Journal of Coloproctology

www.jcol.org.br

Original Article

Surgical treatment of malignant colon polyps

Nuno Telo Preto Ramos[a,*], André Gonçalves[a,b], Pedro Correia da Silva[b], José Barbosa[a,b]

[a] Universidade do Porto, Faculdade de Medicina, Porto, Portugal
[b] Centro Hospitalar São João, Porto, Portugal

ARTICLE INFO

Article history:
Received 3 April 2018
Accepted 6 May 2018
Available online 5 June 2018

Keywords:
Malignant polyp
Colon cancer
Surgery
Residual disease

ABSTRACT

Background: In the therapeutic decision about the malignant colon polyp, several factors predicting residual disease after the endoscopic resection guide the decision of surveillance or surgical intervention. This is a challenging decision, because even in the presence of high-risk predictors currently used, only 15–30% of the patients will have residual disease in the surgical specimen.

Objective: To evaluate patients with a diagnosis of malignant colon polyp at the Hospital Center of São João, who were indicated for surgical treatment, studying the predictors of residual disease in the surgical specimen.

Methods: A retrospective study was carried out, based on the patients with malignant colon polyp diagnosed and treated at the Hospital Center of São João in the city of Porto, Portugal, between 2009 and 2016. The endoscopic, anatomopathological, surgical and follow-up data were reviewed.

Results: Of the total number of patients in the study ($n = 96$), 59 (61.5%) were indicated for surgery after a multidisciplinary discussion. Of this group, 21 patients (35.6%) had residual disease in the surgical specimen, with presence of lymph node invasion in 8 patients (13.6%). The presence of malignancy in the surgical resection specimen was statistically significantly associated with: size of the resected polyp ($p = 0.023$); sessile polyp ($p = 0.007$); piecemeal resection ($p = 0.002$).

Conclusions: The persistence of malignancy in the surgical specimen was associated with larger sessile polyps and piecemeal removal. A significant number of patients did not show malignancy in the surgical resection specimen, with more markers being required to better stratify patients.

* *Corresponding author.*
E-mail: telonuno@hotmail.com (N.T. Ramos).

https://doi.org/10.1016/j.jcol.2018.05.004

Tratamento cirúrgico do pólipo maligno do cólon

Palavras-chave:
Pólipo maligno
Cancro do cólon
Cirurgia
Doença residual

RESUMO

Contexto: Na decisão terapêutica do pólipo maligno do cólon diversos fatores preditores de doença residual após a recessão endoscópica norteiam a decisão de vigilância ou intervenção cirúrgica. Esta é uma decisão desafiadora, uma vez que mesmo na presença dos preditores de alto risco usados atualmente, apenas 15% a 30% dos doentes terão doença residual na peça cirúrgica.

Objetivo: Avaliar os doentes com diagnóstico de pólipo maligno do cólon no Centro Hospitalar de São João que foram orientados para tratamento cirúrgico, estudando os preditores de doença residual na peça cirúrgica.

Métodos: Foi realizado um estudo retrospetivo, tendo por base os doentes com pólipo maligno do cólon diagnosticado e tratado no Centro Hospitalar de São João no Porto, Portugal, entre 2009 e 2016. Os dados endoscópicos, anatomopatológicos, cirúrgicos e o seguimento foram revistos.

Resultados: Do total de doentes em estudo (n = 96); 59 (61,5%) tiveram indicação para cirurgia após discussão multidisciplinar. Deste grupo, 21 doentes (35,6%) apresentavam doença residual na peça cirúrgica, com presença de invasão ganglionar em 8 doentes (13,6%). A presença de malignidade na peça de ressecção cirúrgica associava-se de forma estatisticamente significativa a: tamanho do pólipo ressecado (p = 0,023); pólipo séssil (p = 0,007); ressecção em *piecemeal* (p = 0,002).

Conclusões: A persistência de malignidade na peça cirúrgica associou-se a pólipos sésseis, de maiores dimensões e à remoção em *piecemeal*. Um número importante de doentes não apresentava malignidade na peça de ressecção cirúrgica, sendo necessários mais marcadores para melhor estratificar os doentes.

