Oncologic colorectal resection after endoscopic treatment of malignant polyps: Does endoscopy have an adverse effect on oncologic and surgical outcomes?

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Background: Early colorectal cancer is increasingly treated by endoscopic removal. In cases of incomplete resection or high-risk carcinoma, additional surgery is necessary.

Objective: To evaluate the frequency of subsequent oncologic surgery after endoscopic resection of colorectal cancer, the rate of lymph node metastasis, residual cancer, and morbidity and mortality rates of the operation. Any eventual adverse effect of the prior endoscopic therapy on the surgical and oncologic outcome was assessed.

Design: Retrospective review of prospectively collected data.

Setting: University hospital.

Patients: Sixty-six consecutive patients with incomplete endoscopic treatment and need for additional surgery between 2004 and 2011.

Intervention: The data of these patients were compared with those of a group of patients with surgery for early colorectal cancer during the same period without prior endoscopic resection as the control group.

Main Outcome Measurements: Rate of lymph node metastasis and residual cancer, perioperative morbidity and mortality.

Results: The lymph node metastasis rate after oncologic resection was 8.6%, and the residual cancer rate was 41%. Risk factors for residual cancer were macroscopic incomplete resection ($P < .0001$), positive resection margins ($P = .03$), and piecemeal resection ($P = .004$). No mortality was observed. Perioperative morbidity, mortality, and oncologic outcome were not significantly different in the group with prior endoscopic resection compared with the primarily operated group.

Limitations: Retrospective study.

Conclusion: Endoscopic treatment of malignant polyps does not worsen surgical and oncologic outcomes in cases of subsequent surgery. Because mortality and morbidity are low, oncologic resection generally should be done in the presence of risk factors for residual cancer. (Gastrointest Endosc 2014;79:951-60.)

Colorectal cancer develops predominantly on the basis of adenomas, that is, a sequence from adenoma to carcinoma. Through the removal of polyps before malignant transformation, the incidence of colorectal cancer is reduced.[1-3]

Polyps that macroscopically appear benign during colonoscopy may already be invasive carcinoma on histologic examination. Series reveal that up to 11% of endoscopically removed polyps are already malignant. Up to 20% of

Abbreviations: sm1, upper third of the submucosa; sm2, middle third of the submucosa; sm3, lower third of the submucosa; TNM, tumor, nodes, metastasis.

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endoscopically irresectable polyps were found to be malignant after surgical removal.[4-6]

The adequate management of patients with malignant polyps after endoscopic resection remains controversial. It was shown that endoscopic treatment is feasible and oncologically equal to surgery in certain cases of early colorectal cancer, with the advantage that endoscopic resection is less invasive and less expensive.[7,8] On the other hand, some authors primarily propose surgical resection in borderline resectable polyps or polyps that show certain predictors of malignancy (location, size, granularity, and pit pattern).[9-12]

Generally, colorectal polyps are removed during routine diagnostic colonoscopy, and there is no reliable tool to predict whether a polyp is malignant, nor its depth of infiltration or lymph node metastasis. The decision as to whether the endoscopic therapy was adequate or whether additional surgery is necessary is generally based on the macroscopic assessment of resection margins at the end of the EMR procedure and the histologic examination.

Currently, endoscopic therapy is regarded adequate in completely resected, low-risk carcinomas. Supplementary surgery is routinely recommended in case of incomplete endoscopic resection and in high-risk carcinomas, because the risk for lymph node metastasis increases with the depth of invasion, the histologic grading, and the presence of vascular or lymphatic infiltration. Lymph node metastases in up to 23% of carcinomas are reported if the tumor infiltrates the lower third of the submucosa (sm3).[6,13-18]

In this study, we addressed 2 main issues: (1) calculation of the risk of lymph node metastasis and residual cancer of endoscopic therapy against the higher morbidity and mortality rates of surgical therapy; (2) detection of any eventual adverse effect of prior endoscopic therapy on the surgical and oncologic outcomes of a salvage operation.

