Digestive and Liver Disease 48 (2016) 399–403

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Digestive Endoscopy

Outcome and risk of recurrence for endoscopic resection of colonic superficial neoplastic lesions over 2 cm in diameter

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ARTICLE INFO

Article history:
Received 30 March 2015
Accepted 5 October 2015
Available online 22 October 2015

Keywords:
En block
Endoscopic mucosa resection
Piecemeal
Polyps
Superficial neoplastic lesions

ABSTRACT

Background: Large colorectal superficial neoplastic lesions are challenging to remove. This study aimed to assess the outcomes of routine endoscopic resection of large (≥2 cm and <3 cm) and giant (≥3 cm) lesions.
Methods: From 4587 endoscopic resections, 265 (5.7%) large and giant lesions were removed in 249 patients. We retrospectively analyzed 125 patients (141 endoscopic mucosal resection, 73 large and 68 giant lesions) with a follow-up of 6–12 months. Rate of en bloc and piecemeal resection, recurrence and risk factors were analyzed.
Results: En bloc was performed in 92 cases (65.2%) and piecemeal resection in 49 (34.8%). A complete endoscopic resection was achieved in 139 cases (98.5%) with radical resection in 84/139 cases (60.4%). Argon plasma coagulation was applied in 18/141 lesions (12.8%). A recurrence occurred in 16/139 lesions (11.5%). The risk of recurrence at one year was significantly higher for giant than large lesions ($p = 0.03$). The recurrence risk was higher in treated than in non-argon plasma coagulation treated lesions ($p = 0.01$).
Conclusions: endoscopic mucosal resection is a safe and effective routine treatment for large superficial neoplastic lesions. The risk factors for recurrence include giant size, non-protruding morphology, piecemeal technique and argon plasma coagulation.

1. Introduction

Colorectal cancer (CRC) is the second most common cause of death in the Western world [1,2]. Colonoscopy and polypectomy are effective in reducing the incidence of colorectal cancer and CRC-related mortality [3,4]. Most colonic polyps are small or pedunculated and can be easily removed [5], but sessile or non-polypoid adenomas are increasingly detected and have a stronger association with cancer [6]. Large sessile (>2 cm) and flat colonic lesions have been found in 0.8–5.2% of patients undergoing colonoscopy for different indications [6,7]. The large sessile lesions are challenging to remove endoscopically. Therefore, large lesions are often treated surgically in many centres, with significant morbidity (20%) and potential mortality (up to 5%) [8–13]. Large lesion size is often presumed to correlate with increasing risk of adenocarcinoma [14] and are associated with a higher recurrence rate and complications such as bleeding, perforation and post-polypectomy syndrome [7,15]. In particular, endoscopic treatment of polyps larger than 3 cm, which are termed "giant" polyps, remains controversial because of concerns regarding coexistent malignancy, incomplete resection and safety [16]. Endoscopic mucosal resection (EMR) is a minimally invasive technique for the removal of large sessile lesions [10]. EMR has high success rates and minimal morbidity and mortality. However, data on this specific issue are scanty and have several limitations, including single-centre or retrospective designs, non-standardized techniques, and lack of comprehensive follow-up evaluations [10,17–22]. The aim of this study was to assess the outcomes of EMR for large and giant colon polyps with respect to recurrence rate, routinely treated in a single Italian referral centre. We also aimed to identify risk factors for adenoma recurrence after one year of follow-up.

2. Material and methods

This retrospective study included all endoscopic resections for peduncolated or sessile colorectal polyps larger than 2 cm performed at our institution between January 2001 and July 2011, and

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http://dx.doi.org/10.1016/j.dld.2015.10.006
1590-8658/

with at least one surveillance colonoscopy within six months to one year. All procedures were performed by expert endoscopists and the "inject and cut" technique was used. The injection solution contained saline or saline with epinephrine (1:10,000). When an en bloc resection was deemed technically impossible the lesion was removed by the piecemeal technique. Argon plasma coagulation (APC) was applied after EMR on the lateral margins to complete resection if adenomatous tissue remained. Lesions were treated by surgery if endoscopic resection was not possible or, in case of complete endoscopic resection, if cancer was identified by histology. Patients with cancer who were not eligible for surgery because of advanced age or comorbidities were treated with the endoscopic technique and then underwent colonoscopic surveillance. Protruding lesions were classified according to the Paris morphological classification [23]. The non-protruding lesions were classified "lateral spreading tumours" as previously defined [24], mostly homogeneous granular and focal mixed nodular types were included. The polyp size was estimated by comparison with open biopsy forceps. Lesions with diameter ≥2 cm and <3 cm were defined as 'large', while lesions ≥3 cm diameter were defined as 'giant'. [25]. All specimens were stained with haematoxylin and eosin for histopathological assessment. The adenomas were classified as tubular, villous, tubulovillous and serrate. Colorectal adenomas were histologically classified according to the Vienna criteria [26]. The histologic definition of "low grade dysplasia" also included adenomas showing moderate dysplasia while the histologic diagnosis of "high grade dysplasia" included adenomas with severe dysplasia and "intramucosal carcinoma". The "invasive carcinoma" category included adenomas with neoplastic cell invasion into the submucosal layer. Lesions were indicated in the right and left colon if located proximal or distal to the splenic flexure, respectively. We considered bleeding complications that occurred 24–42 hours after endoscopic resection. Bleeding was treated by injection therapy using dilute epinephrine (1:10,000) or haemoclips. Perforation was diagnosed during resection or by free air on plain abdominal film. During follow-up endoscopy, any alteration of the mucosa in the area of the previous polypectomy was resected or biopsied. A recurrence was defined as the presence of adenomatous tissue in the site of the previous resection. The recurrence was treated using EMR with or without APC, APC only, or surgery when indicated.

