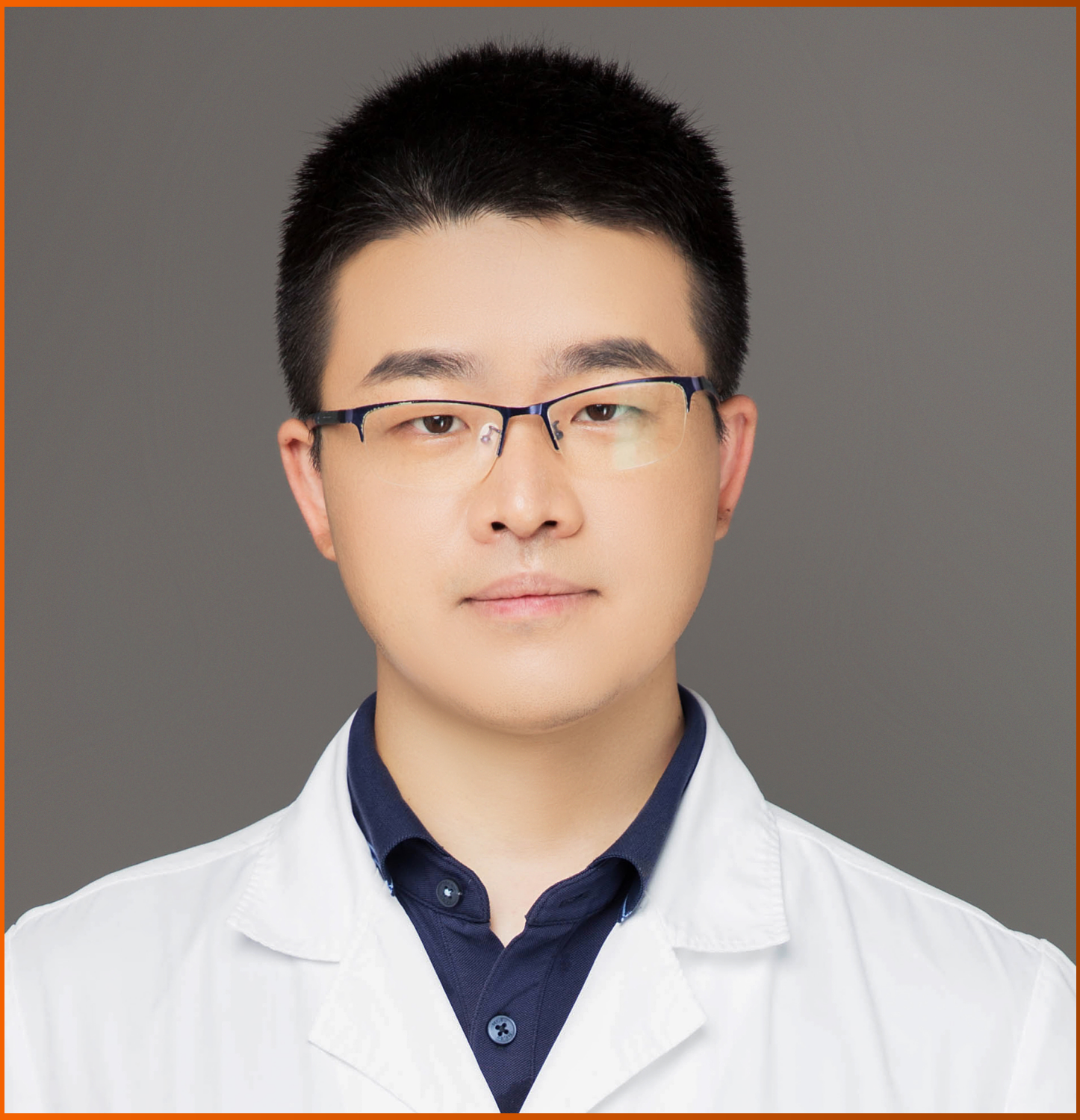
ISSN 1948-5190 (online)

World Journal of *Gastrointestinal Endoscopy*

World J Gastrointest Endosc 2024 September 16; 16(9): 502-544



Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Endoscopy

Contents

Monthly Volume 16 Number 9 September 16, 2024

World Journal of Gastrointestinal Endoscopy

Monthly Volume 16 Number 9 September 16, 2024

Contents

NAME OF JOURNAL
World Journal of Gastrointestinal Endoscopy

ISSN
ISSN 1948-5190 (online)

LAUNCH DATE
October 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Bing Hu, JooYoung Cho

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-5190/editorialboard.htm

PUBLICATION DATE
September 16, 2024

PUBLISHING PARTNER
Digestive Endoscopy Center of West China Hospital, SCU

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

PUBLISHING PARTNER's OFFICIAL WEBSITE
http://www.cd120.com/index.html

World Journal of Gastrointestinal Endoscopy

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Endosc 2024 September 16; 16(9): 502-508

DOI: 10.4253/wjge.v16.i9.502

ISSN 1948-5190 (online)

EDITORIAL

How secure can we expect the surveillance policies to be after the implementation in T1 polyps with carcinoma?

