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Elective colectomy after colonoscopic polypectomy for unexpected polypoid T1 cancer

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Purpose. The treatment of early-stage colorectal adenocarcinoma removed endoscopically depends on histopathologic findings. The aim of this retrospective study was to assess the benefit–risk balance to patients who underwent colectomy after endoscopic polypectomy of T1 carcinoma with unfavourable histological factors.

Methods. Thirty one patients (15 men and 16 women, median age 66 years) who underwent colectomy after endoscopic resection of malignant polyps with T1 carcinoma within the period from 1 January 2004 to 11 February 2015 were included in this retrospective study. Specimens resected after endoscopic polypectomy showed at least one of the following unfavourable factors: no free margin or piecemeal resection. The main objective was to assess the benefit–risk balance of an oncological resection performed after the polypectomy. The oncological benefit was measured by the lymph node metastasis rate. The risk was measured by the occurrence of severe complications of grade III–IV or death.

Results. The most common localisation of T1 cancer was sigmoid colon – 16 cases (51.6%) and upper rectum – 11 cases (35.5%). 11 (35.5%) patients had well-differentiated adenocarcinoma (G1), others (20 patients from 31, 64.5%) had moderate differentiated adenocarcinoma (G2). The main indications of colectomy were two: the margin of resection ≤1 mm (n = 23) and piecemeal resection (n = 9). An oncological benefit of colectomy was reached for four patients (12.9%), who had lymph node metastasis. Six patients (19.4%) presented postoperative complications. All of them were of I–II grade according to the Clavien classification. There were no deaths.

Conclusions. 12.9% of patients, who underwent oncological colectomy after endoscopic polypectomy for unexpected polypoid T1 cancer with unfavourable histology (no free margin or piecemeal polypectomy), had metastasis in the lymph nodes; thus this study suggests the rationale of an oncological surgical resection after endoscopic polypectomy for these patients.

Key words: malignant colonic polyp, endoscopic polypectomy, lymph node metastasis

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INTRODUCTION

A malignant colonic polyp is defined as an endoscopically removed adenomatous polyp, in which cancer cells occur in submucosal lesions (1, 2). The prevalence of malignant polyps in a series of endoscopically removed polyps is between 0.2% and 11% (3). This percentage should increase with increasing numbers being identified in the bowel cancer screening programme (4). Consequently, a clear treatment algorithm is needed to treat patients correctly and safely. There have been various therapeutic options concerning the treatment strategy after endoscopic removal of a malignant polyp, including but not limited to a conservative approach or colectomy with extensive lymph node dissection.

A radical bowel resection is indicated in cases of inadequate excision, i. e. absence of malignant cells 1–2 mm from the transected margin, or if histology reveals undifferentiated adenocarcinoma (3, 5). When polyps are removed using the piecemeal technique, it is impossible to assess the depth of infiltration and the margin of these polyps (3, 5, 6), which then defines further treatment methods. Despite the use of these unfavourable histological criteria to select patients to operate on, many procedures are unnecessary and are sometimes followed by serious complications. The risk of local recurrence and lymph nodes metastasis must also be compared with that of morbidity and mortality following surgery. The number of cases in which high risk is associated with surgical procedures under general anaesthesia has increased due to higher numbers of elderly cases and cases with concurrent diseases in recent years.

We therefore conducted this retrospective study of thirty-one patients to evaluate the oncological benefit (measured by the rate of lymph node metastasis and the persistence of a residual adenocarcinoma) of an additional colectomy after an initial endoscopic polypectomy for T1 colorectal cancer. The morbidity was also analyzed in order to assess the risk–benefit balance of this procedure.

MATERIALS AND METHODS

Subjects

Data was retrospectively collected from 1 January 2004 to 11 February 2015 on all thirty-one patients who underwent an additional colectomy after radical endoscopic removal of malignant polyps with T1 carcinoma at the National Cancer Institute. Resection was done based on at least one of the following unfavourable histological criteria: no free margin or piecemeal resection. All patients gave their signed informed consent. No patient received any neoadjuvant treatment before surgery.

Procedures

The technique of polypectomy is standardized and has been described in literature (7). A majority of large sessile polyps were resected using the piecemeal technique.

All patients underwent elective oncological surgery, including the resection of the concerned segment and regional lymphadenectomy. Accurate localization of the polyp was achieved by metallic clip, endoscopic tattooing, or intraoperative colonoscopy, but it was not systematic. The procedures were performed by laparotomy or laparoscopy depending on the surgeon's preferences and the patient's surgical history. The principles and extent of open and laparoscopic resection were the same.

Resected specimens were fixed in 10% buffered formaline for 12–48 h. Surgical specimens were examined by experienced pathologists and this data was analyzed retrospectively.

