

Prevalence, Histology, Endoscopic Treatment and Long-term Follow-up of Large Colonic Polyps and Laterally Spreading Tumors. The Romanian Experience

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Abstract

Aims. We report the prevalence, histological aspect, endoscopic treatment and follow-up of colonic polyps of 2 cm or larger and of laterally spreading tumors (LSTs) in an eastern European country. **Methods.** All consecutive colonoscopies carried out over a 1-year period (3,856) in the Endoscopy Department of the 3rd Medical Clinic Cluj-Napoca were evaluated. Fifty-two polyps and 12 LSTs of ≥ 2 cm diameter were found. Size, location and histological aspect of large colonic polyps and LSTs were assessed. Endoscopic or surgical resection was recorded. An extensive endoscopic and histological follow-up was performed. **Results.** Median size of polyps was 32mm and of LSTs 41mm. Invasive carcinoma was found in 7 polyps (20.6%) and in 4 LSTs (28.6%). Thirty-six polyps were endoscopically resected (69.2%). A complete endoscopic excision was performed in 35 polyps (98.6%). Histological complete resection was achieved in 30 polyps (83.3%). Thirteen polyps were surgically resected (25%). Eight LSTs were endoscopically resected (64.3%) using endoscopic piecemeal resection (EPMR). A complete endoscopic excision was performed in three LSTs (37.5%). Three LSTs were surgically resected (21.5%). In the polyp group, one patient presented endoscopic recurrence (16.6%) at 6 months follow-up. In the LST group, two invasive recurrences were present at 3 and 30 months of follow-up. **Conclusions.** A complete resection can be performed in the majority of large polyps. LSTs larger than 50mm, incomplete resection and superficial invasive carcinoma were correlated with endoscopic recurrence. EPMR might be a curative method for LSTs but an accurate endoscopic diagnosis and long-term endoscopic follow-up are mandatory.

Key words

Large colonic polyps – laterally spreading tumors – polypectomy – endoscopic resection

Introduction

Colonoscopies for colorectal cancer screening have increased the detection of polyps and early cancers. About 70% of all colorectal cancers are exophytic adenocarcinomas [1]. In European countries, flat adenomas are considered rare tumors [2]. Flat lesions larger than 1 cm are classified as laterally spreading tumors (LSTs) [3]. Lesions larger than 2cm are considered large colonic lesions and have a prevalence of 0.8-5.2% [4-8]. The rate of carcinoma in these large lesions is 5-22.1% [4-8]. It was found that the rate of carcinoma was lower in superficial adenomas than in polypoid adenomas at equal size [4, 8]. From this point of view, these could be suitable for endoscopic treatment even at large size. Therefore it is essential to recognize the features of superficial colonic tumors that might predict a higher incidence of cancer with deep submucosal invasion [8]. Over the past decade, a greater number of large colorectal lesions have been treated by endoscopic methods. The recurrence rate after piecemeal resection of large colonic lesions is 0 to 20% [4-6, 9-12]. Completeness and margins of excision, degree of differentiation and Haggitt level of invasion are the three histological characteristics associated with increased risk of residual disease or potential for metastasis [13]. Most cases of recurrent disease were diagnosed within 6 months from the initial endoscopic resection of superficial tumors [4, 14]. A complete polypectomy or an incomplete polypectomy associated with argon plasma coagulation (APC) achieved a 50% recurrence at 12 month of follow-up [15].

Endoscopic assessment, histological examination and an appropriate follow-up after endoscopic resection of the large colonic lesions are mandatory. We studied the prevalence of large colonic lesions in an eastern European country, the rate of malignancy in these lesions and we present our experience in the endoscopic treatment and follow-up of these lesions.

