

Elective colectomy after colonoscopic polypectomy for unexpected polypoid T1 cancer

Kolektomija po kolonoskopinės piktybinių polipų šalinimo procedūros ir netikėta T1 vėžio histologinė diagnozė

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Objective

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

Methods

From January 1st 2004 to February 28th 2014, twenty-three patients (12 men and 11 women, age median 66 years) who underwent colectomy after endoscopic resection of malignant polyps with T1 carcinoma were included in this retrospective study. Specimens resected after endoscopic polypectomy showed at least one of the two unfavorable factors – no free margin or piecemeal resection. The main objective was to assess the benefit–risk balance of oncological resection performed after polypectomy. The oncological benefit was measured by the lymph node metastasis rate, and the risk was measured by the occurrence of severe (grade III–IV) complications or death.

Results

The most common localisation of T1 cancer was the sigmoid colon (10 cases, 43.5%) and the upper rectum (9 cases, 39.1%). Nine (39.1%) patients had a well-differentiated adenocarcinoma (G1), while others (14 patients from 23, 60.9%) had a moderately differentiated adenocarcinoma (G2). The main indications for colectomy were the margin of resection ≤ 1 mm ($n = 17$) and piecemeal resection ($n = 7$). The most common surgical operation was rectal resection with partial mesorectal excision (9, 39.1%). The oncological benefit of colectomy was reached for two patients (8.7%) who had lymph node metastases. Five patients (21.7%) presented postoperative complications. These complications did not rise surgery risk, because all of them were of I–II grade according to Clavien's classification. There were no deaths.

Conclusions

Among the patients who underwent oncological colectomy after endoscopic polypectomy for unexpected polypoid T1 cancer with unfavorable histology (no free margin or piecemeal polypectomy) 8.7% had metastases in the lymph nodes; thus, this study suggests the rationale of oncological surgical resection after endoscopic polypectomy for these patients.

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

Tikslas

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

Metodika

Į šį retrospektyvų tyrimą įtraukta 23 pacientai (12 vyrų ir 11 moterų, amžiaus mediana 66 metai), kuriems nuo 2004 m. sausio 1 d. iki 2014 m. vasario 28 d. VUOI buvo atlikta kolektomija po kolonoskopinės piktybinių polipų su T1 vėžiu polipektomijos dėl bent vieno iš šių nepalankių histologinių veiksnių: teigiamas rezekcijos kraštas ar polipas pašalintas dalimis. Pagrindinis tikslas buvo įvertinti onkologinės kolektomijos, atliktos po endoskopinės polipektomijos, naudos ir rizikos santykį. Onkologinė nauda vertinta pagal pacientų, kuriems rasta metastazių limfmazgiuose, skaičių. Rizika vertinta atsižvelgiant į III–IV laipsnio komplikacijų dažnį ir mirtingumą.

Rezultatai

Dažniausia piktybinių polipų su T1 vėžiu vieta buvo riestinė žarna – 10 atvejų (43,5 %) ir viršutinis tiesiosios žarnos trečdalis – 9 atvejai (39,1 %). Devyniems (39,1 %) pacientams histologinio tyrimo metu rasta geros diferenciacijos adenokarcinoma (G1), kitiems (14 pacientų iš 23, 60,9 %) – vidutinės diferenciacijos adenokarcinoma (G2). Pagrindinės kolektomijos indikacijos buvo dvi: rezekcijos kraštas ≤ 1 mm (n=17), rezekcija dalimis (n=7). Daugiausia buvo atlikta tiesiosios žarnos rezekcijų su daline mezorektine ekscizija – 9 (39,1 %). Onkologinė kolektomijos nauda pasiekta dviem pacientams (8,7 %), kurie turėjo metastazių limfmazgiuose. Penkiems pacientams (21,7 %) pasireiškė pooperacinių komplikacijų. Šios komplikacijos nedidino operacinės rizikos, nes pagal *Clavien* klasifikaciją buvo I–II laipsnio. Mirties atvejų nepasitaikė.

Išvada

Atliktus onkologinę kolektomiją dėl nepalankių histologinių veiksnių (teigiamas rezekcijos kraštas ar rezekcija dalimis) po endoskopinės polipektomijos, 8,7 % pacientų rasta metastazių limfmazgiuose, todėl šis retrospektyvusis tyrimas pabrėžia onkologinės rezekcijos svarbą šių pacientų grupėje.