We considered the following parameters: age, sex, lesion size (large/giant), shape (protruding/not-protruding), location (left colon/right colon), lift sign (yes/no), EMR resection (en bloc/piecemeal), complications (bleeding/perforation), treatment of complications, histology, grade of dysplasia and cancer, invasion of deep and lateral margins, recurrence, recurrence treatment, surgery, and indication for surgery. The primary endpoint was to evaluate EMR recurrence rate and to identify risk factors of adenoma recurrence at one year of follow-up. The secondary endpoints were to evaluate complete resection rate, complication rate and need for surgery of en bloc vs. piecemeal resection.

2.1. Statistical analysis

All results for continuous variables were summarized using mean ± standard deviation (SD). Frequencies (%) were used to summarize categorical variables. The relationships between categorical variables were examined by the Chi-squared test. The Fisher exact test was applied when necessary. The Kaplan–Meier survival method was used to estimate the cumulative probability of recurrence rate after one year of follow-up. The differences between curves were tested using the Log-Rank test. A Cox proportional hazard regression model was used to assess whether the variables analyzed were independently associated with the probability of recurrence. The following covariates were considered: (1) sex (M vs. F); (2) age (< or ≥ 60 years); (3) location (left colon vs. right colon); (4) size (< or ≥3 cm); (5) endoscopic technique (en bloc vs. piecemeal); (6) dysplasia (low-grade dysplasia vs. high-grade dysplasia/Ca in situ/Cancer) (7) histology (villous/vs. tubular/tubulovillous/serrate). A p-value <0.05 was considered statistically significant. The Stats Direct statistical tools (copyright © 1990–2001) and Epistat (copyright © Epistat Services, 1991) were used for all calculations.

3. Results

We reviewed 9873 colonoscopies performed from January 2001 to July 2011. Overall 4587 endoscopic resections performed. The "polyp detection rate" was 46%. Of the 4587 resections, 265 (5.7%) were resections for lesions ≥2 cm performed in 249 patients. We excluded 124 of the 249 patients for the following reasons: 105 cases were lost at follow-up (for advanced age, refusal colonoscopy, death, etc.) and 19 were treated surgically (endoscopic resection technically impossible or invasive carcinoma). Thus, the population eligible for this study was composed of 125 patients with a total of 141 EMRs performed. The mean age of the patients was 66.4 ± 11.02 years (range 38–89 years) and 63%were male. We included 109 protruding (77%) and 32 non-protruding lesions. The characteristics of the 141 resected lesions are presented in Table 1

3.1. Rate of complete resection

En bloc resection was performed in 92 cases (65.2%) and piecemeal resection was performed in 49 cases (34.8%). The en bloc resection was performed in 58/73 large lesions and 35/68 giant lesions (79.4% vs. 51.4%, $p = 0.0009$). Among the giant en bloc resected lesions the pedunculated morphology was most frequent, and occurred in 21/35 cases (60%). The piecemeal resection was performed in 16/73 large and in 33/68 giant lesions (22% vs. 48.5%, $p = 0.001$). APC was applied to the lesion margins in 18 of the 141 lesions (12.8%).

A complete endoscopic resection was performed in 139 cases (98.5%) and among these cases a radical histological resection (R0) was achieved in 84/139 cases (60.4%). However, it should be noted that the lateral margins were not evaluable in 53 cases by histology (38%). Additionally, deep margins were not evaluable by histology in 13 cases (9.3%). The lateral margins that were not evaluable by

Table 1
Characteristics of resected polyps ($N = 141$).

Features	n (%)
Size	
≥2 < 3 cm	73 (51.8)
≥3 cm	68 (48.2)
Morphology	
Protruding	
Sessile (Is)	40 (28)
Peduncolated (Ip)	63 (45)
Subpeduncolated (Ips)	6 (4)
Non protruding	
Lateral spreading tumour	32 (23)
Location	
Left colon	97 (68.8)
Right colon	44 (31.2)
Histology	
Tubular	36 (25.5)
Villous	20 (14.2)
Tubulovillous	74 (52.5)
Serrate	11 (7.8)
Dysplasia	
Low grade dysplasia	68 (48.2)
High grade dysplasia	67 (47.6)
Cancer	6 (4.2)