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Reappraisal of the characteristics, management, and prognosis of intramucosal colorectal cancers and their comparison with T1 carcinomas

Martin Bordet, MD,[1] Jean-François Bretagne, MD, PhD,[2] Christine Piette, MD,[3] Chloé Rousseau, BS,[4] Thomas Grainville, MD,[1] Mathilde Cosson, MD,[3] Astrid Lièvre, MD, PhD[1,2,3,5]

[1] Department of Gastroenterology, University Hospital, 35033 Rennes, France

[2] Rennes 1 University, 35000 Rennes, France

[3] ADECI 35 (Association pour le Dépistage des Cancers en Ille-et-Vilaine), 35040 Rennes, France

[4] Department of Biostatistics, University Hospital, 35033 Rennes, France

[5] COSS (Chemistry Oncogenesis Stress Signaling), UMR_S 1242, Rennes, France

Corresponding author: J.-F. Bretagne; Phone: +33 607491311;

E-mail: jf.bretagne@gmail.com

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SUMMARY

Background and Aims: The recent description of 'invasive' forms of intramucosal carcinomas (IMCs) has rekindled interest in studying the characteristics, management and prognosis of IMCs and comparing them to T1 colorectal cancers (CRCs).

Methods: This population-based study included 282 cases of IMC and 207 cases of T1 CRC diagnosed by colonoscopy after a positive fecal blood test through a screening program.

Results: IMC presented mainly in the form of pedunculated polyps (68.4%) located in the distal colon (69.9%) with a size ≥20 mm (60.6%). IMCs were endoscopically resected in 227 (80.5%) patients and surgically resected in 55 (19.5%) patients. Surgical patients had more right-sided, more sessile, and larger lesions. There was no sign of lymphovascular invasion. Compared with T1 CRC, IMC demonstrated lower rates of sessile polyps (31.6% vs 49.8%, p<0.0001), primary and ultimate surgical treatment (19.5% vs 39.1% and 19.9% vs 78.7%, p<0.0001, respectively), lymph node metastasis in surgical patients (0% vs 9.5%, p=0.041), cancer recurrence and cancer-related mortality (0% vs 5.6% and 0% vs 2.5%, respectively), and bleeding after endoscopic resection (1.8% vs 8.7%, p=0.001). By multivariate analysis of the pooled cohort (IMC + T1 CRC, n=489), the factors significantly associated with first line surgery were shown to be polyp characteristics and the gastroenterologist having performed the colonoscopy.

Conclusions: IMCs account for a quarter of all screen-detected CRC. They have an excellent prognosis regardless of whether endoscopic or surgical treatment is performed. IMCs differ significantly from T1 carcinomas in terms of management and prognosis.

Key words: colorectal cancer, intramucosal cancer, T1 colorectal cancer, endoscopic

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INTRODUCTION

European guidelines for colorectal cancer (CRC) screening have used the revised Vienna classification[1] in a simplified form for the characterization of colorectal neoplastic lesions.[2] Thus, after removing indefinite neoplasia, colorectal lesions are classified into 4 pathological categories: negative for neoplasia, low-grade neoplasia, high-grade neoplasia, and invasive carcinoma.[2] The term intramucosal carcinoma (IMC) was not retained and was substituted with mucosal high-grade neoplasia, whereas invasive carcinomas were characterized by the invasion of neoplastic cells into the submucosa or beyond. This dichotomy was based on patients with IMCs being considered at negligible risk of lymph node metastases, in connection with the lymphatic vessels present in the mucosal layer perhaps being immature or not communicating with the deeper lymphatic network.[3] However, the concept of invasive IMC has recently emerged from studies demonstrating the occurrence of lymphovascular invasion in cases of IMC, although the potential for lymph node metastasis in such cases has yet to be established.[4] All of these considerations have led to various problems: first, the actual incidence of screen-detected carcinomas has been underestimated in most studies of CRC screening programs excluding IMC, whereas in France, IMC were included in the evaluation of the performance of the national screening program and where they represented 27.7% of all of the carcinomas detected with the guaiac test in 2008 to 2009;[5] second, the management and prognosis of screen-detected IMCs are unknown because these carcinomas are only part of the lesions included in the high-grade neoplasia category; and third, little is known about the characteristics, management and prognosis of IMC compared with early invasive carcinomas, ie, those