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Material and methods

Between November 2005 and November 2006, 3,856 consecutive colonoscopies were performed at the Endoscopy Department, 3rd Medical Clinic, Cluj-Napoca. Patients with epithelial tumors (adenoma, carcinoma or both) of 2 cm or larger were included. Patients with non epithelial tumors, endoscopically advanced adenocarcinomas, inflammatory bowel disease, familial adenomatous polyposis, hereditary non-polyposis colon cancer and submucosal tumors were excluded from the study. An informed consent was obtained from all patients.

The patients were examined using video-colonoscopes (Olympus CL160, Olympus CL180). Tumors invading muscularis propria and/or lymph nodes were excluded from endoscopic treatment. Rectal superficial lesions were evaluated by endorectal ultrasonography. Advanced carcinoma was considered when T2, T3, T4 was detected. If perirectal lymph nodes were present, endoscopic treatment was not performed.

Patients with contraindications for endoscopy and those with coagulopathies were also excluded from the study.

Endoscopic assessment

The endoscopic lesions were classified according to the Japanese classification of colorectal cancers in 6 types of carcinomas (0, 1-5). Type 0 is early carcinoma, limited to the submucosa. Type 0 is divided into two subtypes: subtype I pedunculated or sessile protruded and subtype II superficial. Subtype II is divided into: IIa - slightly elevated, IIb - perfectly flat (change in mucosa color) and IIc - depressed. Their breadth and length exceed several times their height. Subtype IIa with a small central depression has been noted as IIa+IIc, and subtype IIc with slight marginal elevation or a central elevation has been noted as IIc+IIa.

Lateral spreading tumors (LSTs) were considered as type 0 subtype II lesions with a diameter larger than 1 cm. Lesions smaller than 1cm in diameter were considered as flat adenomas. Lesions smaller than 2cm were excluded from study. We divided the LSTs in subtype LST-G (granular type) and subtype LST-NG (non-granular type).

All lesions that fulfilled the endoscopic criteria for inclusion were biopsied.

Configuration of the lesion, presence of central depression, presence of ulceration and the lifting sign were evaluated. If the lesions appeared as advanced, the patients were referred to surgery. Colonic resection (laparotomy) and local lymphadenectomy were performed.

Histological assessment

Histological evaluation of the biopsied or removed lesions was made according to the revisited Vienna classification of epithelial neoplasia of the colon [16]. Lesions containing dysplastic cells were classified as neoplastic - adenomas or carcinomas. Dysplasia was defined as low or high-grade dysplasia. The intramucosal carcinoma was noted within the high-grade dysplasia category. Invasive carcinoma was considered when malignant cells were found in the

submucosa or in the deeper tissues. Submucosal invasion less than 1000 µm was considered as superficial submucosal invasion. Invasion more than 1000 µm was considered as deep submucosal invasion. Adenocarcinomas with only submucosal invasion were considered as early carcinomas. If deeper submucosal invasion or vascular/lymphatic invasion was found, the patients were referred for surgical resection.

In case of submucosal invasion <1000µm and negative vertical margin, resection was regarded as complete. In LSTs, a lateral margin evaluation was difficult due to the multiple fragments resected, so completeness of resection could not be evaluated.

Endoscopic treatment

Polyyps with no suspicion of invasive cancer at endoscopy were removed with or without histological evaluation. If deep submucosal invasive carcinoma was suspected at endoscopy, histological evaluation was performed. Adenocarcinomas with no deep submucosal invasion were endoscopically removed.

Pedunculated polyyps were resected *en-bloc* and then recuperated. Sessile polyyps were resected *en-bloc* or in more fragments using multiple polypectomies. The majority of fragments were recuperated.

The superficial colorectal tumors were endoscopically resected after endoscopic, histological and rectal ultrasonographic assessment. Lateral spreading tumors were resected using a snare after performing elevation with saline solution (endoscopic mucosal resection - EMR „lift and cut”).

A complete endoscopic excision was considered when no macroscopic lesions were left. An incomplete endoscopic excision was considered when some macroscopic lesions were left. In these cases, additional APC was performed in the same session.