Analysis

The primary end point was to assess the detailed oncologic features of T1 colorectal cancer removed endoscopically, with unfavourable histological criteria which indicated a need for additional surgery. To this end, a response variable was considered, linking the presence of positive lymph nodes and the insufficiency of the endoscopic excision with the persistence of a residual adenocarcinoma in the specimen.

Another objective was to analyze short-term complications of additional surgery. Mortality and morbidity were defined respectively as death or complications occurring following surgery during the hospital stay. Complications were classified in accordance with Clavien's classification (8). Ultimately, we assessed the benefit–risk balance of this procedure by assuming that the short-term risk assessed by the severe complications of grade 3–4 or death was as serious as the long-term risk measured by the presence of positive lymph nodes (patients with residual disease in the bowel wall were not included).

RESULTS

Thirty-one patients [16 females; median age at surgery 66 years (range 46–73)] were included in the present study. Patient demographics are shown in Table 1. Most patients were of American Society of Anaesthesiologists (ASA) class 2. The minority of patients were with ASA classes 1 and 4. The most common localisation of T1 cancer was sigmoid colon – 16 cases (51.6%) and rectum – 11 cases (36.7%), others (transverse colon, hepatic flexure, ascending colon, caecum) – 3.2% each. The average polyp size was 18 (range, 5–40) mm. The majority of the colorectal polyps were left-sided in location: 87.1% were sited at or distal to the splenic flexure, as shown in Figure. Clinico-pathologic features with adverse histological criteria that led to surgery and surgical procedures are detailed in Table 2. There were no distant metastases found in any of the patients, either intraoperatively or by radiological imaging.

Table 1. Baseline characteristics of patients

Number of patients	n = 31
Age, years	
Median	66 [46–73]
≥66	48.4% (15)
Gender	
Male	48.4% (15)
Female	51.6% (16)
Patient status according to the American Society of Anaesthesiologists (ASA) Classification	
ASA 1	3.2% (1)
ASA 2	64.5% (20)
ASA 3	29.0% (9)
ASA 4	3.2% (1)

The median number of retrieved lymph nodes per patient was 8 (range 0–39). In four patients (12.9%) who had lymph node metastases, polyp localisations were in the upper rectum and sigmoid colon. Their clinico-morphological features are shown in Table 4. No one had residual adenocarcinomas.

Table 2. Clinical and morphological characteristics of patients' data

Characteristics	Percentage (cases)
Cancer Differentiation Grade	
Well differentiated adenocarcinoma (G1)	35.5% (11/31)
Moderately differentiated adenocarcinoma (G2)	64.5% (20/31)
Resection	
Laparoscopic	58.1% (18)
Open	41.9% (13)
Procedure	
Left hemicolectomy	16.1% (5)
Right hemicolectomy	9.7% (3)
Sigmoid resection	35.5% (11)
Resection of transverse colon	3.2% (1)
Rectal resection with partial mesorectal excision	35.5% (11)
Polyp size, mm	
Mean	18 [5–40] mm
Indication for additional colectomy	
Margin ≤1 mm	74.2% (23)
Piecemeal resection	29.0% (9)
Total sampling node	
Median	8 [0–39]
≥8	51.6% (16)
Lymph node metastasis	12.9% (4)

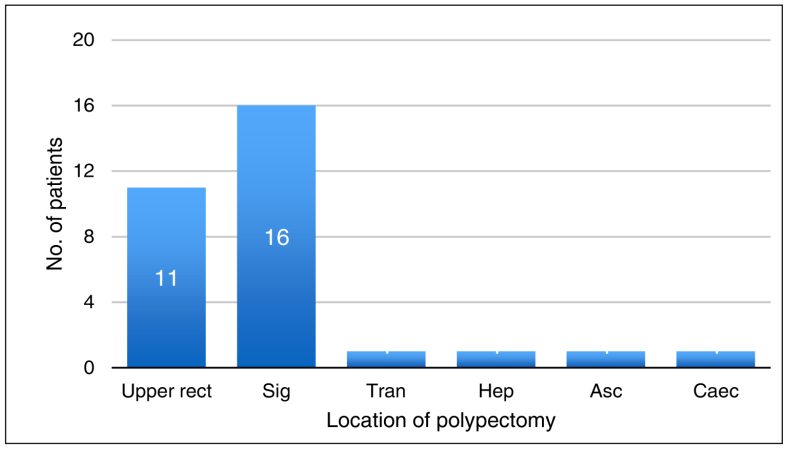

Figure. Location of colorectal polyps (Asc – ascending colon; Caec – caecum; Hep – hepatic flexure; Sig – sigmoid; Upper rect – upper rectum; Tran – Transverse colon)

Overall complication was identified in 6 (19.4%) of the 31 patients. Complications are summarized in Table 3. There were no severe complications of grade III–IV or surgical mortalities. The median length of hospital stay was 11 days (range 5–22).