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limited to the submucosa, also called T1 carcinomas. In this article, IMCs correspond to Tis cancers in the current International Union Against Cancer (UICC) tumor-nodes-metastasis (TNM) classification,[6] ie, cancers with invasion of the lamina propria and eventually into the muscularis mucosae, but not beyond, which excludes intraepithelial cancers, the latter being indistinguishable from what many pathologists call high-grade dysplasia. As for T1 cancers, they invade the submucosa, but not the muscularis propria.[6]

It was stated that the management of screen-detected carcinomas should not differ, stage for stage, from that required for symptomatic disease.[7] However, because screening detects a higher proportion of early disease compared with that diagnosed in the symptomatic population, it is important to check that early cancers are properly managed. We and others have reported the existence of variations in the treatment of significant polyps and early CRC and have pointed out a specialist tribalism continuing to dominate the management of such lesions.[8-10] Although endoscopic therapeutic management can be expected in the vast majority of IMC cases, little is known about the actual conditions for resection of IMC in the literature.[11] Therefore, the primary aim of this study was to use a population-based approach to assess the characteristics of all screen-detected IMCs in one district in France over a 13-year period and to examine the management strategies used and the outcomes of these patients. The secondary purposes of our study were to compare these data with those recently reported for screen-detected T1 carcinoma in the same district at the same time[12] and to assess the factors associated with therapeutic strategies for superficial cancers, ie, the summation of IMC and T1 cancers.

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Study population

This study was a retrospective analysis of a prospective, multicentric cohort including all patients with IMC and T1 adenocarcinomas diagnosed after a positive fecal blood test through the national screening program in the Ille et Vilaine district from 2003 to 2015. Data were prospectively and regularly collected by the ADECI 35 (Association du Dépistage des Cancers en Ille et Vilaine) staff. There were 14,215 (2.5%) positive tests followed by 13,245 colonoscopies (93.2%). The switch from guaiac to immunochemical testing occurred in 2015.[13]

Every patient with screening-detected IMC was included in the study. According to the French recommendations[14] based on the data from the current UICC/TNM classification[6], intraepithelial carcinomas were excluded from the study. Demographic and baseline clinical data and details on the treatment and follow-up were recorded. The CRC screening program was declared and approved by the CNIL (Commission Nationale de l'Informatique et des Libertés) on August 30, 2002 (no. 812571). This research was approved by the CCTIRS (Comité Consultatif pour le Traitement de l'Information en Matière de Recherche dans le Domaine de la Santé).

Colonoscopy data

The date of the colonoscopy, the details of the gastroenterologist who performed the colonoscopy and of the endoscopy center where the colonoscopy was performed, the macroscopic features of colorectal neoplasias, and histological data were recorded. We investigated whether complex polyps were referred to a skilled endoscopist in distinguishing between simultaneous or delayed endoscopic resection, compared with diagnostic

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colonoscopy. The size of the malignant polyps, assessed by the endoscopists by using an open biopsy forceps as a standard, was categorized as <20 mm, 20 to 29 mm, or ≥30 mm. Malignant polyps located in the cecum, the right colon segment, the hepatic flexure or the transverse colon were considered proximal, whereas polyps adjacent or distal to the splenic flexure were considered distal, except for polyps of the rectum, which were isolated in a single category. According to their appearance, polyps were defined as pedunculated or sessile. The rare polyps described as flat were defined as sessile for the study. When 2 IMC were found by the same colonoscopy, the index case was that with the worse pathological features or the larger when the pathological severity was the same. Nonmalignant polyps were also recorded, and polyposis was defined as the presence of 10 polyps or more.

The endoscopic resection techniques used, such as snare polypectomy, endoscopic mucosal resection (EMR), and monobloc or piecemeal resection, were recorded. Postendoscopic adverse events and their severity grades as defined by ASGE were recorded.[15]

Surgery characteristics

The date of surgery, the details of the surgeon and surgery center, modalities (type and indications), postoperative adverse events as defined by the Clavien-Dindo classification,[16] and pathology analysis of surgical specimen were collected. Severe postoperative adverse events were those rated ≥IIIa. Surgery was called primary when the cancer was surgically resected after a diagnostic colonoscopy and secondary when the cancer had been primarily endoscopically resected, but there was an indication for complementary surgery. Data about the lymph nodes (number, invasion) were collected except for transanal resection because lymph nodes were not removed with this technique.