1. Introduction

Colorectal cancer is the third most prevalent cancer in men, and the second most common in women worldwide, being the second leading cause of cancer death in Europe.[1–3]

More than 95% of colorectal cancers arise through the adenoma–carcinoma transformation sequence, over an estimated period of 10–20 years. This supports screening of colorectal cancer, allowing the detection of advanced adenomas and future colorectal cancers through more timely intervention.[3–8]

The increase on implementation of screening programs resulted in a marked increase in the incidence of detection of less advanced neoplastic forms. The malignant colon polyp is defined as a neoplasm that developed and invaded the muscle mucosa through direct continuity, reaching the submucosa, and having lymphatic and vascular dissemination potential.[3,9–11]

After endoscopic resection of a malignant polyp of the colon, the therapeutic decision is divided between endoscopic surveillance or surgical treatment. The decision is currently based on a number of factors, such as deep submucosal invasion, degree of tumor differentiation, lymphovascular invasion, resection margins, and the presence of tumor budding (defined as isolated malignant cells or small groups of malignant cells located at the more advanced end of the tumor invasion).[8]

Yet, the identification and therapeutic decision in these patients remains challenging, because even in the presence of high-risk factors, only 15–30% of the operated patients show residual disease, and a smaller percentage has lymph node disease.[3,7,12,13]

However, neither the malignant colon polyp overtreatment nor the undertreatment is desirable, with this representing a missed opportunity for treatment of a malignant lesion at an early stage and with a significant impact on the prognosis of the disease.[3,8,14,15]

The aim of this study was to evaluate the patients with a diagnosis of malignant colon polyp at the Hospital Center of São João who were indicated for surgical treatment, studying the residual disease predictors in the surgical specimen, aiming at a better future screening of patients with surgery indication after endoscopic resection of the malignant colon polyp.

2. Methods

We developed a retrospective analysis of patients undergoing endoscopic resection of malignant colon polyps between January 2009 and December 2016 at the Hospital Center of São João, reviewing the histology of endoscopically removed polyps. Polyps with in situ carcinoma/high-grade dysplasia, polyps that were only biopsied, polyps located in the rec-

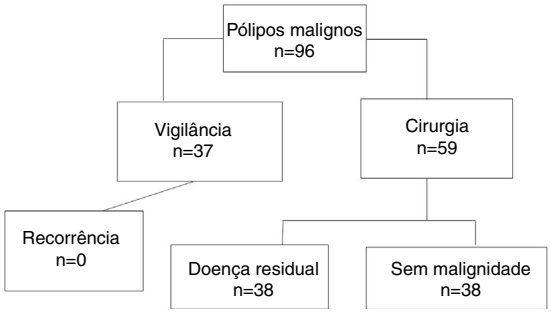

Fig. 1 – Distribution of 96 patients with histology of submucosal invasion following endoscopic resection.

tum, polyps resected in patients with familial syndromes and inflammatory bowel disease were excluded.

Ninety-six patients were included in the study, with gender and age being considered.

The analysis of the endoscopic data involved the characteristics of the polyp [size, type (pediculate or sessile)], location in the colon, type of endoscopic resection (en bloc or piecemeal), and sample fragmentation.

The histological data of endoscopically resected polyps were registered, with determination of distance to the margins, depth of tumor invasion in the submucosa, and histological grade, as well as lymphovascular invasion and presence of tumor budding.

The decisions were made in a multidisciplinary meeting, according to the current protocol, and based on international guidelines.[16–18] Thus, patients were instructed to undergo surgical treatment if: the removed pediculate polyp was fragmented, with invasion of the pedicle polyp axle or unfavorable histological features, which are defined as grades 3–4, lymphovascular invasion, "positive margin" (tumor <2 mm of margin), or presence of tumor budding. Patients with fragmented sessile polyps, with invasion of the axis, margins that were invaded or impossible to be evaluated were also referred for surgical treatment. If the polyp was single, had been completely removed, with favorable histological characteristics and with free margins (≥2 mm), the patients would be oriented for surveillance. A favorable histology is defined as: grades 1–2, absence of lymphovascular invasion, and negative margin of resection.

The remaining cases, such as patients with sessile polyps, with single sessile polyps that were completely removed with favorable histological characteristics and free margins, were discussed in a multidisciplinary meeting and referred for surveillance or radical colectomy.

According to the decision in a multidisciplinary meeting, our analysis was divided into two groups: surveillance group ($n = 37$) and surgery group ($n = 59$) (Fig. 1).

Surveillance patients followed the strict surveillance protocol with early endoscopic reevaluation (3–6 months).