Cristina Mateos Sanchez, Elvira Quintanilla Lazaro, Luis Ramon Rabago

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification
Scientific Quality: Grade A
Novelty: Grade A
Creativity or Innovation: Grade A
Scientific Significance: Grade A

P-Reviewer: Endo Y

Received: June 28, 2024
Revised: August 8, 2024
Accepted: August 20, 2024
Published online: September 16, 2024
Processing time: 75 Days and 7.8 Hours

Cristina Mateos Sanchez, Elvira Quintanilla Lazaro, Department of Gastroenterological, Severo Ochoa Hospital, Madrid, Leganes 28911, Spain

Luis Ramon Rabago, Department of Gastroenterology, San Rafael Hospital, Madrid 28016, Spain

Co-first authors: Cristina Mateos Sanchez and Elvira Quintanilla Lazaro.

Corresponding author: Luis Ramon Rabago, MD, PhD, Chief Physician, Department of Gastroenterology, Hospital San Rafael, Street Serrano 199, Madrid 28016, Spain.
lrabagot@gmail.com

Abstract

Approximately 7% of the polyps resected endoscopically have an adenocarcinoma focus, with no previous endoscopic evidence of malignancy. This raises the question of whether endoscopic resection has been curative. Furthermore, there is no consensus on what the endoscopic and histological criteria for good prognosis are, the appropriate follow-up strategy and what are the long-term results. The aim of the retrospective study by Fábián *et al* was to evaluate the occurrence of local relapse or distant metastasis in those tumors that were resected endoscopically compared to those that underwent oncologic surgery. They concluded that, regardless of the treatment strategy chosen, there was a higher recurrence rate than described in the literature and that adherence to follow-up was poor. The management approach for an endoscopically benign polyp histologically confirmed as adenocarcinoma depends on the presence of any of the previously described poor prognostic histological factors. If none of these factors are present and the polyp has been completely resected *en bloc* (R0), active surveillance is considered appropriate as endoscopic resection is deemed curative. These results highlight, once again, the need for further multicentric clinical practice studies to obtain more evidence for the purpose of establishing appropriate treatment and follow-up strategies.

Key Words: pT1 adenocarcinoma polyps; pT1 follow up management; Histological recurrence rate of pT1 adenocarcinoma; Endoscopic and histologic poor prognostic criteria

Core Tip: The management of endoscopically benign polyps that histopathologically prove to contain pT1 adenocarcinoma is not defined, pending international definition of the required resection and histological criteria to be able to rely on a follow-up without surgery. Based on Fabian's study, it is very likely that the rate of complete resection and the risk of recurrence is much higher than previously published and that we must also consider the risk of insufficient therapy. The follow-up of these patients remains to be clarified and agreed upon in multicenter studies that will make it possible to obtain more data at least for clinical practice and, above all, to insist on the potential risk for survival when patients are lost in follow-up programs.

Citation: Mateos Sanchez C, Quintanilla Lazaro E, Rabago LR. How secure can we expect the surveillance policies to be after the implementation in T1 polyps with carcinoma? *World J Gastrointest Endosc* 2024; 16(9): 502-508
URL: https://www.wjgnet.com/1948-5190/full/v16/i9/502.htm
DOI: https://dx.doi.org/10.4253/wjge.v16.i9.502

INTRODUCTION

The incidence of colorectal cancer (CRC) diagnosed at stage pT1 varies markedly in recent studies, reaching 38% in some series[1].

In most cases the diagnosis of carcinoma is made after resection of the apparently benign polyp, which shows a focus of adenocarcinoma on histological examination[2]. This represents an increase in overall survival but a clinical challenge, given that no specific standardized management guidelines or long-term follow-up have been established.

The aim of the study by Fábián *et al*[3] was to evaluate the incidence of local relapse or distant metastasis of those polyps that were resected endoscopically, comparing it with the evolution of those polyps that after histological analysis were recommended for oncological surgery.

CONCEPT OF PT1 CRC

Definition and predictors of lymphatic and distant invasion

CRC pT1 is defined as a polyp with an adenocarcinoma focus on the submucosa that does not infiltrate the muscularis propria, according to the 8th edition of the classification of the American Joint Committee on Cancer[4]. Different endoscopic and histological risk factors have been described to help predict the presence of adenocarcinoma foci and lymph node spread, thereby indicating the need for subsequent oncological surgery.

When faced with a colonic polypoid lesion, the endoscopist must carry out an exhaustive assessment to consider the most appropriate resection technique[5]. The correct exploration of the characteristics of the polyp will allow prediction of the presence of deep submucosal invasion, *i.e.*, ≥ 1 mm (1000 μm). At present, no highly specific and sensitive endoscopic signs for superficial submucosal invasion (< 1000 μm) have been described, but there are certain endoscopic features associated with a higher risk of submucosal invasion. These include size ≥ 30 mm[6], the presence of depressed areas and the morphology of the polyp, with lateral spreading tumors being the most at risk[7].

It has also been shown that polyps located in the left colon, more specifically in the sigma and rectum, have higher rates of lymphovascular invasion and lymph node metastasis than in other locations[7-9]. In a retrospective study with a large sample size, the rates were significantly different between the two locations (left colon 12.0% *vs* right colon 5.4%, $P < 0.05$)[10].