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Histological features

Histological features were retrospectively assessed by reviewing the patient files. The following parameters were recorded: differentiation, depth of invasion, budding, presence of vascular or lymphatic invasion, perineural neoplastic invasion, and the surgical margins. If a feature was not mentioned in the histopathology report, we did not assume it was absent.

Follow-up

The close follow-up of patients aimed to assess mortality related or not related to tumor progression and local or metastatic recurrence. Data were collected until last follow-up or date of last medical record.

Statistical analysis

Quantitative variables are expressed as the means and standard deviations and were compared with the t-test or the Mann-Whitney Wilcoxon test. Qualitative variables are expressed as numbers or percentages and were compared with X^2 test or the Fisher test. Factors associated with the therapeutic strategy were investigated using univariate logistic regression. Potential covariates ($p \leq 0.20$) were placed into a multivariable logistic regression model that was performed using stepwise backward elimination. Odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) were used to express the association between the studied features and outcomes. By considering patients with IMC or T1 carcinomas as a single group of superficial cancers, we assessed the factors associated with the choice of primary treatment, ie, endoscopic or surgical resection. For this analysis, we selected the gastroenterologists who performed 10 colonoscopies or more harboring one superficial

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cancer, whereas those contributing less than 10 cases of IMC/T1 cancer polyps were all combined together and considered as one gastroenterologist.

All of the analyses were performed using the SAS statistical software program SAS, version 9.4 (SAS Institute, Inc, Cary, NC, USA). A test was interpreted as significant if p was less than 0.05.

RESULTS

Characteristics of the IMC cohort

Over the 13-year period, 1060 cases of CRC were diagnosed, including 282 (26.6%) IMCs and 207 (19.5%) T1 adenocarcinomas, ie, 46.1% of all CRC cases were superficial cancers. The detailed characteristics of the T1 CRC cohort already published are not presented here.[12] Here, we present the data concerning the IMC population and the comparative analysis between IMCs and T1 CRCs.

There were 176 (62.4%) men and 106 (37.6%) women. The mean time between the positive fecal blood test and the diagnostic colonoscopy was 61.4 ± 63.4 days. The colonoscopies were performed by 51 various gastroenterologists in 21 endoscopy centers. The colonoscopies were performed in private centers in 247 (87.6%) cases and in public centers in 35 (12.4%) cases. The number of colonoscopies harboring IMC ranged from 1 to 18 (mean 5.4) per gastroenterologist. Twelve gastroenterologists performed 10 colonoscopies or more. The characteristics of the IMC cohort are reported in **Table 1**.

Characteristics of IMC and associated lesions

The mean size of IMCs was 22.5 ± 11.2 mm. IMCs were preferentially located in the distal colon and particularly in the sigmoid colon (n=174, 61.7%). Most of the malignant polyps

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were pedunculated. In 58.1% of the cases, IMC was associated with at least another polyp (mean 2.4 ± 1.6), and polyposis was diagnosed in 8 (2.8%) patients. A second IMC coexisted in 10 (3.5%) patients.

Management of IMC

Among the 282 patients with IMC, 227 (80.5%) underwent endoscopic resection, and 55 (19.5%) underwent primary surgical resection.

Endoscopic resection

The characteristics of patients and malignant polyps among those endoscopically resected are reported in **Table 1**. The treatment was performed during the diagnostic colonoscopy in 213 cases (93.8%) and was postponed in the others for various reasons. In only 1 (0.4%) case, the patient was referred to an expert in a tertiary endoscopy center. A snare polypectomy was performed in 180 (79.3%) cases and EMR in 47 (20.7%) cases. En bloc resection was performed in 213 (93.8%) cases, whereas 14 (6.2%) were piecemeal, mainly in cases of EMR. Severe bleeding occurred in 4 (1.8%) patients requiring emergency colonoscopy (n=3) or colectomy (n=1) for hemostasis. None of the patients with endoscopically resected IMCs required subsequent surgical resection, except one with residual adenoma and high-grade dysplasia at the time of a close follow-up colonoscopy.