Take-home Message

- The attempt of endoscopic resection is justified in a polyp that the endoscopist believes to be completely endoscopically resectable, even though there is a possibility that it may contain carcinoma.
- In case of incomplete resection or high-risk situations, oncologic radical surgery should be indicated generously because morbidity and mortality rates are low.

PATIENTS AND METHODS

Patients

This retrospective study included all consecutive patients who underwent subsequent colorectal resection after endoscopic resection of malignant polyps, including polypectomy, EMR, and submucosal dissection. All endoscopic and operative procedures were performed in the University Hospital of Mannheim in the study period between January 2004 and June 2011. Patients with previous or synchronous colorectal carcinoma, familial adenomatous polyposis, and inflammatory bowel disease were excluded from the analysis.

Every patient had at least one reason for subsequent surgery: (1) positive resection margin (cancer cells found <1 mm from resection margin) R1/Rx/R2 (R0, no residual tumor; R1, microscopic residual tumor; R2 macroscopic residual tumor; Rx, residual tumor cannot be assessed); (2) lymphovascular invasion; (3) vascular invasion; (4) poor or no differentiation; (5) infiltration of the lower third of the submucosa or deeper.

Low-risk carcinoma was defined as grades 1 to 2 (well or moderate differentiated according to the UICC grading system), maximum T1, sm2 (maximum infiltration of the middle third of the submucosa), and no lymphatic or vascular invasion. All other stages were classified as high risk. A recent review stated that it is debatable whether sm2 lesions should be classified as low risk or high risk, hence needing additional surgery.[19]

In our clinic, sm2 lesions are counted among those of low risk, according to the German colorectal cancer guidelines. In the literature, there are different opinions concerning this topic. A study of 353 patients with early colorectal cancer found only sm3, and not sm2, as a significant predictor for lymph node metastasis.[17]

Surgical and oncologic outcomes were compared with those of a control group consisting of 151 consecutive patients with oncologic resection for colorectal cancer without prior endoscopic resection during the study period. These patients were identified from a prospectively maintained database with all colorectal resections in our department. During the study period, we performed colorectal resections for carcinoma on 805 patients. Patients with tumor stage T1 and T2 without prior endoscopic resection were included. We excluded patients with neoadjuvant treatment and patients with distant metastasis.

We decided to include patients with T2 tumors, because the group of patients with T1 tumors without prior endoscopic resection was very small, and we worried about a statistical bias, because of the small group size. As a result, there was an irregular distribution of patients with T1 and T2 tumors between the 2 study groups. Nevertheless, because all other demographic markers and the Union for International Cancer Control stage did not differ significantly, the groups should be comparable, concerning the short-term outcome.

End points

The effect on operative outcome was measured by perioperative morbidity and mortality, oncologic parameters (rate of R0 resections, number of harvested nodes), and hospital stay. Morbidity was classified according to the Clavien classification introduced in 2004.[20] Grades I and II were adverse events managed by conservative treatment

(pharmaceutical drugs, blood transfusions, parenteral nutrition). Patients with grade III disease were treated surgically or interventionally. Grade IV disease led to organ dysfunction requiring intensive care. Grade V disease equaled death of a patient. Anastomotic leakage was defined as any leakage seen on endoscopy or CT or confirmed during repeat operation.

Endoscopic resection and oncologic surgery

A complete endoscopic resection was intended in each case. Patients were included only when an experienced endoscopic surgeon judged the polyp as endoscopically potentially removable before the beginning of the endoscopic resection (intention to treat).

The endoscopic intervention was performed during a short hospital stay of 2 days. Saline solution with toluidine blue was injected into the submucosal tissue around the polyp either by hand or by hydro jet. Endoscopic resection was done by snare or submucosal dissection. After the resection, the endoscopist judged whether the resection was macroscopically complete or incomplete. Surgery was performed according to the generally accepted oncologic standards (central ligature of the arteries). Operations were done either conventionally or laparoscopically. Location of the resection site was achieved by endoscopic tattooing. The postoperative course followed a standardized clinical pathway, including a fast-track regimen (peridural catheter, early mobilization, and nutrition).