Considering the results of these studies, when a polyp shows endoscopic signs of possible dysplasia, endoscopic mucosal resection (EMR) would not be the appropriate treatment, and it should instead be treated with endoscopic submucosal dissection (ESD). However, when a benign polyp suitable for EMR is found in these locations and is later discovered to harbor an unsuspected submucosal adenocarcinoma (pT1 polyp), EMR might not be considered curative due to the high probability of lymphatic and distant metastasis. Therefore, we must consider additional surgery, even if only one endoscopic/histological high-risk factor is present, unless the patient is at particularly high surgical risk.

Endoscopic characterization of the lesion

Nowadays, advanced technology integrated into endoscopes, such as narrow band imaging (NBI), allows the assessment of the surface and vascular patterns of polyps. This enables risk stratification according to classifications like NBI International Colorectal Endoscopy (NICE), Japanese NBI Expert Team[11] and Kudo[12]. In the prospective multicenter study by Puig *et al*[13], they concluded that the NICE classification has a specificity of over 96% in recognizing deep submucosal invasion, even without magnification and in inexperienced hands.

The morphology of the polyp is also relevant as sessile polyps have demonstrated a higher risk of lymphatic and distant dissemination compared to pedunculated polyps[6].

Endoscopic resection technique

In polyps requiring endoscopic treatment, *en bloc* resection is recommended. Fragmented resection not only carries a

higher risk of residual adenoma but also does not allow for a comprehensive histological study of the entire specimen. Currently, we have local excision techniques that have demonstrated high R0 resection rates, such as transmural resection (full thickness resection (-eFTR-) and ESD. These techniques are particularly indicated for the removal of polyps suspected of high-grade dysplasia or deep submucosal invasion. In the retrospective multicenter study by Didden *et al* [14], an R0 resection rate of 90% was demonstrated for polyps ≤ 15 mm resected by eFTR. However, the study indicated that eFTR should not be performed on polyps larger than 20 mm due to the observed high rates of incomplete resection [14]. Another major advantage of this technique is that its performance would not affect the outcomes of subsequent oncological surgery, if deemed necessary[15].

Histological characteristics

Subsequent anatomo-pathological study should include several features that have been shown to predict the risk of lymphatic spread, including: Lymphovascular invasion, tumoral budding and depth of submucosal invasion of the adenocarcinoma.

Lymphovascular invasion is the strongest independent predictor of risk of nodal metastasis. If present, the risk of lymph node involvement increases up to 7-fold (95%CI: 2.6-19.2)[16].

Tumor budding is defined as a single cell or a group of 4 cells in isolation or in small clusters at the invasion front of the tumor. It is a strong independent predictor of lymph node metastasis, especially grades Bd2 and Bd3[17].

Submucosal invasion was classically assessed using the Kikuchi and Haggitt classifications according to whether it was a sessile or pedunculated polyp, respectively[18]. Nowadays, since assessing the full thickness of the submucosa is sometimes not feasible after endoscopic resection, it has been replaced by measuring submucosal invasion depth. Invasion is considered deep if it extends ≥ 1 mm (1000 μm), which is associated with a significant risk of lymphatic invasion ranging from 11% to 18%[6]. For this reason, it has been considered a strong indicator for the performance of oncological surgery[1,19,20].

Other histological factors associated with the presence of lymph node metastases have been described in the literature, such as affected resection margins (< or > 1 mm), or the degree of differentiation of the adenocarcinoma, with poorly differentiated adenocarcinoma being the worst[7,21]. The histological subtype also plays an important role, with signet ring cells, micropapillary and mucinous subtypes having the worst prognosis[22]. The state of the muscularis mucosae assesses the integrity of the muscularis mucosae, categorized as grade 1 if maintained and grade 2 if fragmented or missing, with the latter presenting the highest risk of lymph node metastasis[16].

Other recently described criteria are *Poorly Differentiated Clusters*. These are defined as aggregates of five or more tumor cells that lack glandular differentiation. Their presence confers an increased risk of lymph node metastasis[19].

Currently, the management approach for an endoscopically benign polyp histologically con-firmed as adenocarcinoma depends on the presence of any of the previously described poor prognostic histological factors (Table 1).

If any of these poor prognostic factors are present, oncological surgery with lymphadenectomy is recommended. However, if none of these factors are present and the polyp has been completely resected *en bloc* (R0), active surveillance is considered appropriate, as endoscopic resection is deemed curative[23].

In the study by Choi *et al*[24], they found that, following these histological criteria for poor prognosis, 70%-80% of patients were considered high risk and therefore underwent oncological surgery. Of the pT1 operated on, more than 90% had no lymph node involvement in the surgical specimen, so that they had been operated on unnecessarily, with the risk that this entails[24]. These data are questionable if we consider the results of Fabian *et al*[3].

Other factors

Biochemical predictors of distant metastasis include carcinoembryonic antigen (CEA) measured at diagnosis[7].

With the intention of predicting with certainty the presence of lymphatic invasion without prior surgery, Wada *et al*[25] proposed a model based on biomarkers in blood. This model is based on the detection of 4 mRNAs and 5 messenger RNAs in blood. In a cohort of 330 patients, they demonstrated high predictive power and reduced the rate of unnecessary cancer surgeries to 17%[25]. This opens the door to new lines of research to provide tools in the management of pT1.