Surgical resection

The characteristics of the patients and malignant polyps among those surgically resected are reported in **Table 1**. The main types of surgery were sigmoidectomy in 18 (32.7%) cases, right colectomy in 14 (25.5%) cases and left colectomy in 9 (16.4%) cases, whereas transanal resection and anterior rectal resection were each performed in 5 cases (9.1%). Two other (3.6%) patients underwent proctectomy, 1 (1.8%) patient a total colectomy and 1 (1.8%)

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patient a cecal resection. The mean number of resected lymph nodes was 14.1 ± 10.8, but 24 (48%) patients had fewer than 12 lymph nodes resected. No lymph nodes metastases were observed in any of the surgically resected cases. Postoperative adverse events were noted in 6 (10.9%) patients, including 2 grade I adverse events and 4 grade III adverse events: peritonitis due to anastomotic leakage requiring emergency surgery and stoma (n=2); and severe bleeding (n=2) requiring one radiologic drainage and one surgical drainage. Among the 55 patients directly operated on, none required reoperation for cancer-related reasons.

Factors associated with surgical resection rather than endoscopic resection

In both univariate and multivariate analyses, factors significantly associated with surgical resection were found to be the characteristics of the malignant polyp (proximal localization, size ≥20 mm, sessile morphology) (**Table 2**). The parameter with the greatest statistical weight was a size ≥30 mm. By univariate analysis, the endoscopists did not seem to be associated with the decision for surgery rather than endoscopic resection (p=0.20).

Histopathological data for IMCs

The lamina propria was invaded in all cases and the muscularis mucosae in two cases. IMCs were reported to be well differentiated in 196 (69.5%) cases and moderately differentiated in 4 cases (1.4%), whereas differentiation was not mentioned in 82 (29.1%) cases. No vascular or lymphatic invasion was reported, and tumor budding was found in 1 (0.35%) case, but these features were not mentioned in approximately half of the pathology reports. Margins were superior to 1 mm in the 55 (100%) IMCs in the surgical group, and 200 patients (88.1%) in the endoscopic treatment group.

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Among the 282 patients with IMCs, follow-up data were available for 268 (95.0%) with a median follow-up of 6.1 ± 3.8 years. All 268 patients were followed up clinically and 259 had colonoscopic follow-up. In addition 47 patients had at least one ultrasound examination and 33 at least one CT scan. Death occurred in 14 cases, but none was cancer related. No local or distant cancer recurrence was found during follow-up. Conversely, metachronous CRC was observed in 2 patients. Of the 49 patients with sessile endoscopically resected IMCs, 45 (91.8%) were followed by colonoscopy, and tumor residue or local recurrence was diagnosed in 7 cases (15.5%). Compared with en bloc resection, piecemeal removal was more frequently associated with residual/recurrent disease (3/36 [8.3%] vs 4/9 [44.4%], OR=8.8 [95% CI, 1.5 - 51.6]; p=0.016). Residual or recurrent disease which corresponded to low-grade dysplasia or high-grade dysplasia adenoma in 4 and 3 cases, respectively, was successfully treated by further endoscopic resection in 6 cases and by surgical resection in one case.

Comparative analysis of IMC and T1 CRC cohorts

There were no differences in the patient and malignant polyp characteristics between the groups, except for a higher proportion of pedunculated polyps in the IMC group than in the T1 group (68.4% vs 50.2%, p<0.0001). The therapeutic strategies were quite different between the groups with a greater proportion of endoscopic resection as first line treatment (80.5% vs 60.9%, p<0.0001) and ultimate treatment (80.1% vs 21.3%, p<0.0001) in the IMC group. Patients with T1 cancers were referred more frequently to expert endoscopists than those with IMC (2.4% vs 0.4%, p=0.045). Among patients undergoing surgical resection with

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lymph node dissection the rate of lymph node metastasis was higher in T1 cancers than IMCs (9.5% vs 0%, p<0.05).

