criteria are easily applicable to pedunculated polyps which have a clear stalk and are easy to resect en bloc. Sessile malignant polyps provide a different set of treatment challenges.

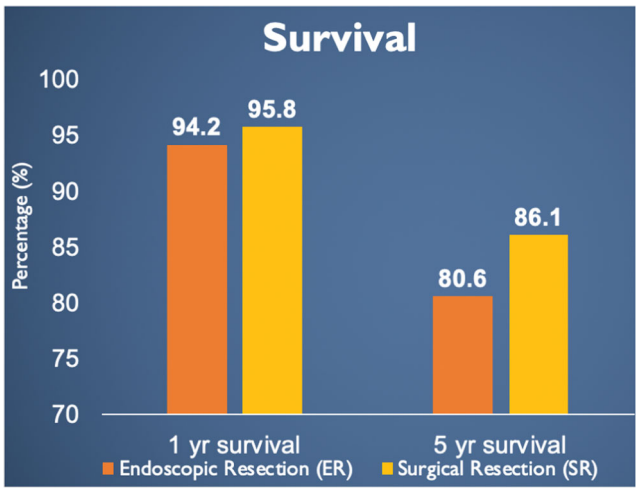

Fig. 2 One- and 5-year survival estimates based on contingency table analysis. ER, endoscopic resection; SR, surgical resection

Lack of a stalk provides shorter access for the spread of the cancer cells from the surface to the bowel wall and therefore leading to a higher rate of lymph node metastasis. Proximal malignant colon polyps are more likely to be sessile and more likely to undergo piecemeal resection. Higher rate of piecemeal resection leads to inadequately assessed resection margins, higher rate of residual tumor, and, thus, higher chance of recurrence.[6, 7, 19, 20]

Only one population-based analysis has been previously performed in an American cohort comparing overall survival between endoscopic resection and surgery in patients with malignant polyps. This study by Cooper et al. was an observational cohort study using SEER database. It included 2077 patients above the age of 65 years diagnosed between 1992 and 2005. Both 1-year and 5-year survival were higher in the surgical group (92% and 75%, respectively) than in the polypectomy group (88% and 62%, respectively). The unadjusted hazard ratio for mortality for polypectomy was 1.51 (95% CI = 1.31–1.74), although when the analysis was adjusted using propensity quintiles, there was no significant difference in mortality between the two groups (hazard ratio was 1.15 (95% CI = 0.98–1.33)). However, this study lacked information regarding important prognostic markers such as involvement of resection margin and presence or absence of lymphovascular invasion.[13]

In our study, a significantly larger proportion of patients underwent surgical resection versus polypectomy alone, when compared with previously reported data.[13, 18, 21] A study using SEER database looking at trends, patterns, and outcomes of surgical treatment in malignant polyps reported a rising trend of surgical resection from 1988 to 2003 (up to 70% from 54%).[23] Majority of polyps in various older series were located in the left colon.[12, 13, 23] Polyps located in the

Table. 3 Multivariate Cox proportional hazards model including treatment status, clinical-, demographic-, and tumor-level factors