On diagnosis of malignant histology after endoscopic resection, patients were informed in detail about the findings, consequences, therapeutic options, and their rationales. The therapeutic concept for every patient was discussed and decided on in an interdisciplinary tumor conference. In particular, the risk of an operation was weighed against the risk of lymph node metastasis or tumor progression or recurrence in cases of unclear resection margins. In cases of high-risk carcinoma or incomplete resection, we generally recommended an oncologic resection, unless the patient had a very high perioperative risk.

In completely resected low-risk carcinomas, we generally recommended an endoscopic follow-up every 3 months for a period of 2 years, which is concordant with the recent German guidelines for colorectal cancer.[2] It was explained to the patients that the risk of lymph node metastasis even in low-risk carcinoma ranges up to 6%.[3-5]

Statistical analysis

The Fisher exact test and the Mann-Whitney test were used for nonparametric data, and the *t* test was used for quantitative data. For quantitative data, medians (range) were calculated. Risk factors for lymph node metastasis and residual cancer were analyzed by the Fisher exact test. A P value $< .05$ was considered statistically significant. Statistical analyses were performed with SPSS 15.0 (SPSS 15.0; Windows version, SPSS Inc, Chicago, IL, USA,).

RESULTS

General data

The total number of colorectal endoscopic resections in the study period was 2169. Colorectal cancer was found in the specimens of 140 patients after endoscopic resection for colorectal polyps in the study period between January 2004 and June 2011 (6.5% of all endoscopic resections). Sixty-eight patients (48.6%) had favorable histology and were classified as having low-risk carcinomas with complete endoscopic resection. In 72 patients (51.4%), a high-risk carcinoma was found or an R0 resection could not be confirmed histologically. These patients were recommended to undergo an oncologic resection after we judged the risk of an operation. Six patients (4.2%) either underwent surgery in other hospitals or refused the operation. A total of 66 patients (47.2%) received a salvage operation in the Department of Surgery of the University Medical Center Mannheim and were included in the study (median age 67.3 years, range 44-91 years). The male to female ratio was 1.54:1, respectively. The operation was performed at a median of 31 days (range 0-109 days) after the endoscopic resection (Fig. 1).

Median size of the resected polyps was 30 mm (range 10-90 mm). Twelve polyps (18.2%) were located in the right side of the colon (cecum to splenic flexure), 24 (36.4%) in the left side of the colon, and 30 (45.4%) in the rectum (Tables 1,2).

Reasons for oncologic resection

In 52 patients (78.8%), the endoscopic resection could be completed and was judged macroscopically complete. In 14 patients (21.2%), the endoscopic intervention was terminated prematurely, and the resection was judged macroscopically incomplete. In these cases, remnants of the polyps were treated with argon plasma coagulation. However, the histologic examination could not confirm a complete resection in 56 patients (84.8%) (resection state R1/Rx/R2). In 24 cases (36.4%), a high-risk carcinoma was found. In 42 patients (63.6%), a carcinoma was classified as low risk (Table 1).

Adverse events of EMR

Adverse events of endoscopic resection were bleeding that required repeat intervention in 4 cases (6.0%) and perforation that required emergency surgery in 3 cases (4.5%). Two perforations (3.0%) were treated conservatively with clipping (Table 1). These 2 patients were discharged after a hospital stay of 3 and 4 days. The 5 patients with perforation during endoscopy were followed-up and showed no local or distant tumor recurrence after a median time of 34 months.