After endoscopic resection, the rate of adverse events, particularly that of bleedings, was significantly higher for T1 than for IMC (8.7% vs 1.8%, p=0.001). After surgical resection, the rate of nonsevere adverse events was significantly higher for T1 than for IMC (20.0% vs 3.6%, p=0.006), but there were no differences for severe adverse events (3.9% vs 7.3%, p=0.45). Finally, as expected, the rates of cancer recurrence and cancer-related death were significantly higher for T1 patients than for IMC patients (5.6% vs 0%, p<0.0001, and 2.5% vs 0%, p=0.013).

Analysis of factors associated with first line surgery rather than endoscopic resection in the whole cohort of superficial cancers (n=489)

By univariate and multivariate analyses, the factors significantly associated with first line surgery were the malignant polyps' characteristics (location, morphology, size) and the gastroenterologist having performed the index colonoscopy (**Table 3**). The factor having the greatest statistical weight was a polyp size ≥30 mm (OR, 66.67; 95% CI, 22.02 - 201.89). Compared with the endoscopist who had endoscopically resected 31 of 32 superficial cancers, the odds ratios for first-line surgery ranged from 1.1 to 159.1 (median=7.2) for the other endoscopists. The lower limit of the CI was greater than 1 for 11 of them by univariate analysis and 4 of them by multivariate analysis.

DISCUSSION

The main outcome of this 13-year population-based study was to determine the characteristics, management and prognosis of IMC. We focused on screen-detected superficial cancers because such lesions are increasingly being detected in screening

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programs and because their treatment should reduce CRC mortality and morbidity.[17–19] In France, unlike other European countries,[2] screen-detected IMC are considered actual CRCs and not high-grade neoplasias. Of course, that fact must be considered when comparing the performance of screening tests and programs between various countries. Thus, the positive predictive value of a positive fecal blood test, which we reported to be 8.5% for CRC with the OC-Sensor test and a cut-off of 30 µg of hemoglobin per gram of feces used for FIT positivity,[13] would become 6.7% after excluding IMCs and considering only invasive cancers.

Little is known about the characteristics, management and prognosis of IMCs, mainly because these lesions are included in the mucosal high-grade neoplasia category.[2] Some authors have even included IMCs in the advanced adenoma category,[20] which from our point of view is questionable because the latter category usually includes adenomas that either are 1 cm or larger in size, have tubulovillous or villous components, or are high-grade dysplasias.[21] In contrast to Hashimoto et al, who reported 9 cases of invasive IMC,[4] we did not observe in the present study any cases of IMC with lymphovascular invasion. This finding, however, must be interpreted cautiously because our study suffered from a large proportion of missing histological data and from the absence of pathology reassessments. Nevertheless, by demonstrating the absence of lymph node metastasis on surgical specimens and the absence of any cancer recurrence after endoscopic or surgical resection with a median follow-up of more than 6 years in almost 300 patients, our study confirmed the excellent prognosis of IMC and therefore the exceptional nature of metastatic IMC occurrence.[22]

The present study showed that the majority of IMCs were in the form of pedunculated polyps located in the distal colon. The proportion of distal polyps was higher in our study than in previous reports,[23] but this study was not devoted exclusively to IMCs. Here, we

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report a high rate (19.5%) of first-line surgical management for IMCs, whereas no patients needed surgery after direct endoscopic resection, except for one patient because of a residual tumor detected by close follow-up colonoscopy. Thus, the fears of the European panel[2] that the use of the term IMC instead of high-grade neoplasia by pathologists could lead to surgical resections after a first endoscopic resection were unfounded. Nevertheless, the question arises as to why there was such a high rate of direct surgical resection, even if, in a U.S. population-based study from 1998 to 2009, a much higher rate of surgery (56.4%) was reported for T0 CRCs, including not solely IMCs but also intraepithelial carcinomas.[11] By both univariate and multivariate analyses, we demonstrated that the factors significantly associated with surgical resection of IMC were the characteristics of the malignant polyps (proximal localization, size ≥20 mm, sessile morphology), knowing that the factor with the greatest statistical weight was a size ≥30 mm. The gastroenterologist who performed the colonoscopy leading to the diagnosis of IMC was not found to be a factor significantly associated with the choice of treatment -- a result identical to that observed for the T1 CRC cohort but quite different from that observed for nonmalignant polyps.[8] However, both studies of IMCs and T1 carcinomas lacked statistical power, given the relatively small number of colonoscopies harboring such neoplastic lesions performed by each gastroenterologist. In fact, by pooling the two cohorts, the present study demonstrated that the gastroenterologist was a significant factor associated with the referral to surgery for superficial CRC. One could speculate that the rate of primary surgery for the IMC cohort would have decreased if patients had been referred to endoscopists with more expertise for the characterization and treatment of complex polyps. The lack of use of the Kudo pit pattern classification[24,25] by French gastroenterologists is to be deplored because these data were not present in any of the colonoscopy reports in the period under review. The