Artificial intelligence (AI) is currently being applied to develop predictive algorithms for the presence of lymphatic invasion. In 2021, Kudo *et al*[26] developed a model that was able to increase the discriminatory power compared to current international guidelines[26] although it has not been validated prospectively or internationally.

CURRENT MANAGEMENT: TREATMENT STRATEGIES AND FOLLOW-UP

There is currently no unified protocol in the published literature for the treatment and follow-up of patients with CRC pT1, who must be assessed in a multidisciplinary manner.

When to opt for surgical treatment

To minimize unnecessary surgeries and enhance the accuracy of predicting lymph node metastases risk, Zwager *et al*[27] conducted a comprehensive meta-analysis reviewing current evidence on histological predictors of poor prognosis. They concluded that deep submucosal invasion, in the absence of other histological risk factors, had a low absolute risk of lymph node metastases (2.6%), compared to the mortality related to surgery (1.7%). Therefore, submucosal invasion alone may be considered a less robust predictor of lymph node metastasis risk in the absence of additional histological factors like lymphovascular invasion and tumor budding. In such cases, EMR could potentially be curative, obviating the need for oncological surgery.

Table 1 Risk factors for poor prognosis

Low risk	High risk
Well or moderately differentiated (G1-2)	Poorly differentiated (G3)
Free resection margins	Affected resection margins
Absence of lymphovascular invasion	Presence of lymphovascular invasion
Absent or low grade budding (Bd0-I)	Intermediate or high budding (Bd2-3)
-	Mucinous, micropapillary or signet ring type
Absence of *Poorly differentiated clusters*	Presence of *Poorly differentiated clusters*
MMI (muscularis mucosae intact)	MM2 (fragmented muscularis mucosae)
Submucosal invasion < 1000 μm	Submucosal invasion > 1000 μm

Recently, an international group led by Dawson *et al*[28] conducted a multicenter study aiming to develop an index that distinguishes low-risk from high-risk patients, termed the International Budding Consortium Score. This score incorporates histological factors such as tumor budding, lymphovascular invasion, depth of submucosal invasion, and degree of differentiation. The study demonstrated high discriminatory power with a sensitivity of 0.9 (95%CI: 0.8-0.95) and a specificity of 0.26 (95%CI: 0.22-0.3)[28]. However, this index is not internationally validated and requires evidence from prospective studies.

Follow-up strategies

The second major challenge posed by this type of tumor is the follow-up protocol, including its frequency and methodology. As mentioned earlier, tumors with a high histological risk undergo oncological surgery and are followed up according to various CRC clinical guidelines. However, the approach for pT1 tumors resected endoscopically without needing surgery remains unclear. Moreover, there is no international consensus, and protocols vary between centers, highlighting the need for further research in the coming years. To determine a good strategy, it is essential to know the incidence of recurrence and time to recurrence.

Dang *et al*[29] analyzed 71 studies involving a total of 5167 patients with pT1 treated exclusively endoscopically. They reported a cumulative incidence of recurrence (local and/or distant) of 3.3%, with 40.8% of these patients succumbing to the tumor itself. Most recurrences (> 90%) occurred within 72 months of follow-up. Higher recurrence rates were observed among pT1 cases with poor prognostic histological factors compared to those without (7% *vs* 0.7%). These findings underscore the importance of comprehensive histological examination of resected specimens, including all features that have demonstrated a strong predictive value for poor prognosis.

Based on these results, a follow-up strategy has been proposed: For low-risk polyps with complete endoscopic resection (R0) after histological examination, no further extension study is required. These patients are recommended to undergo colonoscopy at one year and subsequently according to international polyp follow-up guidelines.

For high histological risk pT1 polyps, a closer follow-up plan is suggested, including surveillance for both local and distant recurrence. This involves colonoscopy at 3, 6, and 12 months after resection, followed by every 6 months until the second year, and then annually until the fifth year. Additionally, for monitoring distant recurrence, they recommend blood tests for CEA levels, abdominal ultrasound, and chest X-ray every 6 months until the fifth year[29].

The use of computed tomography (CT) for follow-up is not recommended due to its low sensitivity and specificity in assessing local and nodal recurrence[20]. However, in Great Britain and Ireland it is recommended to conduct a thoraco-abdominal CT scan four weeks after endoscopic resection. This practice allows for a baseline comparison in case of suspected recurrence during future radiological studies[30].

Discussion

The management of stage pT1 CRC lacks standardization in both treatment and follow-up protocols in local and international guidelines. Much of the evidence is derived from retrospective studies, like the one conducted by Fábián *et al*[3], which is a retrospective, descriptive, non-randomized study covering a 10-year period, with a median follow-up of 67 months. This duration is significantly longer compared to the median follow-up of approximately 36 months seen in most similar studies[31]. Its main strength lies in its focus on routine clinical practice, involving patients with benign polyps lacking endoscopic signs of malignancy. These patients underwent endoscopic resection and were subsequently followed for up to 10 years to assess recurrences. When it comes to decision-making processes, a single-center study is deemed suitable because it assumes standardized criteria for treatment decisions. Given the challenges and potential ethical concerns surrounding randomized studies, the preference leans towards prospective rather than retrospective descriptive multicenter studies, like Fabian's but with a significantly larger patient cohort[3]. Such studies would aid in resolving uncertainties in management practices. Moreover, there is a growing emphasis on leveraging new tools like AI and recently described biomarkers to enhance decision-making capabilities. It is noteworthy that despite widespread documentation of histologic criteria for determining high risk in the literature, the histologic descriptions were deficient in this study. While tumor differentiation (82.4%) and resection margins (86.8%) were frequently described, factors with significant predictive value like lymphovascular invasion and tumor budding were reported less frequently than