Table 3. Postoperative complications in 26 patients

Postoperative outcomes	Number of patients, %
Dindo-Clavien grade II complications	6 (19.4)
Pneumonia	1 (3.2)
Hypovolemic shock	1 (3.2)
Postoperative ileus	1 (3.2)
Urinary infection	2 (6.4)
Wound infection	1 (3.2)

DISCUSSION

In our study 12.9% of patients had lymph node metastases and no one had residual adenocarcinoma in the specimen, although we selected patients whose polypectomy was considered complete by the endoscopist, and where adenocarcinoma was incidentally found on histopathological examination with no free margin, or after polypectomy using the piecemeal technique. However, to claim complete endoscopic removal requires an experience with polypectomy (9). The absence of remnant cancer could be explained by the fact that coagulation artefacts of snare polypectomy make it difficult for the pathologist to confirm tumour-free margins (6). Moreover, our study design contributed to the low rate of residual tumours, since only macroscopically benign-appearing polyps revealing malignancy at histology were included in this study. Furthermore, it is difficult to reconstruct polyp's anatomy on histopathological examination after polypectomy using the piecemeal technique (10). Accordingly, the aim of this study was to assess the oncological benefit of additional colectomy in these cases.

Our sample size is moderate, but it included highly-selected patients. For patients with T1 colorectal cancer, the lymph node metastasis rate varies from 0 to 17.3% (6, 11, 12). In our study, 12.9% of patients had lymph node metastases, which is the upper limit of the rate usually reported in the literature. As seen in Table 4, in all cases malignant polyps were found in the left-sided location, which correlates with malignancy in various studies of T1 colorectal adenocarcinomas (12–16). According to the current literature, incomplete or doubtfully complete resection, poor differentiation, budding, submucosal invasion >1 mm and lymphatic invasion are the main risk factors for positive lymph nodes (3, 5, 6, 17–19). Additional surgery is required for patients who present multiple adverse histological criteria. If only one criterion is selected, the indication should be discussed, especially for patients with multiple comorbidities (20). Most authors claim that a clear resection margin is anywhere from 1 mm (21) (as this definition was used in our study) to 2 mm (22). According to Naqvi et al., even those with <1 mm clearance of cancer cells can be treated with surveillance (23). Nevertheless, Bosch et al. find that the 1 mm cut-off is not an optimal method for risk stratification for additional colectomy, and although it has a high sensitivity (96.7%), it still carries a low specificity (24.1%) (18). Budding, submucosal and lymphatic invasion were not evaluated in our specimens, because in daily practice endoscopically resected

Table 4. Clinico-morphological features of patients with lymph node metastases. F – female; ASA – American Society of Anaesthesiologists class; Hosp. – hospitalization; Loc. – localization; Dif. – differentiation; G2 – moderate differentiation

Patient	Age	Sex	ASA	Hosp. days	No free margin	Piecemeal	Loc.	Diff.	Diameter (mm)	Positive lymph nodes
1	72	F	3	13	+	+	Upper rectum	G2	20	1/13
2	51	F	2	10	+	–	Sigmoid	G2	40	1/16
3	63	F	2	7	+	–	Upper rectum	G2	40	1/8
4	71	F	2	8	+	–	Upper rectum	G2	25	1/16

specimens, especially when carcinoma was not expected to be found by an endoscopist, often miss the muscularis propria and therefore it is hard to estimate the invasion depth rendered difficult by polypectomy artefacts. Submucosal lymphatics are often difficult to see and there is a wide inter-observer error (24). The assessment of lymphatic invasion may sometimes be too subjective to draw any valid conclusion. While early reports found no enhanced risk in cases with lymph vascular invasion alone, others show that it is an independent risk factor for lymph node metastasis (25–27). According to a value-of-information analysis published by Hassan et al., venous invasion had the highest predictive value for lymph node metastasis (28).

There is also a debate about the number of lymph nodes which should be examined for an adequate staging of colorectal cancer. The Guidelines 2000 for Colon and Rectal Cancer Surgery published by the National Cancer Institute in the USA recommended that 12 lymph nodes should be examined (29). Nevertheless, these results are based on data collected from T3 and T4 tumours. According to Benhaim et al., the number of lymph nodes is not a reliable indicator of the quality of surgery or of the histopathological examination when colectomy is done for malignant polyps removed endoscopically (30). Maggard et al. have reported that the examination of ≥4 lymph nodes is enough for staging T1 cancer. With a median of eight lymph nodes examined per specimen, our results are consistent with the literature (31).