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subjective impression left by the polyp to the endoscopist and the endoscopist's confidence in his(her) own ability to resect a probably malignant polyp are nonmeasurable factors which probably play an important role in the therapeutic decision. In other words, we suspect that the comfort level of the endoscopist with resection has an important impact on the management of malignant polyps. It is hoped that the appropriation of tools, such as the recently developed JNET[26] and CONNECT[27] classifications, for the characterization and the training of gastroenterologists in the various endoscopic resection techniques, including submucosal dissection not used in this series, will in the future reduce the rate of referral to surgeons for IMC. Our study shows that piecemeal removal of sessile IMCs exposes to the risk of residual or recurrent disease, but in every case it was nonmalignant disease. The rate of residual or recurrent disease we found in this study for sessile IMCs (15.5%) was rather lower than that observed in other series of malignant polyps.[28] Nevertheless, we agree with the justification for performing a second-look colonoscopy in these cases of piecemeal resection.[28]

We are not aware of any studies in the literature comparing IMCs and T1 CRCs. The present study showed first that there were no significant differences between the characteristics of both cohorts' patients (age, sex). There were also no significant differences between the two cohorts in the morphology of the malignant polyps (size, localization), except for the morphology with a higher rate of sessile polyps for T1 than IMC (49.8% vs 31.6%, $p<0.0001$). The latter result, in agreement with another study[29], argues in favor of the transformation of pedunculated polyps into sessile polyps during colorectal carcinogenesis. Sessile morphology of malignant polyps was a factor significantly associated with surgical treatment in both the IMC and T1 cohorts, partly explained the higher direct surgical referral rate observed in the T1 cohort, compared with the IMC cohort (39.1% vs 19.5%, $p<0.0001$). Of course, the rate of

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second-line surgery after primary endoscopic resection was higher for the T1 cohort than the IMC cohort (65.0% vs 0.44%, p<0.0001) due to the presence of high-risk pathological features of lymph node metastasis for T1 carcinomas. Similarly, the higher rate of lymph node metastasis found in patients operated on for T1 CRCs compared with IMCs (9.5% vs 0%, p=0.0409) was expected. Thus, our study highlights the excellent prognosis of patients with IMCs with the absence of any cancer recurrence and cancer-related mortality for IMCs, in contrast to TI CRCs (5.6% and 2.5%, respectively). Finally, we must emphasize the large difference in the rate of postendoscopic bleeding that we observed between the IMC and T1 CRC cohorts (1.8% vs 8.7%, p=0.001). The rate of postendoscopic bleeding in the IMC cohort is in agreement with that of other studies,[30,31] whereas the relatively high rate of postendoscopic adverse events that we registered for the T1 carcinoma cohort was a topic of debate for us.[12] We previously evoked the possible inexperience of some endoscopists in the endoscopic treatment of T1 carcinomas, but this hypothesis no longer holds because it was the same endoscopists who performed the endoscopic treatment of malignant polyps in both cohorts. In their meta-analysis including 50 studies of endoscopic resection of large (≥20 mm) colorectal polyps, including 58% invasive cancers, Hassan et al[23] reported a mean rate of 6.5% for bleeding. A recent Dutch study including T1 CRCs reported rates of 3.7% and 1.2% for bleeding and perforation, respectively.[32] In accordance with these data, our findings raise questions about the safety of endoscopic resection for T1 CRC, which should be explored more extensively.