anticipated, at 75.6% and 14.5%, respectively. Only 19% of pT1 cases had a comprehensive histologic assessment that included tumor differentiation, resection margins, depth of submucosal invasion, lymphovascular invasion, and tumor budding. This limitation may have affected the homogeneity in stratifying between surgical resection and endoscopic resection groups. Additionally, despite guidelines recommending additional surgery for 53% of patients, only half of them underwent the procedure.

Based on the histological data obtained from the initial polypectomy, surgery was performed on 41 of the 88 patients who presented endoscopic or histological data with a high risk of recurrence (non-evaluable margins, piecemeal resection or histological data with a high risk of recurrence). With this group we compared the evolution and recurrences, and made it possible to estimate the effectiveness of polypectomy by studying the rate of residual lesion, adenopathy, *etc*.

The study included a small number of patients, and considering the anticipated low recurrence rate and the fact that it was not a randomized study, comparisons between the surgically treated group and the endoscopically treated group are scientifically untenable due to significant biases, among other limitations. However, they do provide epidemiological clues of great interest that should be considered with respect to the treatment and follow-up strategies that we will consider later.

Firstly, endoscopic resection was considered complete in 87% and the histological study showed complete resection in only 56%, and in 19% could not be determined, indicating a high rate of incomplete resections much higher than the endoscopic estimate.

Secondly, the histological analysis of the polyps had significant rates of "missing" histological data, which made it difficult to assess critical items such as tumor differentiation or deep margins that are predictive of recurrence risk. In this study, the overall recurrence rate (local and distant) was 9%, notably higher than that reported in other studies such as the one by Belderbos *et al*[32], where recurrence was around 6.3%. Importantly, there were no significant differences between the two groups, like the findings in the study by Fábián *et al*[3]. The only factor that was statistically significant in predicting local and distant recurrence in this study was the non-pedunculated morphology of the polyp, as had been previously proven[6]. This may be related to a lower rate of complete resection compared to pedunculated polyps (47% *vs* 82%). The authors acknowledge not having had access to advanced endoscopic resection techniques with DSE or eFTR, which could imply a higher *en bloc* resection rate and a more complete histological study.

Finally, in the surgical resection specimens that allowed for a thorough evaluation of the outcomes of polypectomy, at least one high-risk item for recurrence was present in 82.2% of cases (including unassessable resection margins as high-risk features). Importantly, residual neoplasia was found in 15 polyps among 10 patients (24.4%), and lymphatic involvement was observed in 4 patients (9.8%). In univariate regression analyses, piecemeal polypectomy was associated with a risk of residual neoplasia, although this association did not hold in multivariate analyses, possibly due to the small sample size of the study. Therefore, in considering management, treatment, and follow-up strategies, it is crucial to acknowledge that polypectomies of endoscopically apparently benign polyps, not removed with DSE or full-thickness resection, have a high rate of incomplete resections, resulting in residual tumor and affected lymph nodes. Piecemeal resection specifically correlates with incomplete resections.

The second crucial point in the study by Fábián *et al*[3] is the clinical recurrence rate, which appears to be higher than previously reported, with 8.9% of patients developing metastases during the follow-up period and 3.6% experiencing local recurrence. Importantly, there was a significant loss to follow-up, particularly among patients who did not undergo surgery, indicating a lack of awareness about the importance of monitoring for carcinoma recurrence. Adherence to follow-up was poor, with only 54% of patients remaining in the study after the first year, a number that declined over time. Moreover, there was a notable disparity at the 5-year mark between patients who underwent surgery and those who had only endoscopic resection (48% *vs* 18%), suggesting a potential lack of disease awareness among the latter group. Follow-up with CT and CEA was also not included, although it has not been protocolized in endoscopic guidelines, it should be considered as another strategy in the follow-up of patients with pT1 CRC.

CONCLUSION

The exhaustive review on the management of colorectal tumors in stage pT1 shows that we still have a long way to go in terms of management and follow-up, being necessary to review and deepen the endoscopic criteria of the resection technique and the histologic criteria that must be studied in relation to incomplete resection or recurrence; and specifically, the depth of invasion questioned. It is very likely that the rate of incomplete resection and the risk of recurrence is much higher than previously published, and that we must also consider the risk of insufficient therapy. The follow-up of these patients remains to be clarified, detailed and agreed upon in multicenter studies, and above all we must insist on the potential risk to survival when patients are lost in follow-up programs. In addition, we must bet on new tools that can be useful in decision making, such as AI and the new biomarkers described above.

FOOTNOTES

Author contributions: Mateos Sanchez C oversaw the complete review and update of the topic, and wrote the preliminary Spanish and English drafts; Quintanilla Lazaro E assisted Mateos Sanchez C, gave her vision, helped Mateos Sanchez C with her tasks, reviewed the topic, and contributed various critical comments on the original article that made the editorial writing possible; Rabago LR made the final revision of all the tasks and provided the final critical comments on the original article, upon which this editorial has been written. Mateos Sanchez C and Quintanilla Lazaro E contributed equally to this work as co-first authors.