If hemorrhage occurred, continuous snaring was performed or adrenalin solution was injected submucosally. Perforations were treated conservatively (hemoclips).

Follow-up

The lesions included in the study were endoscopically treated, surgically removed or included in a follow-up program. The patients with polyyps treated endoscopically were monitored by endoscopy and histology at 3, 6 and 12 months. The patients with LSTs were monitored by endoscopy, histology and endorectal ultrasonography (in case of rectal lesions) at 3, 6, 12, 24 and 30 months. The patients with surgically removed lesions were monitored by endoscopy and histological examination at 12 months.

Recurrent lesions were resected by polypectomy or EMR with or without APC. Remnant samples were assessed. Lesions with vascular/lymphatic invasion or deeper submucosal invasion were referred to surgery.

Statistics

Statistical analysis was performed using SPSS version 13.0 for Windows. Comparisons within groups were

undertaken using the paired t test whereas comparisons between groups were made using the unpaired t test. For statistical analyses, p values of less than 0.05 were considered significant.

Results

In 575 from 3,856 consecutive colonoscopies, 802 polyps and 14 LSTs were found: 52 pedunculated and sessile polyps and 12 LSTs of ≥ 2 cm diameter. Two patients with LSTs < 2cm were excluded from the study. The prevalence of the ≥ 2 cm colonic lesions was 1.69%.

In the polyp group, 31 patients (59.6%) were males and 21 (40.4%) females. Mean age was 60.0 years (range 37-78) in males and 64.2 years (range 42-84) in females.

Superficial tumors (LSTs) were found in 12 patients. Of these, 7 were males, mean age 63.0 years (range 50-75) and 5 were females, mean age 61.8 years (range 51-82). Most of the superficial tumors were elevated subtype IIa (11/12; 91.6%), 1 was subtype IIa+IIc (8.33%). All belonged to the LST-G subtype.

From the 52 polyps, 30 were pedunculated and 22 sessile. The size of 30 polyps ranged between 20-29mm (57.6%), of 17 polyps between 30-39mm (30.7%), of 4 polyps - 40-49mm (7.6%) and 1 polyp was > 50mm (1.9%).

The majority of protruding tumors were located in the sigmoid colon (33 out of 52, 63.46%), more frequently than in other location (p<0.05). Most of the LSTs (66.6%) were found in the rectum (Figs. 1, 2), more frequently than in other location (p<0.05). The size of two LSTs ranged between 20-29mm, three superficial lesions had 30-39mm, one had 40mm and 6 were ≥ 50 mm.

In the polyp group, 34 lesions were adenomas and adenocarcinomas. One was non-neoplastic and was excluded, and 17 polyps were lost. Seven polyps had invasive carcinoma (20.5%). All the 12 patients with subtype II tumors had adenomas or adenocarcinomas. Invasive carcinoma was found in three LSTs (3/12; 25%). No significant difference was found between the polyp group and the LST group regarding presence of invasive carcinoma.

High grade dysplasia was found in 11 polyps (32.3%) and in 5 subtype II lesions (41.6%), without significant difference

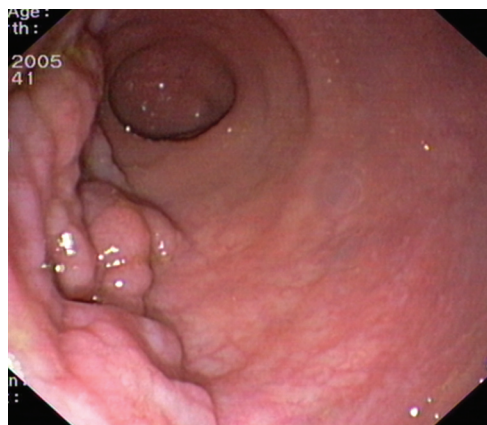


Fig 2. Lateral spreading tumors located in rectum.

between groups. Low grade dysplasia was found in 15 polyps (44.1%) and in only one subtype II lesion (8.3%) (p<0.05). Adenoma without dysplasia was observed in one polyp (2.9%) and in three subtype II tumors (25%) (no significant difference) (Table I).