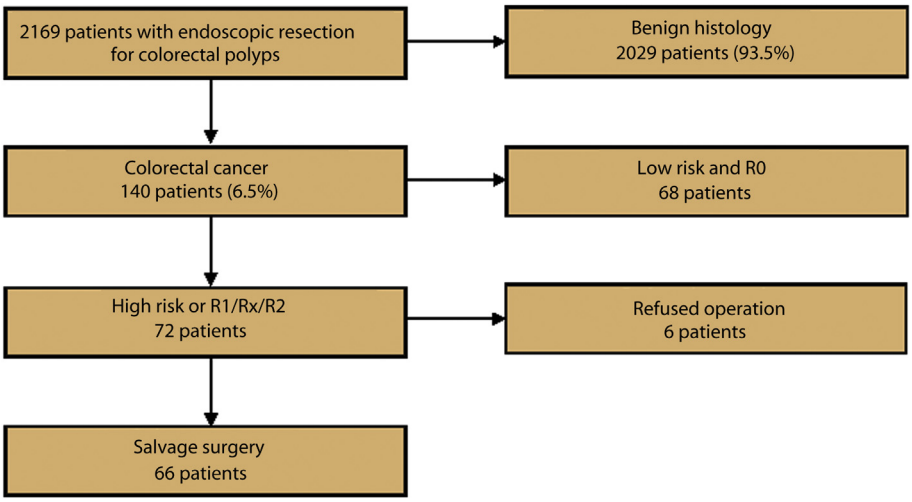

Figure 1. Patients with endoscopic resection for colorectal polyps between 2004 and 2011.

Results of colorectal resection

Low anterior resection or anterior resection was performed in 22 cases (33.3%), transanal resection (transanal endoscopic microsurgery) in 8 cases (12.1%), right colectomy in 12 cases (18.2%), left colectomy and sigmoid resection in 23 cases (34.8%), and subtotal colectomy in 1 case (1.5%).

Three patients had emergency surgery because of perforation during endoscopic resection (1 patient with high-risk carcinoma, 2 patients with incomplete resection). These operations also were performed oncologically. A stoma was not necessary.

No residual tumor was found in the operation specimens of 39 patients (59.1%). Tumor remnants were found in the operation specimens of 27 patients (40.9%), carcinoma was found in 25 patients (37.9%), adenoma with high-grade dysplasia in 1 patient (1.5%), and adenoma with low-grade dysplasia in 1 patient (1.5%). Table 3 shows the frequency of tumor remnants in the surgical specimens in relation to the resection state after the endoscopic intervention. Lymph node metastases were detected in the operation specimens in 5 cases (8.6%). Three of these patients had high-risk carcinomas, and 2 cases were classified as low-risk carcinomas. The rate of positive lymph nodes was 5.9% in the low-risk group and 12.5% in the high-risk group. For the calculation of the rate of positive lymph nodes, patients with transanal operations and therefore no lymphadenectomy were excluded.

The polypectomy and the primary surgery (control) groups were comparable in age, male to female ratio, and body mass index (Table 2). In the group without prior endoscopic resection, a higher percentage of polyps was located in the right side of the colon (36% vs 17%; $P = .05$). The frequency of rectal cancer was equal in both groups (44% vs 45%).

Postoperative mortality and morbidity were similar in the 2 groups. Overall mortality was low (1%), and occurrence of major adverse events such as anastomotic leakage were similar between the groups. The 2 patients in the group without prior endoscopic resection died of septic multiple organ failure after anastomotic leakage. There were no differences in the rates of R0 resection and the number of harvested lymph nodes between groups (Table 2).

The 3 patients who had emergency surgery because of perforation during endoscopic resection had no postoperative adverse events, and they had oncologic outcomes comparable to those of electively operated patients (harvested nodes, n = 14; R0 resection rate 100%). A statistical analysis was not done because of the small sample size.

Univariate analysis identified macroscopic incomplete resection ($P < .0001$), positive resection margins ($P = .03$), and piecemeal resection ($P = .004$) as potential risk factors for residual cancer. Multivariate analysis showed incomplete resection as significantly associated with residual cancer ($P < .0001$) (Tables 4,5).

DISCUSSION

Cancer in endoscopically removed polyps and adenomas is a frequent finding.[4-6] The discussion of whether surgery or endoscopy is the adequate treatment of early colorectal cancer is ongoing. Supporters of endoscopic treatment argue with lower morbidity and mortality rates and the good functional results, especially in comparison to low rectal resections in the case of middle and low rectal lesions. Opponents of the endoscopic method argue with the risk of residual tumor in cases of unknown deeper penetration of bowel layers; the inherent risk of

TABLE 1. Histologic characteristics of resected polyps and adverse events related to endoscopic resection, n = 66