Of the patients undergoing surgical treatment, we evaluated the type of surgery, the approach pathway, and morbidity and mortality according to the Clavien–Dindo classification.[19]

From the histological analysis of the surgical specimens, the following was considered: the length of the surgical specimen, the number of resected ganglia, the metastasized ganglia/resected ganglia ratio, and the presence of residual disease. Histological grade and lymphovascular invasion were evaluated in patients with residual disease.

Univariate analysis was performed for the presence of residual disease in patients undergoing surgical treatment, using the one-way ANOVA test for continuous variables, and the chi-square test for categorical variables, using the SPSS software 19. A p-value < 0.05 was considered to represent a statistically significant difference.

Patients in the study were followed for at least 12 months after polypectomy.

The Ethics Committee of the Hospital Center of São João/Medical School of the University of Porto unanimously approved the study with process no. 250/17.

3. Results

Patients' characteristics were assessed in both study groups and presented in Table 1, with all values rounded to one decimal place.

The distribution of male vs. female genders is similar between the two groups, with a preponderance of male patients (total 64.6%). The mean age was slightly higher in the surveillance group compared to the surgery group (67.5 vs. 63.9 years).

Regarding the gross characteristics of the polyps, despite a higher percentage of pediculate polyps in the series (59.4%), in the surgery group there was a higher proportion of sessile polyps compared to the surveillance group (40.1% vs. 27.0%).

We registered a greater preference for the left colon in both study groups; 97.3% in the surveillance group, and 84.7% in the surgery group. The results were divided into right colon, including blind, ascending colon and the proximal two-thirds of the transverse colon; and left colon, including the distal third of the transverse colon, the descending colon, and the sigmoid colon.

The analysis of median polyp size revealed that it was larger in the surgery group (24.6 mm) compared to the surveillance group (24.4 mm), and that the mean polyp size among the 96 patients studied was 24.6 mm.

Table 2 shows the univariate analysis of the surgery group, evaluating the variables for the presence of residual disease in the surgical specimen in 59 patients undergoing surgery, corresponding to 61.5% of the population of patients with malignant colon polyp.

It should be noted that of the group of patients operated on, only 21 out of 59 had residual disease in the surgical specimen (35.6%) compared to 38 patients whose specimen was negative for residual disease, corresponding to 64.4% of the operated patients.

The analysis showed no statistically significant difference for the presence of malignancy in the surgical specimen in relation to gender ($p = 0.78$) and age ($p = 0.33$).

The polyp size was statistically significantly associated with the presence of residual disease in the surgery group ($p = 0.02$); the type of polyp was also statistically significant to the presence of residual disease in the surgery group ($p < 0.01$), and sessile polyps were associated with the presence of residual disease. The piecemeal resection was also statistically

Table 1 – Patients' characteristics.

	Surveillance group $n = 37$ (38.5%)	Surgical group $n = 59$ (61.5%)	Total $n = 96$
Gender			
Male	25 (67.6%)	37 (62.7%)	62 (64.6%)
Female	12 (32.4%)	22 (37.3%)	34 (35.4%)
Age (mean ± SD)	67.5 ± 14.4 years	63.9 ± 11.7 years	65.2 ± 13.2 years
Polyp			
Sessile	10 (27.0%)	24 (40.1%)	34 (35.4%)
Pediculate	24 (64.9%)	33 (55.9%)	57 (59.4%)
Location in the colon			
Right	1 (2.7%)	9 (15.3%)	10 (10.4%)
Left	36 (97.3%)	50 (84.7%)	86 (89.6%)
Polyp size (mean ± SD)	24.6 ± 10.9 mm	24.4 ± 9.4 mm	24.6 ± 10.3 mm

Table 2 – Comparison among patients undergoing surgery ($n = 59$).

	Group of the operated with residual disease ($n = 21$)	Group of the operated with no evidence of residual disease ($n = 38$)	*p*-Value
Gender			0.78
Male	14	23	
Female	7	15	
Age at polipectomy (mean ± SD)	65.1 ± 8.7 years 95% CI 62.1–68.0	61.9 ± 15.6 years 95% CI 54.9–69.1	0.33
Polyp size (mean ± SD)	28.1 ± 11.8 mm 95% CI 22.7–33.5	21.5 ± 9.6 mm 95% CI 18.3–24.6	0.02
Type of polyp			<0.01
Sessile	14	10	
Pediculate	6	27	
Type of resection			<0.01
En Bloc	4	27	
Piecemeal	11	8	
Resection margin			0.19
Free	3	13	
Invaded	7	15	
Impossible to evaluate	4	6	
Distance of free at margin (mean ± SD)	5.3 ± 5.1	4.9 ± 4.5	0.08
Histology grade			0.44
Well differentiated	0	1	
Moderately differentiated	5	11	
Slightly differentiated	4	12	
Unknown	12	14	
Location of lesion			0.31
Right colon	5	5	
Left colon/sigmoid	16	33	
Lymphovascular invasion (presence)	5	5	0.12
Tumor budding (present)	2	0	0.09