Parameter		Parameterestimate	Standarderror	*p* value	Hazardratio	95% hazard ratio confidence limits	
Surgical status	ER (reference)						
	SR	−0.63364	0.07344	< 0.0001	0.531	0.460	0.613
Sex	Male (reference)						
	Female	−0.17621	0.04389	< 0.0001	0.838	0.769	0.914
Race/ethnicity	NH White (Reference)						
	NH Black	0.09950	0.06579	0.1304	1.105	0.971	1.257
	NH NA/API	−0.45352	0.16053	0.0047	0.635	0.464	0.870
	Hispanic/Latino	−0.21960	0.12386	0.0762	0.803	0.630	1.023
	Other/unknown	−0.41649	0.26913	0.1217	0.659	0.389	1.117
Age category	< 65 (Reference)						
	≥ 65	0.73585	0.07391	< 0.0001	2.087	1.806	2.413
Charlson-Deyo comorbidity score	0 (reference)						
	1	0.49262	0.05120	< 0.0001	1.637	1.480	1.809
	2	0.99208	0.06842	< 0.0001	2.697	2.358	3.084
	≥ 3	1.37933	0.08203	< 0.0001	3.972	3.382	4.665
Urban/rural status	Metro counties (reference)						
	Urban Counties	−0.04133	0.06741	0.5398	0.960	0.841	1.095
	Rural Counties	−0.25766	0.19540	0.1873	0.773	0.527	1.134
Insurance status	Not insured (reference)						
	Private insurance	−0.27714	0.21548	0.1984	0.758	0.497	1.156
	Medicaid	0.16027	0.24738	0.5171	1.174	0.723	1.906
	Medicare	0.30860	0.21743	0.1558	1.362	0.889	2.085
	Other government	0.13793	0.33302	0.6787	1.148	0.598	2.205
	Insurance status unknown	0.55556	0.27542	0.0437	1.743	1.016	2.990
Facility type	Community Ca. program (reference)						
	Comprehensive community cancer program	0.07885	0.06867	0.2509	1.082	0.946	1.238
	Academic/research program	−0.05391	0.07732	0.4857	0.948	0.814	1.103
	Integrated network cancer program	−0.00760	0.08966	0.9324	0.992	0.832	1.183
Facility location	Northeast (reference)						
	Southeast	0.14912	0.06770	0.0276	1.161	1.017	1.326
	Northcentral	0.01978	0.06324	0.7544	1.020	0.901	1.155
	Southcentral	−0.00956	0.07516	0.8987	0.990	0.855	1.148
	West	−0.17751	0.08370	0.0339	0.837	0.711	0.987
Lymphovascular invasion	Absent (reference)						
	Present	0.33006	0.07673	< 0.0001	1.391	1.197	1.617

Table. 3 (continued)

Parameter		Parameterestimate	Standarderror	*p* value	Hazardratio	95% hazard ratio confidence limits	
	Not applicable	1.66471	0.70930	0.0189	5.284	1.316	21.219
	Unknown	−0.09612	0.07024	0.1712	0.908	0.792	1.042
Tumor grade	Well differentiated (reference)						
	Moderately differentiated	0.02044	0.05416	0.7058	1.021	0.918	1.135
	Poorly differentiated	0.18255	0.09877	0.0646	1.200	0.989	1.457
	Undifferentiated, anaplastic	0.42016	0.20254	0.0380	1.522	1.023	2.264
	Cell type not determined	−0.17764	0.08970	0.0477	0.837	0.702	0.998
Primary site	Right colon (reference)						
	Missing	0.15943	0.20658	0.4403	1.173	0.782	1.758
	Left colon	−0.03374	0.04719	0.4746	0.967	0.881	1.061
	Colon, NOS	0.30108	0.16256	0.0640	1.351	0.983	1.858

ER, endoscopic resection; *SR*, surgical resection; *NH*, non-Hispanic; *NA/API*, Native American/Asian Pacific Islanders

proximal or right colon in the same studies were much more likely to undergo surgery compared with polypectomy. In our series, approximately 50% of all polyps were located in the right colon. This suggests a rising trend of right colonic malignant polyps, possibly accounting for a proportion of the increase in surgery cases. Patients with a positive margin of resection (presence of tumor cells < 1 mm of resection margin) have been shown to have a recurrence rate up to 33%.[24] In a series by Belderbos et al., it was shown to be the only independent risk factor for long-term recurrence after polypectomy with a HR of 6.88 (95% CI = 2.27, 20.87).[12] Surgical resection is recommended by current guidelines if the resection margin is positive or indeterminate.[18] Therefore, we excluded patients with a positive or indeterminate resection margin. This may have led to exclusion of a greater number of patients who had polypectomy but added an important advantage to our study by excluding patients who were more likely to have an adverse outcome with endoscopic resection alone.