Reikšminiai žodžiai: piktybinis tiesiosios žarnos polipas, endoskopinė polipektomija, limfmazgių metastazės

Introduction

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 the series of endoscopically removed polyps is between 0.2% and 11% [3]. This is set to rise with increased numbers being identified in the bowel cancer screening programme. Consequently, a clear treatment algorithm is needed to treat patients correctly and safely. There have been various therapeutic options concerning treatment strategy after endoscopic removal of a malignant polyp, ranging from a conservative approach to colectomy with an 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 the histology

reveals undifferentiated adenocarcinoma [3, 4]. 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], on which the further treatment may also be based. Despite the use of these unfavorable histological criteria to select patients for operating, many procedures are unnecessary and are sometimes followed by serious complications. The risk of local recurrence and lymph node metastases 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 anesthesia has increased due to the increased numbers of elderly cases and cases with concurrent diseases.

Therefore, we have conducted this retrospective study to evaluate the oncological benefit (measured by the rate of lymph node metastases and the persistence of

residual adenocarcinoma) of an additional colectomy after the 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

Data were collected retrospectively from January 1st 2004 to February 28th 2014 on all twenty-three patients who underwent additional colectomy after a radical endoscopic removal of malignant polyps with T1 carcinoma at the Vilnius University Oncology Institute. Resection was done based on at least one of the two unfavorable histological criteria – no free margin or piecemeal resection. All patients gave their signed informed consent. No patient had received any neoadjuvant treatment before surgery.

The technique of polypectomy is standardized and has been described elsewhere [6]. The 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 with a 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 of the extent of open and laparoscopic resections were the same.

Resected specimens were placed into a sample bottle and fixed in 10% buffered formaline for 12–48 h. Surgical specimens were examined by experienced pathologists, and these data were analyzed retrospectively.

The primary end point was to assess the detailed oncologic features of T1 colorectal cancer, removed endoscopically, with unfavorable 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 on the specimen.

Table 1. Baseline characteristics of patients

Number of patients	N = 23
Age (years)	
Median	66 (46–73)
≥ 66	52.2% (12)
Gender	
Male	52.2% (12)
Female	47.8% (11)
American Society of Anaesthesiologists class	
1	4.3% (1)
2	60.9% (14)
3	30.4% (7)
4	4.3% (1)

Table 2. Clinical and morphological characteristics of patients

Differentiation grade	
Well differentiated adenocarcinoma (G1)	39.1% (9/23)
Moderately differentiated adenocarcinoma (G2)	60.9% (14/23)
Resection	
Laparoscopic	43.5% (10)
Open	56.5% (13)
Procedure	
Left hemicolectomy	21.7% (5)
Right hemicolectomy	13.0% (3)
Sigmoid resection	21.7% (5)
Resection of transverse colon	4.3% (1)
Rectal resection with partial mesorectal excision	39.1% (9)
Polyp size (mm)	
Mean	16.5 [5–40]
Indications for additional colectomy	
Margin ≤ 1mm	73.9% (17)
Piecemeal resection	30.4% (7)
Total sampling node	
Median	8 [0–39]
≥ 8	52.2% (12)
Lymph node metastases	8.7% (2)

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 [7]. Finally, we assessed the benefit–risk balance of this procedure, with the assumption 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 or residual adenocarcinoma on the specimen.

Results

Twenty-three patients [12 males; 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 of ASA classes 1 and 4. The most common localisation of T1 cancer was sigmoid colon (10 cases, 43.5%) and rectum (9 cases, 39.1%), others (transverse colon, hepatic flexure, ascending colon, caecum) – 4.3% each. The average polyp size was 16,5 (range, 5–40) mm. The majority of colorectal polyps were left-sided in location: 82.6% were sited at or distal to the splenic flexure (Figure 1). Clinicopathologic features with adverse histological criteria that led to surgery and the surgical procedures are de-

tailed in Table 2. There were no distant metastases found in any of the patients, either intraoperatively or by radiological imaging. The median number of retrieved lymph nodes per patient was 8 (range, 0–39). In two patients (8.7 %) who had lymph node metastases, polyps were localised in the upper rectum and the sigmoid colon. Their clinicomorphological features are shown in Table 4. No one had residual adenocarcinomas.

Overall complication was identified in 5 (21.7 %) of the 23 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 12 days (range, 5–22).