Table I. Correlation between size and histological aspect in protruding tumours.

	20-29 mm	30-39 mm	40-49 mm	50-59 mm	Total
Adenoma without dysplasia	1				1
with low dysplasia	9	6			15
with high dysplasia	4	1	2		7
Carcinoma	4	6		1	11
Total	18	13	2	1	34

Eleven patients (11/52; 21.1%) with protruding tumors had endoscopic synchronous advanced tumors and 20 patients had two or more polyps (40.4%).

Most of the type I adenomas were endoscopically treated. Thirty-six polyps (30 pedunculated and 6 sessile) (69.2%) were endoscopically resected using a snare. Thirty of them (all pedunculated) were resected into one fragment. Six (sessile type) were resected in two or three fragments. Piece-meal polypectomy was performed preferentially in 5 sessile polyps > 30mm. A complete endoscopic excision was achieved in 35 polyps (98.6%). APC after piecemeal polypectomy was performed for one 20mm polyp because of suspected macroscopic fragments remnants. Bleeding occurred in two piece-meal polypectomies and was stopped after adrenalin injection. No perforation occurred.

Thirteen polyps were referred per primam for surgical resection (13/52; 25%). The reasons were the technical level of difficulty, the distal location, deep invasion suspected endoscopically, and deep submucosal invasion on histological evaluation. Three patients were not referred to endoscopy or surgery: one had liver cirrhosis and coagulopathy, two refused the treatment. After histological assessment, complete resection was considered in 30 cases (83.3%). In six cases (13.9%) with deep submucosal invasive

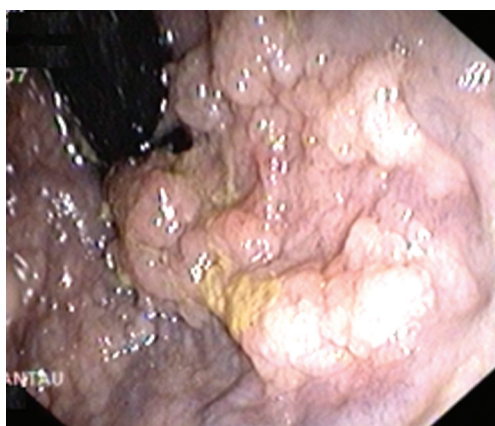


Fig 1. Lateral spreading tumors, retrovision aspect.

carcinoma found after endoscopic resection, curative surgery was performed.

Eight type II lesions were resected endoscopically (8/12; 66.6%) by endoscopic piece meal resection (EPMR). In cases treated by EPMR, no significant co-morbidities were detected (Table II). Three lesions were referred directly to surgery (3/12; 25%). These had the following features: one IIa+IIc subtype 20mm lesion with invasive carcinoma; one 50mm lesion located in the cecum with non-dysplasia adenoma and one 30 mm lesion with high dysplasia adenoma located in the sigmoid colon.

In the endoscopically treated group, three LSTs were treated using EPMR (Figs.3, 4) and 5 using EPMR associated with APC. When incomplete resection was considered an additional destruction of the remnants with APC was applied. In one case (with superficial invasive carcinoma at initial histological evaluation) after three months of follow-up, muscularis propria invasion was detected by rectal ultrasonography and the patient was referred to surgery. Bleeding occurred in 4 cases (4/8; 50%) but stopped spontaneously or after adrenalin injection. Pain during and after resection occurred in one case and was relieved by analgetics.

In the polyp group, 6 patients with polypectomy were monitored at 3, 6 and 12 months. Only one presented endoscopic recurrence at 6 months follow-up.