Conflict-of-interest statement: We do not have any conflict-of-interest.

Country of origin: Spain

ORCID number: Cristina Mateos Sanchez 0009-0005-5680-3018; Elvira Quintanilla Lazaro 0000-0002-2384-0227; Luis Ramon Rabago 0000-0001-7801-2181.

S-Editor: Qu XL
L-Editor: Webster JR
P-Editor: Cai YX

REFERENCES

1 **Cubiella J**, González A, Almazán R, Rodríguez-Camacho E, Fontenla Rodiles J, Domínguez Ferreiro C, Tejido Sandoval C, Sánchez Gómez C, de Vicente Bielza N, Lorenzo IP, Zubizarreta R. pT1 Colorectal Cancer Detected in a Colorectal Cancer Mass Screening Program: Treatment and Factors Associated with Residual and Extraluminal Disease. *Cancers (Basel)* 2020; **12** [PMID: 32899974 DOI: 10.3390/cancers12092530]

2 **Asheer ZE**, Bisgaard T, Mjåland O, Angenete E, Bulut O, Souzani KL. Scandinavian surveillance follow-up programmes in patients with malignant colorectal polyps. *Dan Med J* 2021; **68** [PMID: 33543697]

3 **Fábián A**, Bor R, Vasas B, Szűcs M, Tóth T, Bősze Z, Szántó KJ, Bacsur P, Bálint A, Farkas B, Farkas K, Milassin Á, Rutka M, Resál T, Molnár T, Szepes Z. Long-term outcomes after endoscopic removal of malignant colorectal polyps: Results from a 10-year cohort. *World J Gastrointest Endosc* 2024; **16**: 193-205 [PMID: 38680198 DOI: 10.4253/wjge.v16.i4.193]

4 **Amin MB**, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, Meyer L, Gress DM, Byrd DR, Winchester DP. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. *CA Cancer J Clin* 2017; **67**: 93-99 [PMID: 28094848 DOI: 10.3322/caac.21388]

5 **Hassan C**, Wysocki PT, Fuccio L, Seufferlein T, Dinis-Ribeiro M, Brandão C, Regula J, Frazzoni L, Pellise M, Alfieri S, Dekker E, Jover R, Rosati G, Senore C, Spada C, Gralnek I, Dumonceau JM, van Hooft JE, van Cutsem E, Ponchon T. Endoscopic surveillance after surgical or endoscopic resection for colorectal cancer: European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Digestive Oncology (ESDO) Guideline. *Endoscopy* 2019; **51**: C1 [PMID: 30763965 DOI: 10.1055/a-0854-5925]

6 **Guo K**, Feng Y, Yuan L, Wasan HS, Sun L, Shen M, Ruan S. Risk factors and predictors of lymph nodes metastasis and distant metastasis in newly diagnosed T1 colorectal cancer. *Cancer Med* 2020; **9**: 5095-5113 [PMID: 32469151 DOI: 10.1002/cam4.3114]

7 **Shaukat A**, Kaltenbach T, Dominitz JA, Robertson DJ, Anderson JC, Cruise M, Burke CA, Gupta S, Lieberman D, Syngal S, Rex DK. Endoscopic Recognition and Management Strategies for Malignant Colorectal Polyps: Recommendations of the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2020; **159**: 1916-1934.e2 [PMID: 33159840 DOI: 10.1053/j.gastro.2020.08.050]

8 **Yasue C**, Chino A, Takamatsu M, Namikawa K, Ide D, Saito S, Igarashi M, Fujisaki J. Pathological risk factors and predictive endoscopic factors for lymph node metastasis of T1 colorectal cancer: a single-center study of 846 lesions. *J Gastroenterol* 2019; **54**: 708-717 [PMID: 30810812 DOI: 10.1007/s00535-019-01564-y]

9 **Vermeer NCA**, Backes Y, Snijders HS, Bastiaannet E, Liefers GJ, Moons LMG, van de Velde CJH, Peeters KCMJ; Dutch T1 Colorectal Cancer Working Group. National cohort study on postoperative risks after surgery for submucosal invasive colorectal cancer. *BJS Open* 2019; **3**: 210-217 [PMID: 30957069 DOI: 10.1002/bjs5.50125]

10 **Mochizuki K**, Kudo SE, Ichimasa K, Kouyama Y, Matsudaira S, Takashina Y, Maeda Y, Ishigaki T, Nakamura H, Toyoshima N, Mori Y, Misawa M, Ogata N, Kudo T, Hayashi T, Wakamura K, Sawada N, Ishida F, Miyachi H. Left-sided location is a risk factor for lymph node metastasis of T1 colorectal cancer: a single-center retrospective study. *Int J Colorectal Dis* 2020; **35**: 1911-1919 [PMID: 32548720 DOI: 10.1007/s00384-020-03668-x]