Size of polyp, median (range), mm	30 (10-90)
Resection status, no. (%)*	
R0	10 (15.2)
R1	22 (33.3)
R2	13 (19.7)
Rx	21 (31.8)
Resection type, no. (%)	
En bloc	43 (65.2)
Piecemeal	23 (34.8)
Resection status, macroscopic, no. (%)	
Complete	52 (78.8)
Incomplete	14 (21.2)
High risk, no. (%)	24 (36.4)
Lymphatic invasion	13 (19.7)
Vascular invasion	1 (1.5)
Grading, G3/4†	7 (10.6)
Invasion sm3 and more	15 (22.7)
Residual tumor, no. (%)	27 (40.9)
Carcinoma	25 (37.9)
Low-grade dysplasia	1 (1.5)
High-grade dysplasia	1 (1.5)
No residual tumor	39 (59.1)
Adverse events, no. (%)	
Bleeding	4 (6.1)
Perforation (clipped)	2 (3.0)
Perforation (operation)	3 (4.5)

R0-Rx, R0, no residual tumor; *R1*, microscopic residual tumor; *R2*, macroscopc residual tumor; *Rx*, residual tumor cannot be assessed; sm3, lower third of the submucosa.
*Resection status.
†Grading system.

lymph node metastasis, for lymph nodes that are not removed; and the uncertain histologic assessment in cases of piecemeal resection. Some studies report accelerated tumor growth after incomplete endoscopic resection.[21,22] Furthermore, tumor cell dissemination may occur during endoscopic resection, especially when tumors are cut through with a piecemeal technique.[23] Although the prognostic impact of such tumor cell dissemination remains controversial, it may contribute to tumor metastasis.

Finally, perforation during endoscopic resection of a malignant polyp, although rare, is likely to increase the recurrence rate, at least in analogy to intraoperative tumor perforation, which is known to severely impair the oncologic prognosis.[24]

Generally, endoscopic treatment is regarded sufficient in cases of completely resected low-risk carcinomas. In all other cases, a subsequent surgical resection is recommended.[18] Some studies report the repeated endoscopic treatment in cases of R1 and/or Rx resections in low-risk carcinomas with good oncologic outcomes.[4,7] Still, a certain insecurity remains, because the probability of lymph node metastases in some studies ranges up to 20%, even for low-risk rectal cancer.[25]

Many studies have examined the feasibility and outcome of endoscopic treatment of early colorectal cancer and especially the usefulness of the classification into low-risk and high-risk carcinomas, with the latter showing a significantly worse outcome. Several authors have shown that a positive resection margin significantly predicts residual disease, that poorly differentiated carcinomas are associated with increased mortality, and that vascular invasion is associated with a higher risk of lymph node metastasis.[7,11,14,26,31] The conducted studies have mainly focused on risk factors for residual cancer and lymph node metastasis. Despite the high clinical relevance, there are few reports on surgical and oncologic outcomes of colorectal resections after prior endoscopic resection, and the number of patients examined in these studies is generally small.

However, these parameters are important in deciding between a solely endoscopic approach or additional surgery. The frequency of residual disease and lymph node metastasis, and thus the risk of tumor progression and adverse outcomes, in cases of no further surgical treatment versus the morbidity and mortality of subsequent surgery in cases of insufficient endoscopic treatment have to be weighed against each other.

We report a series of 66 patients who had surgery after incomplete endoscopic treatment of a malignant polyp or presentation of a high-risk carcinoma in the histologic examination. The primary aim was to investigate any potential influence of a prior endoscopic resection on the surgical and oncologic outcomes by comparing patients with colorectal resection for cancer with and without prior endoscopic treatment. We found that residual tumor was, indeed, detected in all but one patient in whom curative surgery had been performed because of a macroscopically incomplete resection.