The main limitations of the present study were its retrospective nature and the suboptimal collection of data regarding some histopathological items. A reassessment of histological specimens by a gastrointestinal pathologist could have confirmed or not the poor interobserver agreement of the diagnosis of lamina propria invasion, which was reported in

a short Japanese series.[33] Furthermore, it cannot be ruled out that such an analysis could have revealed signs of lymphovascular invasion in some cases of IMC. But this relative pathological weakness is largely compensated by the quality and duration of the follow-up never reported to date, which is one of the strengths of the study.

CONCLUSION

This long-term population-based study of 282 screening-detected IMCs highlights the excellent prognosis of these CRCs, which did not result in any specific mortality or long-term cancer recurrence regardless of the endoscopic or surgical treatment performed. Surgical patients had more right-sided, more sessile and larger lesions. We speculate that the rate of surgery of 19.6% could be decreased by referring patients to expert endoscopists. The comparison between IMCs and T1 CRCs showed that they are different cancers in terms of their management and prognosis. In addition, the much higher rate of bleeding observed after endoscopic resection of T1 CRCs compared with IMCs raises questions about the safety of endoscopic resection for T1 carcinomas.

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TABLE 1. Characteristics of patients, colonoscopies, and polyps according to the treatment of intramucosal carcinomas

Variable	Total IMC cohort	Endoscopic resection	Surgical resection	*P* value
PATIENTS' CHARACTERISTICS	282 (100%)	227 (80.5%)	55 (19.5%)	< 0.0001
Age (years)				
Median age	63.81 ± 7.11	63.81 ± 7.00	63.80 ± 7.60	0.992
50-54	42 (14.9%)	31 (13.7%)	11 (20.0%)	0.581
55-59	34 (12.1%)	30 (30.2%)	4 (7.3%)	
60-64	62 (22.0%)	51 (22.5%)	11 (20.0%)	
65-69	74 (26.2%)	58 (25.6%)	16 (29.1%)	
70-74	70 (24.8%)	57 (25.1%)	13 (23.6%)	
Sex				
Male	176 (62.4%)	141 (62.1%)	35 (63.6%)	0.834
Female	106 (37.6%)	86 (37.9%)	20 (36.4%)	

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COLONOSCOPY AND POLYPS' CHARACTERISTICS				
IMC size				
<20 mm	111 (39.4%)	109 (48.0%)	2 (3.6%)	< 0.0001
20-29 mm	97 (34.4%)	84 (37.0%)	13 (23.6%)	
⩾30 mm	74 (26.2%)	34 (15.0%)	40 (72.7%)	
IMC localization				
Proximal colon	30 (10.6%)	12 (5.3%)	18 (32.7%)	< 0.0001
Distal colon	197 (69.9%)	172 (75.8%)	25 (45.5%)	
Rectum	55 (19.5%)	43 (18.9%)	12 (21.8%)	
IMC morphology				
Pedunculated	193 (68.4%)	178 (78.4%)	15 (27.3%)	< 0.0001
Sessile	89 (31.6%)	49 (21.6%)	40 (72.7%)	
Distribution of patients according to the number of associated polyps (excluding the index case)				

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No associated polyps	118 (41.8%)	93 (41.0%)	25 (45.5%)	0.253
1 to 9 polyps	156 (55.3%)	129 (56.8%)	27 (49.1%)	
Polyposis (⩾10)	8 (2.8%)	5 (2.2%)	3 (5.5%)	
Year of the colonoscopy				
Before 2007	163 (57.8%)	133 (81.6%)	30 (18.4%)	0.586
After 2007	119 (42.2%)	94 (79.0%)	25 (21.0%)	

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TABLE 2. Factors associated with surgical resection rather than endoscopic resection of intramucosal carcinomas

Variable	Univariate analysis			Multivariate analysis		
PATIENTS CHARACTERISTICS	Odd ratio	95% CI	*P* value	Odd ratio	95% CI	*P* value
Age (years)	1.00	[0.96 - 1.04]	0.992			
Sex						
Men Women	1 (ref) 0.94	[0.51 - 1.73]	0.834			
POLYPS CHARACTERISTICS						
Localization						
Rectum Proximal colon Distal colon	1 (ref) 5.37 0.52	[2.04 - 14.19] [0.24 - 1.12]	< 0.0001	1 (ref) 4.45 3.10	[1.25; 15.89] [0.98; 9.74]	0.0461
Size						