11 **Sumimoto K**, Tanaka S, Shigita K, Hirano D, Tamaru Y, Ninomiya Y, Asayama N, Hayashi N, Oka S, Arihiro K, Yoshihara M, Chayama K. Clinical impact and characteristics of the narrow-band imaging magnifying endoscopic classification of colorectal tumors proposed by the Japan NBI Expert Team. *Gastrointest Endosc* 2017; **85**: 816-821 [PMID: 27460392 DOI: 10.1016/j.gie.2016.07.035]

12 **Kudo S**, Tamura S, Nakajima T, Yamano H, Kusaka H, Watanabe H. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. *Gastrointest Endosc* 1996; **44**: 8-14 [PMID: 8836710 DOI: 10.1016/s0016-5107(96)70222-5]

13 **Puig I**, López-Cerón M, Arnau A, Rosiñol Ò, Cuatrecasas M, Herreros-de-Tejada A, Ferrández Á, Serra-Burriel M, Nogales Ó, Vida F, de Castro L, López-Vicente J, Vega P, Álvarez-González MA, González-Santiago J, Hernández-Conde M, Díez-Redondo P, Rivero-Sánchez L, Gimeno-García AZ, Burgos A, García-Alonso FJ, Bustamante-Balén M, Martínez-Bauer E, Peñas B, Pellise M; EndoCAR group, Spanish Gastroenterological Association and the Spanish Digestive Endoscopy Society. Accuracy of the Narrow-Band Imaging International Colorectal Endoscopic Classification System in Identification of Deep Invasion in Colorectal Polyps. *Gastroenterology* 2019; **156**: 75-87 [PMID: 30296432 DOI: 10.1053/j.gastro.2018.10.004]

14 **Didden P**, van Eijck van Heslinga RAH, Schwartz MP, Arensman LR, Vleggaar FP, de Graaf W, Koch AD, Doukas M, Lacle MM, Moons LMG. Relevance of polyp size for primary endoscopic full-thickness resection of suspected T1 colorectal cancers. *Endoscopy* 2022; **54**: 1062-1070 [PMID: 35255517 DOI: 10.1055/a-1790-5539]

15 **Zwager LW**, Bastiaansen BAJ, van der Spek BW, Heine DN, Schreuder RM, Perk LE, Weusten BLAM, Boonstra JJ, van der Sluis H, Wolters HJ, Bekkering FC, Rietdijk ST, Schwartz MP, Nagengast WB, Ten Hove WR, Terhaar Sive Droste JS, Rando Munoz FJ, Vlug MS, Beaumont H, Houben MHMG, Seerden TCJ, de Wijkerslooth TR, Gielisse EAR, Hazewinkel Y, de Ridder R, Straathof JA, van der Vlugt M, Koens L,

Fockens P, Dekker E; Dutch eFTR Group. Endoscopic full-thickness resection of T1 colorectal cancers: a retrospective analysis from a multicenter Dutch eFTR registry. *Endoscopy* 2022; **54**: 475-485 [PMID: 34488228 DOI: 10.1055/a-1637-9051]

16 **Hassan C**, Zullo A, Risio M, Rossini FP, Morini S. Histologic risk factors and clinical outcome in colorectal malignant polyp: a pooled-data analysis. *Dis Colon Rectum* 2005; **48**: 1588-1596 [PMID: 15937622 DOI: 10.1007/s10350-005-0063-3]

17 **Kye BH**, Jung JH, Kim HJ, Kang SG, Cho HM, Kim JG. Tumor budding as a risk factor of lymph node metastasis in submucosal invasive T1 colorectal carcinoma: a retrospective study. *BMC Surg* 2012; **12**: 16 [PMID: 22866826 DOI: 10.1186/1471-2482-12-16]

18 **Haggitt RC**, Glotzbach RE, Soffer EE, Wruble LD. Prognostic factors in colorectal carcinomas arising in adenomas: implications for lesions removed by endoscopic polypectomy. *Gastroenterology* 1985; **89**: 328-336 [PMID: 4007423 DOI: 10.1016/0016-5085(85)90333-6]

19 **Yim K**, Won DD, Lee IK, Oh ST, Jung ES, Lee SH. Novel predictors for lymph node metastasis in submucosal invasive colorectal carcinoma. *World J Gastroenterol* 2017; **23**: 5936-5944 [PMID: 28932085 DOI: 10.3748/wjg.v23.i32.5936]

20 **Saraiva S**, Rosa I, Fonseca R, Pereira AD. Colorectal malignant polyps: a modern approach. *Ann Gastroenterol* 2022; **35**: 17-27 [PMID: 34987284 DOI: 10.20524/aog.2021.0681]

21 **Caputo D**, Caricato M, La Vaccara V, Taffon C, Capolupo GT, Coppola R. T1 colorectal cancer: poor histological grading is predictive of lymph-node metastases. *Int J Surg* 2014; **12**: 209-212 [PMID: 24378911 DOI: 10.1016/j.ijsu.2013.12.012]

22 **Dano H**, Baldin P, Demetter P, Driessen A, Hoorens A, Sagaert X, Van Huysse J, Verset L, Jouret-Mourin A. Guidelines for an optimal management of a malignant colorectal polyp. What is essential in a pathology report ? *Acta Gastroenterol Belg* 2020; **83**: 53-59 [PMID: 32233272]