associated with the presence of residual disease in the surgical specimen ($p = 0.002$), with 32.2% of the operated patients undergoing piecemeal endoscopic resection.

Regarding the free margin of invasion of the malignant polyp and the invasion of the same margin, no statistically significant association with presence of residual disease ($p = 0.08$ and $p = 0.19$, respectively) was reported. Both the tumor differentiation and the location of the polyp also showed no association with residual disease ($p = 0.44$ and 0.31, respectively).

Regarding tumor budding, although not statistically associated with the presence of malignancy in the surgical specimen, it should be noted that all patients ($n = 2$) who presented with tumor budding also had residual disease in the surgical specimen ($p = 0.09$). Lymphovascular invasion was not statistically significantly associated with the presence of malignancy in the surgical specimen ($p = 0.09$). Thus, both tumor budding and lymphovascular invasion seem to show a tendency toward statistical significance, although not significant for the presence of malignancy in the surgical specimen.

Table 3 summarizes the surgical characteristics and outcomes of the 59 patients who were operated on. The presence of lymph node invasion was observed in 8 patients (13.6%), all of which presenting residual disease in the surgical specimen, corresponding to 38.1% of patients with residual disease and lymph node invasion.

In the total of patients operated on, the type of surgery performed was sigmoidectomy in 42.9% of the cases; left hemi-

Table 3 – Surgical characteristics and *outcomes*.

	Group of the operated with residual disease ($n = 21$)	Group of the operated with no evidence of residual disease ($n = 38$)	Total of operated ($n = 59$)
Types of surgery			
Sigmoidectomy	9 (42.9%)	25 (65.8%)	34 (57.6%)
Left hemicolectomy	3 (14.3%)	6 (15.8%)	9 (15.3%)
Right hemicolectomy	3 (14.3%)	4 (10.5%)	7 (11.9%)
Transverse segmental colectomy	0 (0%)	2 (5.3%)	2 (3.4%)
Total colectomy	4 (19.0%)	2 (5.3%)	6 (10.2%)
Approach			
Laparoscopy	7 (33.3%)	23 (60.5%)	30 (50.8%)
Laparotomy	14 (66.7%)	15 (39.5%)	29 (49.2%)
Days of hospital stay (mean–min–max)	7.9 (4–15) days	9.5 (4–55) days	8.9 (4–55) days
Complications			
Total number of events	5 (23.8%)	7 (18.4%)	12 (20.3%)
Clavien's classification			
Type 1	1 (4.8%)	1 (2.6%)	2 (3.4%)
Type 2	3 (14.3%)	1 (2.6%)	4 (6.8%)
Type 3b	0 (0%)	5 (13.2%)	5 (8.5%)
Type 5	1 (4.8%)	0 (0%)	1 (1.7%)
Total of resected ganglia (mean–min/max) < 12 ganglia	13.8 (9–29) ganglia; 7 (33.3%)	11.6 (0–55) ganglia; 27 (71.1%)	12.4 (0–55) ganglia; 34 (57.6%)
Length of surgical specimen (mean–min–max)	35.4 (10–136.5) cm	20.5 (6–145) cm	25.8 (6–145) cm
Follow-up (mean ± SD)	41.3 ± 24.1 months	42.5 ± 22.1 months	43.4 ± 22.7 months
Disease recurrence/progression	2 (9.5%)	0 (0%)	2 (3.4%)

colectomy in 15.3% of the cases; right hemicolectomy in 11.9%; segmental colectomy of the transverse colon was performed in 3.4%; and six patients (10.2%) underwent total colectomy due to synchronous malignant polyps in the right and left colon.