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<20 mm	1 (ref)			1 (ref)		
20-29 mm	8.43	[1.85 - 38.39]	< 0.0001	7.69	[1.58; 37.31]	< 0.0001
≥ 30 mm	64.11	[14.72 - 279.2]		54.61	[11.34; 262.9]	
Morphology						
Pedunculated	1 (ref)		< 0.0001	1 (ref)		< 0.0001
Sessile	9.69	[4.95 - 18.98]		10.68	[3.99; 28.58]	
COLONOSCOPY CHARACTERISTICS						
Number of polyps	1.02	[0.86 - 1.22]	0.787			
Years of the first colonoscopy						
Before 2007	1 (ref)		0.586			
After 2007	1.18	[0.65 - 2.13]				

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TABLE 3. Analysis of factors associated with first line surgery rather than endoscopic resection in the whole cohort of superficial cancers (n=489)

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	***P* value**	**OR**	95% CI	***P* value**
POLYPS CHARACTERISTICS						
Localization						
Rectum	1 (ref)		< 0.0001	1 (ref)		0.026
Proximal	3.90	[1.9 - 8.2]		3.97	[1.42 - 11.1]	
Distal	0.49	[0.3 - 0.8]		1.97	[0.90 - 4.31]	
Size						
<20 mm	1 (ref)		< 0.0001	1 (ref)		< 0.0001
20-29 mm	9.68	[4.3 - 22.1]		19.37	[6.62 - 56.63]	
≥30 mm	42.14	[18.27 - 97.21]		66.67	[22.02 - 201.9]	
Morphology						
Pedunculated	1 (ref)		< 0.0001	1 (ref)		< 0.0001
Sessile	8.31	[5.28 - 13.06]		10.80	[5.4 - 21.67]	
INDIVIDUAL ENDOSCOPISTS WHO PERFORMED AT LEAST 10 COLONOSCOPIES						

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A	1 (ref)		0.0004	1 (ref)		0.0028
B	3.97	[0.52 -		2.04	[0.15 -	
C	28.32	30.37]		24.72	27.43]	
D	11.31	[4.51 -		7.19	[2.21 -	
E	9.95	77.64]		8.03	276.79]	
F	4.61	[1.81 -		2.13	[0.67 -	
G	17.65	70.55]		25.22	77.28]	
H	5.00	[1.31 -		3.49	[0.54 -	
I	21.00	75.81]		15.90	119.29]	
J	11.87	[0.65 -		9.24	[0.16 -	
K	13.23	32.83]		9.01	28.00]	
L	5.14	[2.74 -		3.86	[2.22 -	
M	10.12	113.7]		13.14	286.95]	
N	28.64	[0.56 -		159.51	[0.18 -	
O	50.99	45.03]		11.89	68.13]	
P	5.73	[2.64 -		2.28	[0.85 -	
Q	3.27	67.24]		1.11	299.12]	
R	5.45	[1.71 -		4.47	[0.73 -	
S	1.84	82.29]		1.25	117.26]	
Other	8.84	[2.02 -		5.43	[0.81 -	
endoscopists		86.81]			100.73]	
		[0.76 -			[0.33 -	
		34.87]			45.38]	

		[1.48 - 69.05] [3.80 - 215.85] [6.17 - 421.13] [0.79 - 41.38] [0.43 - 24.68] [0.70 - 42.66] [0.22 - 15.36] [1.59 - 49.22]			[1.12 - 154.33] [9.8 - 2609.3] [0.78 - 180.59] [0.15 - 34.61] [0.07 - 17.31] [0.28 - 72.03] [0.08 - 18.64] [0.59 - 49.93]	

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List of abbreviations

IMC : intramucosal carcinoma
CRC : colorectal cancer
ADECI: Association de Dépistage des Cancers en Ille et Vilaine
CNIL: Commission Nationale de l'Informatique et des Libertés
CCTIRS: Comité Consultatif pour le Traitement de l'Information en Matière de Recherche dans le Domaine de la Santé.
ASGE: American Society of Gastrointestinal Endoscopy
EMR: Endoscopic Mucosal Resection
OR: Odd Ratio
CI: Confidence Interval

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