Endoscopic and histological features in patients of the

LST group treated endoscopically were the following: lesions larger than 50mm (3/8; 37.5%), superficial submucosal carcinoma (2/8, 25%) and incomplete resection (3/8; 37.5%). The patients were monitored by endoscopy, histology and rectal endosonography at 3, 6, 12, 24, 30 months. At three months of follow-up, five of them presented no recurrence (5/8; 42.5%), but two had non-invasive recurrence (2/8; 25%) and were treated by EPMR. In one case (16.6%), an invasive recurrence was detected. In this case a fibrotic scar was observed at endoscopy, but rectal endosonography detected invasion of muscularis propria and the patient was referred to surgery. At 6 months follow-up, six patients had no recurrence and two patients had endoscopic recurrence, treated by EPMR. At 12 and 24 months of follow-up, the proportion was the same. At 30 months of follow-up, three patients presented endoscopic recurrence: two of them were the patients who had endoscopic recurrence at 3, 6, 12, and 24 months, treated by EPMR. In one case endoscopic recurrence occurred only after 30 months of follow-up. An invasive carcinoma was detected by histological evaluation and the case was referred to surgery. Endoscopy, histology and follow-up parameters are presented in Table II.

Discussion

Although reporting only a small number of cases, this is the first study addressing prevalence, clinicopathological

Table II. Clinico-pathological characteristics, initial or/and additional treatment and endoscopic follow-up at 3, 6,12, 24 and 30 months of lateral spreading tumors.

Patient	Location	II sub-type	Size	Rectal EUS	Histology	Initial treatment	Additional treatment	Local recurrence
1	ascending	IIa	20 mm	NA	low dysplastic	EMR pm	APC	at
2	sigmoid	IIa+c	20 mm	NA	submucosal invasion	surgery	no	no
3	rectum	IIa	40 mm	yes	tubular adenoma	missed	no	missed
4	descending	IIa	60 mm	NA	high dysplasia adenoma	EMR pm	no	no
5	rectum	IIa	10 mm	yes	low dysplasia adenoma	no	no	growing
6	rectum	IIa	30 mm	yes	high dysplasia adenoma	surgery	no	no
7	cecum	IIa	50 mm	NA	tubular-villous adenoma	surgery	no	no
8	descending	IIa+c	15 mm	NA	invasive carcinoma	no	no	growing
9	rectum	IIa	50 mm	yes	superficial submucosal invasion	EMR pm	APC	at 30 months
10	rectum	IIa	30 mm	yes	high dysplasia adenoma	EMR pm	APC	no
11	rectum	IIa	50 mm	yes	superficial submucosal invasion	EMR pm	surgery	at 3 months
12	rectum	IIa	30 mm	yes	high dysplasia adenoma	EMR pm	no	no
13	rectum	IIa	50 mm	no	high dysplasia adenoma	EMR pm	APC	at 3, 6, 12, 24, 30 months
14	rectum	IIa	80 mm	no	tubular adenoma	EMR pm	APC	no

Rectal EUS: rectal ultrasonography; NA: not applicable; APC: argon plasma coagulation; EMR pm: piece-meal endoscopic mucosal resection.

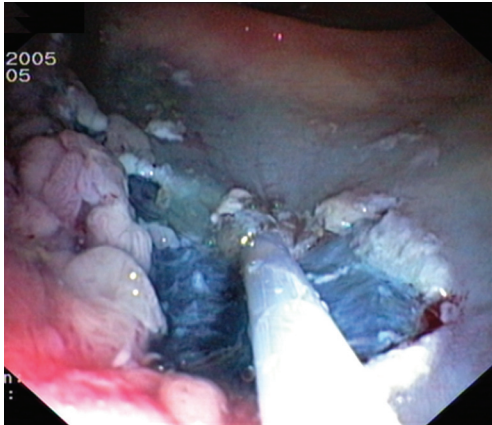


Fig 3. Piece-meal mucosectomy.