Discussion

In our study, 8.7% of patients had lymph node metastases, and no one had residual adenocarcinoma on

Table 3. Postoperative complications in 23 patients

Postoperative outcomes	Number of patients (%)
Dindo–Clavien grade II complications	5 (21.7)
Pneumonia	1 (4.3)
Hypovolemic shock	1 (4.3)
Postoperative ileus	1 (4.3)
Urinary infection	1 (4.3)
Wound infection	1 (4.3)

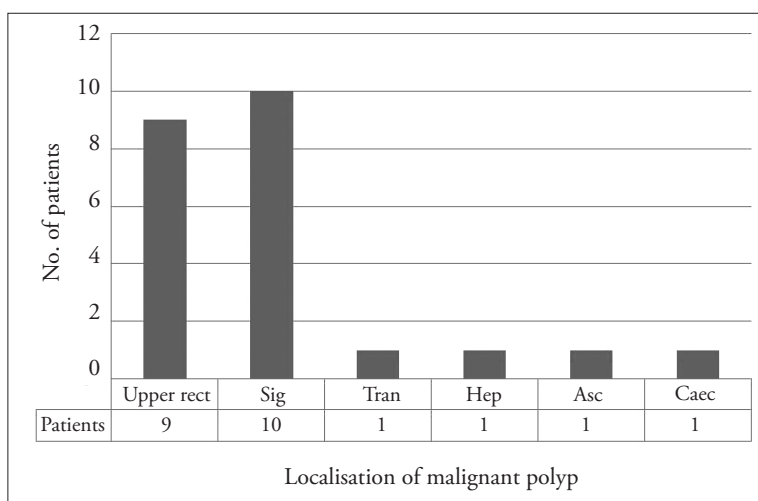


Figure 1. Location of colorectal polyps. Asc, ascending colon; Caec, caecum; Hep, hepatic flexure; Sig, sigmoid; Upper rect, upper rectum; Tran, Transverse colon

Table 4. Clinicomorphological features of patients with lymph node metastases

Patient	Age	Sex	ASA	Hosp. days	No free margin	Peace-meal	Loc.	Diff.	Diame-ter (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

F – female; ASA – American Society of Anaesthesiologists class; Hosp. – hospitalization; Loc. – localization; Dif. – differentiation; G2 – moderate differentiation.

the specimen, although we selected patients whose polypectomy was considered complete by the endoscopist and adenocarcinoma was incidentally found in a histopathological examination with no free margin or after polypectomy using the piecemeal technique. However, to claim a complete endoscopic removal requires experience with polypectomy [8]. 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 [5]. Moreover, our study design contributed to the low rate of residual tumours, since only macroscopically benign looking polyps revealing malignancy at histology were included in this study. Furthermore, it could be hard to reconstruct polyp's anatomy on histopathological examination after polypectomy using the piecemeal technique [9]. Accordingly, the aim of this study was to assess 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 6 to 8% [10]. In our study, 8.7% of patients had lymph node metastases, which is the upper limit of the rate usually reported in the literature. According to the current literature, incomplete or doubtfully complete resection, poor differentiation and lymphovascular invasion are the main risk factors for positive lymph nodes [3–5, 11]. 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 [12]. Most authors claim that a clear resection margin is anywhere from 1 mm [13] (as this definition was used in our study) to 2 mm [2, 14]. According to Naqvi et al.,

even those with a <1mm clearance of cancer cells can be treated with surveillance [15].

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, recommend that 12 lymph nodes should be examined [16]. Nevertheless, these results are based on data collected from T3 and T4 tumors. 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 [17]. Maggard et al. have reported that the examination of ≥ 4 lymph nodes is enough for staging the T1 cancer. With a median of eight lymph nodes examined per specimen, our results are consistent with the literature [18].

According to Fielding et al. [19], up to 12% of patients older than 70 years die during or after a curative resection of colon cancer. They also claim that the risk of local recurrence or persisting lymph node metastases might be acceptable in these patients [19]. 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 the mortality of the elderly. Of the patients operated on, 21.7% presented just grade II complications. The current literature shows that surgery for colorectal cancer is still marked by a mortality of 2 to 5% and the overall morbidity approaching 30% [20].

Of course, 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 unfavorable histologic grade, such as poorly differentiated or mucinous adenocarcinoma, is a risk factor for lymph node metastases in colorectal cancer [13, 21], but we had no patient with such factors in this study, because their incidence is usually lower than 5% [22]. A multicentric prospective study could provide additional results, in particular to weigh each adverse histological criterion. Despite these limitations, our patients were included consecutively, and the population was

perfectly homogeneous with the strict inclusion criteria. We, therefore, believe that these results reflect the reality.

Conclusions

Of the patients who underwent oncological colectomy after endoscopic polypectomy for unexpected polypoid T1 cancer with unfavorable histology (no free margin or peacemeal polypectomy) 8.7% had metastases in the lymph nodes. Thus, this study underlines the rationale of oncological surgical resection after endoscopic polypectomy for these patients.

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