However, residual tumor was detected in only one-third of patients having resection margins pathologically classified as R1 and Rx. There are 2 explanations for these results: the first is that the use of diathermy during endoscopic resection leads to thermal tumor necrosis at the resection margin. The second explanation is that piecemeal resection makes it impossible to verify clear margins. On the other hand, piecemeal

TABLE 2. Comparison of patients with and without endoscopic resection prior to surgery

	With ER, n = 66	Without ER n = 151	*P* value
Age, median (range), y	67.3 (44.4-91.4)	67.2 (33.5-91.4)	.788
Male, no. (%)	40 (60.1)	82 (54.3)	.390
Body mass index, median (range)	27.2 (19.7-40.1)	26.3 (17.8-36.4)	.160
Tumor location, no. (%)			
Right side of colon	12 (18.2)	55 (36.4)	.004
Left side of colon	24 (36.4)	30 (19.9)	.005
Rectum	30 (45.4)	66 (43.7)	.883
ASA classification,* no. (%)			
ASA 1/2	54 (81.8)	122 (80.8)	1
ASA 3	12 (18.2)	29 (19.2)	1
TNM stage†, no. (%)			
T1	56 (84.8)	36 (23.8)	.000
T2	6 (9.1)	114 (75.5)	.000
T3	4 (6.1)	0 (0)	.000
N0[1]	53 (91.4)	131 (86.8)	.823
N1	5 (8.6)	20 (13.2)	.482
T1N1	2 (4.2)	2 (5.6)	1
T2N1	1 (16.7)	18 (15.4)	1
T3N1	2 (50)	0	1
UICC stage‡			
UICC 1	59 (89.4)	131 (86.8)	.915
UICC 2	2 (3.0)	0 (0)	.095
UICC 3	5 (7.6)	20 (13.2)	.357
Patients without adverse events, no. (%)	45 (68.2)	103 (68.2)	.911
Patients with adverse events, no. (%)	21 (31.8)	48 (31.8)	1
Dindo-Clavien grades I + II§, no. (%)	17 (25.8)	42 (27.8)	.873
Bleeding requiring transfusion	1 (1.5)	1 (0.7)	.519
Bowel paralysis	7 (10.6)	16 (10.6)	1
Urinary tract infection	1 (1.5)	2 (1.3)	1
Pneumonia	2 (3.0)	5 (3.3)	1
Cardiac	1 (1.5)	6 (4.0)	.677
Wound infection‖	5 (8.6)	12 (7.9)	.626
Dindo-Clavien grades III + IV, no. (%)	8 (12.1)	15 (9.9)	.642
Anastomotic leak colon¶	2 (5.6)	4 (5.4)	.638
Anastomotic leak rectum**	2 (8.6)	5 (7.1)	1
Ileus	2 (3.0)	2 (1.3)	.170

(*continued on next page*)

TABLE 2. Continued

	With ER, n = 66	Without ER n = 151	*P* value
Burst abdomen	0	1 (0.7)	.546
Bleeding requiring repeat operation	1 (1.5)	1 (0.7)	.546
Myocardial infarction	1 (1.5)	1 (0.7)	.546
30-day mortality, no. (%)	0 (0)	2 (1.3)	.349
Harvested nodes, median (range)	12 [3-25]	13 [4-25]	.504
Resection status, †† no. (%)			
R0	65 (98.5)	151 (100)	.307
R1	1 (1.5)	0 (0)	.307
Hospital stay, median (range), d			
Without TEM	12 (6-74)	12 (5-127)	.963
All	11 (4-74)		

ER, Endoscopic resection; *ASA,* American Society of Anesthesiologists; *TNM,* tumor, nodes, metastasis; *UICC,* Union for International Cancer Control; *TEM,* transanal endoscopic microsurgery.
*ASA Physical Status Classification System.
†TNM; T1, tumor invades submucosa; T2, tumor invades muscularis propria; T3, tumor invades subserosa; T4, tumor invades adjacent organs or penetrates visceral peritoneum; N1, metastases in 1-3 nodes; N2, metastases in more than 3 nodes; M1, distant metastases.
‡UICC-stages, I, T1/T2; II, T3/T4; III, any T N+; IV, any T, any N M1.
§Dindo-Clavien grades; Grade I, any deviation from normal postoperative course without need for pharmaceutic, interventional or surgical treatment except analgetics, antiemetics, antipyretics; Grade II, requring pharmaceutical drugs, blood transfusions, parenteral nutrition; Grade III, requring surgical, endoscopic, or radiological intervention; Grade IV, leading to organ dysfunction requiring intensive care; Grade V, death of a patient.
‖Patients with transanal endoscopic microsurgery excluded.
¶Only patients with colon anastomosis.
**Only patients with rectum anastomosis.
††Resection status; R0, no residual tumor; R1, microscopic residual tumor; R2, macroscopc residual tumor; Rx, residual tumor cannot be assessed.