23 **Watanabe T**, Muro K, Ajioka Y, Hashiguchi Y, Ito Y, Saito Y, Hamaguchi T, Ishida H, Ishiguro M, Ishihara S, Kanemitsu Y, Kawano H, Kinugasa Y, Kokudo N, Murofushi K, Nakajima T, Oka S, Sakai Y, Tsuji A, Uehara K, Ueno H, Yamazaki K, Yoshida M, Yoshino T, Boku N, Fujimori T, Itabashi M, Koinuma N, Morita T, Nishimura G, Sakata Y, Shimada Y, Takahashi K, Tanaka S, Tsuruta O, Yamaguchi T, Yamaguchi N, Tanaka T, Kotake K, Sugihara K; Japanese Society for Cancer of the Colon and Rectum. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2016 for the treatment of colorectal cancer. *Int J Clin Oncol* 2018; **23**: 1-34 [PMID: 28349281 DOI: 10.1007/s10147-017-1101-6]

24 **Choi YS**, Kim WS, Hwang SW, Park SH, Yang DH, Ye BD, Myung SJ, Yang SK, Byeon JS. Clinical outcomes of submucosal colorectal cancer diagnosed after endoscopic resection: a focus on the need for surgery. *Intest Res* 2020; **18**: 96-106 [PMID: 32013317 DOI: 10.5217/ir.2019.00092]

25 **Wada Y**, Shimada M, Murano T, Takamaru H, Morine Y, Ikemoto T, Saito Y, Balaguer F, Bujanda L, Pellise M, Kato K, Saito Y, Ikematsu H, Goel A. A Liquid Biopsy Assay for Noninvasive Identification of Lymph Node Metastases in T1 Colorectal Cancer. *Gastroenterology* 2021; **161**: 151-162.e1 [PMID: 33819484 DOI: 10.1053/j.gastro.2021.03.062]

26 **Kudo SE**, Ichimasa K, Villard B, Mori Y, Misawa M, Saito S, Hotta K, Saito Y, Matsuda T, Yamada K, Mitani T, Ohtsuka K, Chino A, Ide D, Imai K, Kishida Y, Nakamura K, Saiki Y, Tanaka M, Hoteya S, Yamashita S, Kinugasa Y, Fukuda M, Kudo T, Miyachi H, Ishida F, Itoh H, Oda M, Mori K. Artificial Intelligence System to Determine Risk of T1 Colorectal Cancer Metastasis to Lymph Node. *Gastroenterology* 2021; **160**: 1075-1084.e2 [PMID: 32979355 DOI: 10.1053/j.gastro.2020.09.027]

27 **Zwager LW**, Bastiaansen BAJ, Montazeri NSM, Hompes R, Barresi V, Ichimasa K, Kawachi H, Machado I, Masaki T, Sheng W, Tanaka S, Togashi K, Yasue C, Fockens P, Moons LMG, Dekker E. Deep Submucosal Invasion Is Not an Independent Risk Factor for Lymph Node Metastasis in T1 Colorectal Cancer: A Meta-Analysis. *Gastroenterology* 2022; **163**: 174-189 [PMID: 35436498 DOI: 10.1053/j.gastro.2022.04.010]

28 **Dawson H**, Bokhorst JM, Studer L, Vieth M, Oguz Erdogan AS, Kus Öztürk S, Kirsch R, Brockmoeller S, Cathomas G, Buslei R, Fink D, Roumet M, Zlobec I, van der Laak J, Nagtegaal ID, Lugli A. Lymph node metastases and recurrence in pT1 colorectal cancer: Prediction with the International Budding Consortium Score-A retrospective, multi-centric study. *United European Gastroenterol J* 2024; **12**: 299-308 [PMID: 38193866 DOI: 10.1002/ueg2.12521]

29 **Dang H**, Dekkers N, le Cessie S, van Hooft JE, van Leerdam ME, Oldenburg PP, Flothuis L, Schoones JW, Langers AMJ, Hardwick JCH, van der Kraan J, Boonstra JJ. Risk and Time Pattern of Recurrences After Local Endoscopic Resection of T1 Colorectal Cancer: A Meta-analysis. *Clin Gastroenterol Hepatol* 2022; **20**: e298-e314 [PMID: 33271339 DOI: 10.1016/j.cgh.2020.11.032]

30 **Williams JG**, Pullan RD, Hill J, Horgan PG, Salmo E, Buchanan GN, Rasheed S, McGee SG, Haboubi N; 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 [PMID: 23848492 DOI: 10.1111/codi.12262]

31 **Yeh JH**, Tseng CH, Huang RY, Lin CW, Lee CT, Hsiao PJ, Wu TC, Kuo LT, Wang WL. Long-term Outcomes of Primary Endoscopic Resection vs Surgery for T1 Colorectal Cancer: A Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol* 2020; **18**: 2813-2823.e5 [PMID: 32526343 DOI: 10.1016/j.cgh.2020.05.060]

32 **Belderbos TD**, van Erning FN, de Hingh IH, van Oijen MG, Lemmens VE, Siersema PD. Long-term Recurrence-free Survival After Standard Endoscopic Resection Versus Surgical Resection of Submucosal Invasive Colorectal Cancer: A Population-based Study. *Clin Gastroenterol Hepatol* 2017; **15**: 403-411.e1 [PMID: 27609703 DOI: 10.1016/j.cgh.2016.08.041]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com