Of the 59 patients undergoing surgery, the laparoscopy was used in 30 patients, corresponding to 50.8% of the cases in the group, laparotomy in 29 patients (49.2%). Regarding length stay, a mean time of 8.9 days of hospitalization, with a maximum of 55 days and a minimum of 4 days of hospitalization was recorded.

Regarding complications after surgery, 13 patients (22%) had history of complications or changes in the normal postoperative course. The complications were presented according to the Clavien–Dindo classification, and are compiled in Table 3. The major morbidity of the series (defined by Clavien–Dindo ≥3) was 10.2%; among them a mortality of 1.7% (1 case).

More than half of the patients (57.6%) had less than 12 ganglia resected in the surgery, and a mean of 12.4 ganglia resected. The average length of the surgical specimen was 25.8 cm.

The mean follow-up was 41.3 ± 24.1 months in the group with residual disease; of 42.5 ± 22.1 months in the group without residual disease, and 43.4 ± 22.7 months in the total of operated patients.

Recurrence/progression of the disease was reported in two patients with residual disease, corresponding to 9.5% of this group, and 3.4% of the total of patients operated. One event of liver metastases and one of ganglion metastasis were reported. It should be noted that, in addition, six of the operated patients were not followed in subsequent consultations, either due to death from postoperative complications (1), lack of patient compliance (4), or other causes (1).

No recurrence events (local or disease progression) were recorded in the 37 patients undergoing a surveillance program, nor were any of them subsequently surgically treated for this cause.

4. Discussion

The identification and therapeutic decision in patients with malignant colon polyp remains challenging, due to the high percentage of patients who, despite having high-risk criteria for residual disease, do not show residual disease in the surgical specimen/lymph node invasion. In the study developed, only 35.6% of operated patients showed residual disease in the surgical specimen, and no recurrence was observed in the surveillance group. This value is above the variation between 15% and 27% reported in the literature, between residual disease in both the intestinal wall and in the lymph nodes.[5]

This study showed that polyp size can be considered an important predictor of malignancy of the surgical specimen, and the piecemeal resection and the type of sessile polyp showed an association with malignancy outcome of the surgical specimen.

Currently, the literature shows that there is no consensus on the definition of neoplasia-free distance of the resection margins, and our study did not allow the demonstration of the importance of this distance; however, some authors argue that even patients with a resection margin of carcinoma <1 mm can be safely treated through surveillance and that polyps with invaded or unknown margins should be treated through surgery.[9,12] There are even studies reporting that absence of neoplasia in the resection margin seems sufficient to avoid surgery if other risk factors are not present.[20]

The limitation of the study is the impossibility of assessing the margins invasion in all polyps, either because they are fulgurated or because a piecemeal resection was performed, making it impossible to correctly analyze the polyp and as such, inducing a selection bias in the surgery group. Bruno Gonçalves et al.[4] recommend the development of endoscopic techniques in order to prevent unnecessary surgeries due to incorrect polypectomy or inability to evaluate polyps.

Although our study failed to show statistically significant differences in the differentiation, there are studies that showed that an adverse histology (slightly differentiated carcinoma) was associated with an increased risk of lymph node metastases.[18] However, the undifferentiated histological type rarely appears in the malignant colon polyp, with a mean incidence of 3.1%.[9,21]

The submucosa invasion classification is based on Haggitt's classifications for the pediculate (1–4), and Kikuchi's (sm1–sm3) for the sessile polyps (indication for surgery: Haggitt 3 and 4; Kikuchi sm3).[22] In polyps undergoing endoscopic removal, particularly in sessile polyps, it is not always possible to use these classifications. In this study, this classification was not used uniformly/routinely in the histological analysis and therefore was not included in the collected data. In addition, a significant proportion of the polyps was removed in piecemeal (32.2%), making it impossible to proceed with correct orientation, and the muscular layer was not represented in all polypectomy pieces. As a solution, Kitajima et al.[23] suggest the measurement in μm of the depth of invasion of the neoplasia beyond the muscularis mucosae, and observed that the risk of lymph node metastasis is zero if <1000 μm for malignant sessile polyps.

It was demonstrated that tumor budding was associated with the clinical aggressiveness of the polyps, being a factor of poor prognosis.[8] In this series, only a small proportion of the patients ($n=2$) shows tumor budding, thus not allowing more conclusions. We believe, however, that it should be routinely investigated in the histology of polypectomy specimens, and that it is an important factor to include in the therapeutic decision.[22]

For surgical treatment of the malignant polyp, a formal oncological resection is used[24] and in this series, major morbidity, all requiring surgical reintervention was 10.2%. This is consistent with the literature.[20]

This is one of the key points in this discussion, because if only a fraction of the patients will have a malignant surgical piece, morbidity is not negligible.