TABLE 3. Residual tumor after surgery in relation to histologic resection status after endoscopic resection

	R after endoscopy and histology of endoscopic specimen	Residual tumor (no. [%]) found in specimen of subsequent radical surgery
All	66	27 (40.9)
R1/R2/Rx	56	26 (46.4)
R0	10	1 (10.0)
R1	22	7 (31.8)
R2	13	12 (92.3)
Rx	21	7 (33.3)

R, Resection status; R0, no residual tumor; R1, microscopic residual tumor; R2, macroscopc residual tumor; Rx, residual tumor cannot be assessed.

resection was a risk factor for residual cancer in this study. In one case in which pathologic examination after endoscopic resection failed to reveal any cancer at all, residual cancer was found in the specimen after surgery. The rate of residual tumor after R1 resection in former studies ranged from 15% to 30%.[7,8,14,27-29] Our statistical analysis showed that a positive resection margin, incomplete resection, and piecemeal resection were risk factors for residual disease. These risk factors also were identified in another study.[27]

In our study, the risk of lymph node metastasis was 12.5% in high-risk carcinoma and still 6% in low-risk carcinoma, which is concordant with results of most published studies. However, certain studies found lymph node metastasis in up to 26% in high-risk cancer and 20% in low-risk rectal cancer.[17,21,25]

Colorectal resections still have an average mortality of 2% and a morbidity of 30%.[30] Detailed data about mortality and morbidity of oncologic resections after prior endoscopic treatment are rare. In a review from 2005,[14] the overall rate of surgically related death was 0.8% in colorectal resections after endoscopic treatment of early colorectal cancer (28 studies, 951 patients). This implies a relatively small patient number in every single study. Surgical adverse events are not mentioned in this review. Other studies found no surgical morbidity or mortality at all,[7,8] which is somewhat difficult to discuss regarding the earlier-mentioned rates of adverse events in a large review.

In our study, mortality was about 1%, the rate of severe adverse events (Dindo classification III-V) was about 10%,

TABLE 4. Risk factors for residual cancer, n = 66*

	Residual cancer	*P* value
Sex		.485
Male (n = 40)	15 (37.5)	
Female (n = 26)	12 (46.2)	
Tumor location		1.000
Proximal (n = 12)	5 (41.7)	
Distal (n = 54)	22 (40.7)	
Size of polyp		.663
<20 mm (n = 27)	10 (37.0)	
>20 mm (n = 39)	17 (43.6)	
Invasion		.563
Sm3 (n = 15)	5 (33.3)	
Sm1-2 (n = 51)	22 (43.1)	
Lymphovascular invasion		1.000
No (n = 53)	21 (39.6)	
Yes (n = 13)	6 (46.2)	
Margin <1 mm		.03
Positive (n = 56)	26 (46.4)	
Negative (n = 10)	1 (10)	
Differentiation		.036
G1-2 (n = 59)	27 (45.8)	
G3-4 (n = 7)	0 (0)	
Resection status		.000
Complete (n = 52)	14 (26.9)	
Incomplete (n = 14)	13 (92.8)	
Resection type		.004
En bloc (n = 43)	12 (27.9)	
Piecemeal (n = 23)	15 (65.2)	

sm, 1, 2, or 3, third of the submucosa; sm1, infiltration of upper third of submucosa; sm2, infiltration of middle third of submucosa; sm3, infiltration of lower third of submucosa. *G 1-4*, differentiation group; tumor grading system: grade 1, well differentiated; grade 2, moderately differentiated; grade 3, poorly differentiated; grade 4, undifferentiated.
*Data are absolute numbers (%).