Distribution of demographic characteristics was similar in our study compared with previously reported data including gender, race, co-morbidities, and tumor characteristics such as grade of differentiation.[13] Our study included a much wider age distribution with approximately 44% of the patients less than 65 years. This adds an important aspect to our study especially given the rising incidence of colon cancer in those below the age of 50.[25] Another important advantage of our study is availability of information regarding lymphovascular invasion. Presence of lymphovascular invasion has been associated with higher chance of lymph node metastasis, recurrence, and poor survival.[4–7] In our study, absence of lymphovascular invasion was associated with improved survival along with female gender, younger age at diagnosis, and lack of co-morbidities (Table 3).

One-year and 5-year survival estimates were in favor of the group that had surgery, similar to the study by Cooper et al.[13] To adjust for potential confounding factors, multivariate Cox proportional analysis was performed and the adjusted Hazard ratio remained consistent with a survival advantage for surgery. The exact reasons for this variation are not entirely clear. Our study included a significantly larger number of patients than in prior studies.[12, 13, 21–23] Median age of patients was younger, and a significant majority had lack of any co-morbidity compared with the study by Cooper et al.[13] Therefore, they were more likely to tolerate surgery and any post-operative complications better than older patients with multiple co-morbidities. Fifty percent of the polyps in our study were located in the right colon, and thus less likely to be removed adequately with polypectomy alone.[13, 20, 23] Field cancerization or field effect is the tendency of normal appearing mucosa surrounding a primary malignancy to form metachronous neoplasms. This has been described in colon adenocarcinoma.[26] Removal of the colonic segment surgically

may help decrease the risk of such metachronous neoplasms and possibly improve survival. Improvement in surgical techniques and increasing use of laparoscopic approach have led to quicker recovery of bowel function, shorter hospital stay, and decrease in post-operative morbidity.[27] In our study, patients who underwent surgery had longer length of stay, had higher chance of unplanned readmission within 30 days related to the surgery for the cancer, and had slightly increased 30-day mortality risk. There was no difference in 90-day mortality. The slight increase in 30-day mortality risk is likely a reflection of higher chance of surgery in patient with one or two co-morbidities (Charlson-Deyo score 1 and 2) in our series (Table 2). Over an extended time period, this increased risk did not sustain.

Our study does have limitations. Like other published series, ours is an observational study using a hospital registry database. Thus, patients were not matched and selection bias may exist in allocation of treatment. In order to mitigate that, we adjusted our analysis for various demographic, clinic, and tumor level factors using multivariate Cox proportional hazard model as shown in Table 3. Data regarding morphology of polyps was not available. However, a recent paper that assessed polyp morphology using a large database of asymptomatic patients who underwent screening colonoscopy showed that only 13% of all polyps were pedunculated. The rest were classified as sessile or flat.[28] Information about appropriate risk stratification such as family history of colon cancer or prior history of colon polyps was lacking. By excluding patients with a prior cancer diagnosis, we attempted to limit the confounding effect on overall survival for patients with increased risk. The data on lymphovascular invasion was not reported prior to 2010; nevertheless, as most of our cases were diagnosed later than that, majority of our patients had this information available for analysis. Although survival data were available, the cause of mortality and information regarding progression or recurrence of the disease was not available in the database. Information regarding surveillance follow-up after definitive treatment was lacking. This would have added valuable information to the study. Nonetheless, overall survival is still considered a gold standard and definitive end point for cancer patients.[29]

Conclusion

Our study is the largest population-based analysis of patients with T1N0M0 malignant colon polyps. Overall survival was found to be higher in patients who underwent surgery compared with polypectomy alone, even after adjusting for various clinical, demographic, and tumor level factors. Current guidelines state that malignant polyps with favorable histological features and clear resection margins can be managed through polypectomy alone, but our study suggests that it has not led to improved survival in usual clinical practice. Larger prospective series or a randomized clinical trial if possible are needed to shed more light on this increasingly frequent clinical problem.

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