According to L. P. Fielding et al., up to 12% of patients older than 70 years die during or after curative resection for colon cancer. They also claim that the risk of local recurrence or persisting lymph node metastases might be acceptable in these patients (32). In our study the median age of patients was 66 years and we had no deaths. Technical advances during the last two decades, such as more developed laparoscopic surgery, could have a positive influence on mortality of the elderly. 19.4% of the patients operated on presented just grade II complications. Current literature shows that surgery for colorectal cancer is still marked by a mortality of 1% and an overall morbidity approaching 20% (33, 34).

Obviously, this study has some drawbacks, since it is a retrospective study with a moderate sample size. This study did not focus on long-term oncological results. However, the risk of recurrence in patients without lymph node metastases or residual adenocarcinoma on the specimen is exceptional. Many studies have clarified that an unfavourable histologic grade, such as poorly differentiated or mucinous adenocarcinoma, is a risk factor for lymph node metastasis in colorectal cancer (21, 35), but we did not have any patient with such factors in this study, because their incidence is usually lower than 5% (36). A multicentric prospective study could provide additional results, in particular by weighing each adverse histological criterion. Despite these limitations, our patients were included consecutively and the population was perfectly homogeneous with a strict inclusion criteria. We therefore believe that these results reflect reality.

CONCLUSIONS

In conclusion, 12.9% of patients, who underwent oncological colectomy after endoscopic polypectomy for unexpected polypoid T1 cancer with unfavourable histology (no free margin or piecemeal polypectomy), had metastasis in the lymph nodes, and thus this study suggests the rationale of oncological surgical resection after endoscopic polypectomy for these patients.

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KOLEKTOMIJA PO KOLONOSKOPINĖS PIKTYBINIŲ POLIPŲ ŠALINIMO PROCEDŪROS SU NETIKĖTA T1 VĖŽIO HISTOLOGINE DIAGNOZE: ONKOLOGINĖ NAUDA IR OPERACINĖ RIZIKA

Santrauka

Tikslas. Ankstyvosios stadijos storosios ir tiesiosios žarnos vėžio, pašalinto endoskopiniu būdu, tolimesnė gydymo taktika priklauso nuo histologinio ištyrimo radinių. Šio tyrimo tikslas – įvertinti kolektomijos naudos ir rizikos santykį pacientams, kuriems atlikta endoskopinė polipektomija ir histologinio tyrimo metu rasti nepalankūs histologiniai veiksniai.

Metodika. Šiame retrospektyviniame tyrime dalyvavo 31 pacientas (15 vyrų ir 16 moterų, amžiaus mediana – 66 metai), jiems 2004 sausio 1 – vasario 11 d. NVI buvo atlikta kolektomija po kolonoskopinės piktybinių polipų su T1 vėžiu polipektomijos dėl bent vieno iš šių nepalankių histologinių veiksnių: teigiamo rezekcijos krašto ar polipo, pašalinto dalimis. Pagrindinis tikslas – įvertinti onkologinės kolektomijos, atliktos po endoskopinės polipektomijos, naudos ir rizikos santykį. Onkologinė nauda vertinta pagal pacientų, kurių limfmazgiuose rasta metastazių, skaičių. Rizika vertinta atsižvelgiant į III–IV laipsnio komplikacijų dažnį ir mirtingumą.

Rezultatai. Dažniausia piktybinių polipų su T1 vėžiu vieta buvo riestinė žarna – 16 atvejų (51,6 %) ir tiesioji žarna – 11 atvejų (35,5 %). 11 (35,5 %) pacientų histologinio tyrimo metu rasta gerai diferencijuota adenokarcinoma (G1), likusiesiems (20 pacientų iš 31, 64,5 %) – vidutinės diferenciacijos adenokarcinoma (G2). Pagrindinės kolektomijos indikacijos buvo dvi: rezekcijos kraštas ≤1 mm (n = 23), rezekcija dalimis (n = 9). Vienas pacientas turėjo abi šias indikacijas. Onkologinė kolektomijos nauda pasiekta keturiems pacientams (12,9 %), turėjusiems metastazių limfmazgiuose. 6 pacientams (19,4 %) pasireiškė pooperacinės komplikacijos. Šios komplikacijos nedidino operacinės rizikos, nes pagal Clavien klasifikaciją yra I–II laipsnio. Mirties atvejų nebuvo.

Išvada. 12,9 % pacientų, kuriems atlikta endoskopinė polipektomija ir histologinio tyrimo metu rasti nepalankūs histologiniai veiksniai, onkologinė kolektomija buvo naudinga.

Raktažodžiai: piktybinis storosios žarnos polipas, endoskopinė polipektomija, metastazės limfmazgiuose