TABLE 5. Risk factors for lymph node metastasis, n = 58*

	Residual cancer	*P* value
Sex		.634
Male (n = 34)	4 (11.8)	
Female (n = 24)	1 (4.2)	
Tumor location		1.000
Proximal (n = 12)	1 (8.3)	
Distal (n = 46)	4 (8.7)	
Size of polyp		1.000
<20 mm (n = 24)	2 (8.3)	
>20 mm (n = 34)	3 (8.8)	
Invasion		.584
Sm3 (n = 13)	2 (15.4)	
Sm1-2 (n = 45)	3 (6.7)	
Lymphovascular invasion		.306
No (n = 46)	3 (6.5)	
Yes (n = 12)	2 (16.7)	
Margin <1 mm		.206
Positive (n = 49)	3 (6.1)	
Negative (n = 9)	2 (22.2)	
Differentiation		.505
G1-2 (n = 51)	4 (7.8)	
G3-4 (n = 7)	1 (14.3)	
Resection status		1.000
Complete (n = 44)	4 (9.1)	
Incomplete (n = 14)	1 (7.1)	
Resection type		1.000
En bloc (n = 37)	3 (8.1)	
Piecemeal (n = 21)	2 (9.5)	

*Data are absolute numbers (%), n = 58 without patients with transanal endoscopic microsurgery; sm1, Infiltration of upper third of submucosa; sm2, infiltration of middle third of submucosa; sm3, infiltration of lower third of submucosa.

and overall morbidity was 30%, which is comparable to findings in the literature.

An important finding is that morbidity and mortality were not significantly different between patients who primarily underwent surgery and patients who had prior endoscopic resections. The same holds true for accepted surgical surrogate parameters of oncologic outcome—lymph node harvest and R0 resection rate. Hence, prior endoscopic resection should not have any negative effect on surgical outcome.

Benizri et al[32] recently analyzed study results of 64 patients with additional colectomy after endoscopic resection. They measured oncologic benefits by the lymph node metastasis rate and residual carcinoma. The risk was measured by the occurrence of severe adverse events after surgery (Dindo classification III/IV). A benefit-risk balance was calculated, which was in favor of surgery when 2 or more adverse histologic criteria (low differentiation,

lymphovascular invasion, R1 resection, piecemeal resection, etc) were present. The authors concluded that all patients with at least 2 adverse histologic criteria after polypectomy for T1 adenocarcinoma must be recommended for surgery; for young patients ($\leq$65 years), a single criterion was deemed sufficient to recommend operation. A drawback to this study is certainly the low rate of lymph node metastases (8%) and residual cancer (3%), which is low compared with the existing literature and may lead to a bias in measuring the potential oncologic benefit of an operation.

Drawbacks to our study are its retrospective character and the lack of long-term oncologic data. The latter may have contributed to shedding light on the influence of tumor cells that potentially disseminated during endoscopic resection and on the long-term oncologic outcome in comparison to tumor cell dissemination during radical surgical resection. This will have to be looked at in the further follow-up of the patients.

A further limitation is the fact that in the control group more tumors are staged T2. This is because only a few patients with T1 lesions and no prior endoscopic therapy were eligible. We worried about the small sample size and a potential statistical bias, so we decided to include patients with T2 lesions to achieve valid rates of adverse events, mortality, and oncologic outcomes as a benchmark to compare patients who underwent endoscopic resection. Because this tumor stage is limited to the bowel wall, this should be a homogenous group regarding the short-term outcome. The analysis showed that the groups were comparable in demographic markers.

Our study is the first that compares surgical and oncologic outcomes of resections for colorectal cancer with and without prior endoscopic treatment. We found no negative effect of a prior endoscopic resection on perioperative morbidity and mortality and oncologic surrogate quality markers. Therefore, we conclude that the attempt at endoscopic resection is justified in a polyp that the endoscopist believes to be completely endoscopically resectable, even though there is a possibility that it may contain carcinoma.

In cases of incomplete resection or high-risk situations, oncologic radical surgery should be indicated because morbidity and mortality rates are low. Because of the lack of sufficient evidence, the treatment strategy has to be discussed with every patient and individualized, especially in elderly patients and those with multiple comorbidities.

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