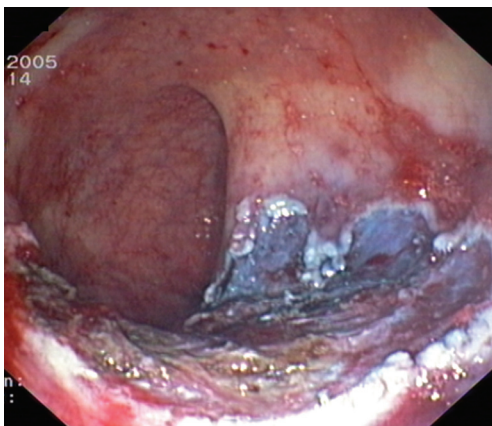


Fig 4. Complete endoscopic resection.

features and endoscopic treatment of large colonic lesions in Romania. Large lesions may include pedunculated, sessile or flat polyps. Flat lesions larger than 1 cm, classified as LSTs, are sometimes difficult to distinguish from sessile polyps. The height of a LST lesion is usually less than the height of the closed cups of a biopsy forceps, but LST-G lesions might be higher.

The incidence of superficial colorectal tumors has increased recently [4, 6]. A prevalence of 1.4% [8] or of 5.2% [18] of lesions larger than 2 cm was found in patients undergoing colonoscopy. The rate of carcinoma in these large lesions was 5-15% [8, 17-21]. We found a prevalence of 1.69% for the large colonic lesions.

Laterally spreading tumors typically extend laterally and circumferentially rather than vertically along the colonic wall [20, 21] and the frequency of invasive carcinoma is lower than of the polypoid lesions of similar size [8]. The rate of carcinoma was reported to be 10.4% for LSTs of 16-20mm and 22.1% for LSTs larger than 20mm [8]. In our patients, carcinoma was present in 32.3% of the large polyps, and in 25% of the LSTs. Carcinoma was present in 16.6% of the LSTs of 30-59mm diameter, a rate lower than in the polyps of same size (43.7%).

In a series of flat and polypoid adenomas, rectosigmoidian location, large size and villous component were found to be associated with higher rates of malignancy. The authors did

not find a different rate of high-grade dysplasia or carcinoma for similar size [22].

The combination of chromoscopy magnifying colonoscopy improves detection of this type of lesions, assessing the lateral margins and the depth of lesions. High-resolution magnification endoscopy and chromoscopy can help to diagnose invasive carcinoma, allowing the choice of endoscopic or surgical treatment [23]. Applying non-vital staining method allowed a detailed morphology with particular reference to central depression [24]. Previous reports showed that NG-type lesions were more common in the right colon (77%) as compared to G-type (39%) and more often associated with invasive disease (stage T2) [4, 25].

In the past several years, endoscopic resection of superficial colorectal tumors has reduced the morbidity associated with surgery [12, 26]. A recent report from the AGA Institute has predicted the decline of screening colonoscopy and increased the focus on complex endoscopic procedures by the gastroenterologist [27]. In the latter years, more authors have reported endoscopic curative success in large colonic lesions [4, 5, 8, 19, 20]. Rate of *en-bloc* resection of large colonic polyps varies (0-59%) and the rate of EPMR was reported to be 41-100% [5, 20, 27]. Recently, endoscopists have become more aggressive. In our patients, *en-bloc* resection was achieved in 83.3% of the polyps. Complete endoscopic excision was achieved in 98.6% of the polyps and in 27.5% of LSTs. A limit of our study was that in the LST group, complete resection could not be properly evaluated due to the multiple fragments resected.

In order to choose the appropriate treatment, it is essential to recognize the endoscopic criteria for predicting submucosal invasion. Endoscopic findings which might predict a higher incidence of cancer with deep submucosal invasion are: presence of depression, large (>10mm) nodule, uneven nodularity and a size > 30mm. Only presence of depression and histological type were identified as independent risk factors [28]. The pit pattern (invasive pattern), sclerous wall change, and larger tumor size were significantly associated with higher submucosal invasion in LST-NG type while large nodule in LST-G type was associated with higher rate of submucosal invasion [25]. Most of the carcinoma invasions of the submucosal layer in LST-G type occurred under the largest nodule [28].