In addition, the numbers of resected lymph nodes in the 59 surgeries were very variable, but more than half of the patients (57.8%) had less than the 12 ganglia recommended in the guidelines for surgical resection specimens. This is a problem already addressed in the literature, because even when undergoing oncologic surgery, the number of resected lymph nodes is often less than 12 in malignant polyp surgery.[24,25]

In the guidelines, the number of ganglia to be removed in a T1 tumor is not well defined.[26] Some authors question the type of surgery performed, while others highlight the relation between the T stage and the number of excised lymph nodes. On one hand, Benhaim et al.[24] concluded that this fact does not appear to have any meaning in the long-term prognosis of the patients, with no more residual disease events occurring, even though less than 12 lymph nodes have been resected. On the other hand, Backes, Y. et al., demonstrated that the resection of less than 10 lymph nodes was associated with an increased risk of colorectal cancer recurrence, noting the importance of appropriate oncologic resection even in T1 neoplasias.[26]

The rate of disease relapse/progression was 3.4% in the surgery group (9.5% in the residual disease group). This is consistent with the data of the literature.[22] Patients had a mean follow-up of 43.4 months; however, some of the patients under study were only followed for 12 months, due to the nature of the study design, namely in patients operated in 2016, making it impossible to register any relapses of the disease, presumably underestimating the risk of disease recurrence.

In a future approach, and with the objective of improving the clinical decision making process, biomarkers appear as predictors of malignancy, and the importance of certain microenvironmental factors of lymphocytes and neutrophils, such as NIC and MMP-7[27] or markers such as CITED1, which have been shown to be an independent risk factor for ganglion metastasis and residual disease, is increasingly recognized.[28] Increased COL11A1 expression has also been reported in the diagnosis of invasive carcinoma in endoscopically removed malignant polyps.[29]

5. Conclusion

Patient orientation after endoscopic malignant polyp resection is challenging because of the possibility of residual disease on the one hand, and the possibility of performing "unnecessary" surgery on the other hand. The full clarification of the endoscopic, histological and clinical characteristics is of vital importance when deciding the best treatment for each patient.

The persistence of malignancy in the surgical specimen was associated with larger sessile polyps, which makes it difficult to perform an endoscopic en block/complete removal.

Nevertheless, a significant number of patients did not present malignancy in the surgical resection, and other factors/markers had to be explored to better stratify the patients and better predict the risk of lymph node metastasis, through the development of endoscopic, histological and surgical techniques.

Discussion at multidisciplinary meetings is necessary to resolve the risk/benefit dilemma of surgical treatment of malignant polyps with high risk of residual disease, and the decision should always take into account patients' wishes and medical conditions.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources,

methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136:E359–86.
2. Neilson LJ, Rutter MD, Saunders BP, Plumb A, Rees CJ. Assessment and management of the malignant colorectal polyp. Frontline Gastroenterol. 2015;6:117–26.
3. Hassan C, Zullo A, Winn S, Eramo A, Tomao S, Rossini FP, et al. The colorectal malignant polyp: scoping a dilemma. Dig Liver Dis. 2007;39:92–100.
4. Gonçalves BM, Fontainhas V, Caetano AC, Ferreira A, Gonçalves R, Bastos P. Oncological outcomes after endoscopic removal of malignant colorectal polyps. Rev Esp Enferm Dig. 2013;105:454–61.
5. Fasoli R, Nienstedt R, De Carli N, Monica F, Guido E, Valiante F, et al. The management of malignant polyps in colorectal cancer screening programmes: a retrospective Italian multi-centre study. Dig Liver Dis. 2015;47:715–9.
6. Levic K, Kjær M, Bulut O, Jess P, Bisgaard T. Watchful waiting versus colorectal resection after polypectomy for malignant colorectal polyps. Dan Med J. 2015;62:A4996.
7. Aarons CB, Shanmugan S, Bleier JI. Management of malignant colon polyps: current status and controversies. World J Gastroenterol. 2014;20:16178–83.
8. Church JM. Colon cancer screening update and management of the malignant polyp. Clin Colon Rectal Surg. 2005;18:141–9.
9. Naqvi S, Burroughs S, Chave HS, Branagan G. Management of colorectal polyp cancers. Ann R Coll Surg Engl. 2012;94:574–8.
10. Bujanda L, Cosme A, Gil I, Arenas-Mirave JI. Malignant colorectal polyps. World J Gastroenterol. 2010;16:3103–11.
11. Wu XR, Liang J, Church JM. Management of sessile malignant polyps: is colonoscopic polypectomy enough? Surg Endosc. 2015;29:2947–52.
12. Jung EJ, Ryu CG, Paik JH, Hwang DY. Undetermined margins after colonoscopic polypectomy for malignant polyps: the need for radical resection. Anticancer Res. 2015;35:6887–91.
13. Jang EJ, Kim DD, Cho CH. Value and interpretation of resection margin after a colonoscopic polypectomy for malignant polyps. J Korean Soc Coloproctol. 2011;27:194–201.
14. Fischer J, Dobbs B, Dixon L, Eglinton TW, Wakeman CJ, Frizelle FA, et al. Management of malignant colorectal polyps in New Zealand. ANZ J Surg. 2017;87:350–5.
15. Freeman HJ. Long-term follow-up of patients with malignant pedunculated colon polyps after colonoscopic polypectomy. Can J Gastroenterol. 2013;27:20–4.
16. Labianca R, Nordlinger B, Beretta GD, Mosconi S, Mandalà M, Cervantes A, et al. Early colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24 Suppl. 6:vi64–72.
17. Guidelines N. Clinical practice guidelines in oncology – colon cancer, version 2; 2016.
18. Brown IS, Bettington ML, Bettington A, Miller G, Rosty C. Adverse histological features in malignant colorectal polyps: a contemporary series of 239 cases. J Clin Pathol. 2016;69:292–9.
19. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD. The Clavien–Dindo classification of surgical complications: five-year experience. Ann Surg. 2009;250:187–96.
20. Gill MD, Rutter MD, Holtham SJ. Management and short-term outcome of malignant colorectal polyps in the North of England. Colorectal Dis. 2013;15:169–76.
21. Fleming M, Ravula S, Tatishchev SF, Wang HL. Colorectal carcinoma: pathologic aspects. J Gastrointest Oncol. 2012;3:153–73.
22. Williams JG, Pullan RD, Hill J, Horgan PG, Salmo E, Buchanan GN, et al. Association of Coloproctology of Great Britain and Ireland. Management of the malignant colorectal polyp: ACPGBI position statement. Colorectal Dis. 2013;15 Suppl. 2:1–38.
23. Kitajima K, Fujimori T, Fujii S, Takeda J, Ohkura Y, Kawamata H, et al. Correlations between lymph node metastasis and depth of submucosal invasion in submucosal invasive colorectal carcinoma: a Japanese collaborative study. J Gastroenterol. 2004;39:534–43.
24. Benhaim L, Benoist S, Bachet JB, Julié C, Penna C, Nordlinger B. Salvage colectomy for endoscopically removed malignant colon polyps: is it possible to determine the optimal number of lymph nodes that need to be harvested? Colorectal Dis. 2012;14:79–86.
25. Wasif N, Etzioni D, Maggard MA, Tomlinson JS, Ko CY. Trends, patterns, and outcomes in the management of malignant colonic polyps in the general population of the United States. Cancer. 2011;117:931–7.
26. Backes Y, Elias SG, Bhoelan BS, Groen JN, van Bergeijk J, Seerden TCJ, et al. The prognostic value of lymph node yield in the earliest stage of colorectal cancer: a multicenter cohort study. BMC Med. 2017;15:129.
27. Akishima-Fukasawa Y, Ishikawa Y, Akasaka Y, Uzuki M, Inomata N, Yokoo T, et al. Histopathological predictors of regional lymph node metastasis at the invasive front in early colorectal cancer. Histopathology. 2011;59:470–81.
28. Nasu T, Oku Y, Takifuji K, Hotta T, Yokoyama S, Matsuda K, et al. Predicting lymph node metastasis in early colorectal cancer using the CITED1 expression. J Surg Res. 2013;185:136–42.
29. Zhang D, Zhu H, Harpaz N. Overexpression of alpha1 chain of type XI collagen (COL11A1) aids in the diagnosis of invasive carcinoma in endoscopically removed malignant colorectal polyps. Pathol Res Pract. 2016;212:545–8.