Recognition of depression is very important because depressed lesions often are associated with invasive cancer even when very small. We found a subtype IIa+IIc lesion presenting invasive carcinoma at a size of 20mm, while two superficial tumors without depression were associated with invasive cancer at a size of 50mm.

One previous study described 41 polyps \geq 2cm, of which 60% were removed surgically [29]. In another study of 179 sessile polyps of \geq 2cm diameter, only 4% were referred to surgery without an attempt of endoscopic resection [30]. In our study, the majority of the polyps were endoscopically treated and 25% of the polyps were referred per primam to surgery. The type II lesions were in a large proportion endoscopically resected and 25% were referred to surgery.

EMPR should be the first line treatment for most LSTs because of the lower invasive carcinoma rate as compared with the polypoid lesions of similar size. Lymph node metastasis is more frequent in cases of deeper submucosal invasive cancer [31, 32]. Lesions with submucosal invasion < 1000 μm , without lymphovascular involvement and poorly differentiated component do not involve lymph node metastases and for lesions < 2cm standard EMR is recommended [3]. Both our patients in whom invasive recurrence occurred at 3 and 30 months of follow-up had lesions of 50mm and a superficial submucosal invasion at the first histological examination.

Laterally spreading tumors in the colorectum are usually removed by EMR even when large. Saito et al recommended that the area including a large nodule in LST-G type should be resected first endoscopically followed by resection of the remaining tumor [25]. Curative rate for LSTs using endoscopic mucosal resection at two years of follow-up was 96% in a European study [4].

At present, endoscopic submucosal dissection is recommended for the large flat lesions (especially LST-NG type >20mm in size) or for lesions with submucosal fibrosis, residual tissue and recurrence after polypectomy/EMR [33].

Uraoka et al did not recommend LSTs with deeper submucosal invasion to be treated by EMR because of the higher risk of lymph node metastasis [25]. Therefore, we should avoid EMR for deeper submucosal invasive cancer because histological assessment is difficult. Incomplete EMR is considered to accelerate growth of any residual cancer, and is considered as a risk factor for distant metastasis [34]. Although the risk of local nodal metastasis is low (5–10%) for stage T1 type G and for flat LSTs, there still is a risk that EMR may leave untreated nodal disease in situ [35].

APC treatment along with EMPR was shown to achieve an equal recurrence rate (50%) to complete polypectomy, while incomplete polypectomy without APC had a 100% recurrence rate [15]. Tanaka et al found that 83% of cases of recurrent disease were diagnosed within six months of the index EMR. Tanaka's cohort developed a recurrent adenoma at 13.5 months post resection of a 20 mm type G ascending colonic lesion [14], while recurrence in Brooker's series of sessile polypectomy without APC was in excess of 50% at 12 months post polypectomy [36].

Risk for recurrence of the advanced adenoma is greater for high-risk adenomas at baseline than for those with low risk [37]. Due to the high rate of malignant transformation, it is essential to perform an oncologically radical operation [38]. Actual guidelines recommend a total colonoscopy within 12 months after curative resection of colorectal cancer [38].

Conclusions

The rate of carcinoma is lower in the LSTs than in the polyps of similar size. In the LSTs, type, depression and size larger than 50mm suggest invasive carcinoma. LSTs larger than 50mm, incomplete resection and superficial invasive

carcinoma are correlated with endoscopic recurrence. In the majority of polyps a complete resection can be performed. Piecemeal EMR can be a curative method for large lesions but an accurate pretreatment assessment and prolonged endoscopic follow-up is mandatory.

Conflicts of interest

Nothing to declare.

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