Management of large polyps in a colorectal cancer screening programme with faecal immunochemical test: a population- and community-based observational study

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Abbreviations
ASGE: American Society for Gastrointestinal Endoscopy
BCSP: Bowel cancer screening programme
CI: confidence interval
CRC: colorectal cancer
EMR: endoscopic mucosal resection
ER: endoscopic resection
ESD: endoscopic submucosal dissection
ESGE: European Society for Gastrointestinal Endoscopy
FIT: faecal immunochemical test
gFOBT: guaiac-based faecal occult blood test
LNM: lymph node metastasis

NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
LP: large polyp

NPV: negative predictive value

PPV: positive predictive value

SD: standard deviation

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Ethical approval

Not required.

Competing interests

None declared

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ABSTRACT

Objective: To analyse presentation, management and outcomes of large (≥20 mm) polyps (LPs) detected in a colorectal cancer (CRC) screening programme using a faecal immunochemical test (FIT) and to compare them with those of a previous guaiac-based faecal occult blood test (gFOBT) programme.

Design: Retrospective population-based study of all LPs detected in patients aged 50-74 years between 2015 and 2019 during FIT-positive colonoscopies within the screening programme organised in Alsace (France).

Results: Overall, 1256 LPs (8.5% malignant and 51.8% non-pedunculated) were detected by 102 community gastroenterologists in 1164 patients (one in 12 colonoscopies). Endoscopic resection rate was 82.7% for benign LPs (70.2% non-pedunculated, 95.2% pedunculated, p<0.001), varying from 0 to 100% depending on the endoscopist. It was correlated with endoscopist’s LP resection volume, not with adenoma detection rate. More than 50% of endoscopists did not refer patients to experienced endoscopists, resulting in unwarranted surgery in 60 to 90% of patients with benign LPs. The sensitivity of optical diagnosis of malignancy was 54% for non-pedunculated and 27% for pedunculated T1 CRCs. Endoscopic resection was curative for 4.3% of non-pedunculated and 37.8% pedunculated T1 CRCs. One surgery was avoided for 57 endoscopic submucosal dissections. Management practices did not vary significantly between the gFOBT and FIT periods.

Conclusion: Compared with current recommendations, there is tremendous room for improvement of community endoscopy practices for the diagnosis and management of LPs. Endoscopic resection is curative in 15.9% of T1 CRCs only. The benefit of endoscopic submucosal dissection is marginal in community practice.
INTRODUCTION

Colorectal cancer (CRC) is the second most common cancer in Europe (500,000 estimated cases in 2018) and the second leading cause of death from malignant disease, resulting in 243,000 estimated deaths in 2018 [1]. Most are preventable whatever the screening method used: faecal occult blood test (FOBT), flexible sigmoidoscopy, and colonoscopy and polypectomy are effective at reducing CRC incidence and mortality [2]. Many countries have thus launched CRC screening programmes.

Most colorectal polyps are small or diminutive and easily removed. Large (≥ 20 mm) polyps (LPs) are increasingly detected in FOBT-enriched colonoscopies, malignant in a non-negligible proportion of cases and challenging to remove endoscopically. Several guidelines have been recently published on colorectal polypectomy and management of LPs [3-6] along with systematic reviews and meta-analyses [7-9]. Some authors claim that all benign colorectal polyps can be removed by endoscopic resection (ER), using endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD) or hybrid techniques. In a meta-analysis of 50 studies, over 90% of LPs could be removed endoscopically by experienced endoscopists [8]. Population-based studies are far less optimistic, with referral rates for surgery of 21-22% for benign LPs [10,11]. In 2015, the US recommendations for quality indicators for colonoscopy proposed two research priorities concerning the management of LPs and the success rate of ER of non-pedunculated LPs in community practice [12]. In 2020, there is still no direct answer to these questions. An indirect disappointing answer is the high volume of surgery for benign colorectal polyps observed in several countries. In the US, they represented 25% of surgeries for colorectal neoplasia [13]. Yet, the pooled 1-month complication and mortality rates of surgery for benign polyps are 24% and 0.7%, respectively, significantly higher than those of ER (perforation 1.5%, bleeding 6.5%, mortality 0.08%) [8,14]. There is no data on the management of LPs in community practice and in population-based faecal immunochemical test (FIT) and colonoscopy screening programmes. Only two studies within guaiac-based FOBT (gFOBT) CRC screening programmes have been reported [10,11]. Precise data on the management and outcomes of LPs in an organised CRC screening programme are of utmost importance for transparent information of the invited population, all the more so since the invited population is asymptomatic and non-seeking, and the organised programme is supposed to offer an equally high-quality screening service to all individuals.
Our aim was to analyse presentation, management and outcomes of colorectal LPs detected in the French CRC FIT screening programme and to compare them with those of the previous gFOBT programme.

**METHODS**

We conducted a population-based retrospective observational study of prospectively collected data. We analysed data concerning all LPs detected from June 2015 to June 2019 in residents undergoing colonoscopy for a positive FIT within the CRC screening programme organised in Alsace, part of the French national programme. We further compared them with those concerning LPs detected between 2007 and 2014 in residents undergoing colonoscopy for a positive gFOBT.

**FOBT screening programmes**

A gFOBT CRC screening programme was initiated in 2003 in Alsace, a region in eastern France, 1.8 million inhabitants. Its design has been previously described [15,16]. People with serious illness, recent CRC screening or high CRC risk were excluded. Residents aged 50-74 years (0.57 million persons in 2018) were invited by mail every other year to participate. The gFOBT (Hemoccult II) was replaced by a quantitative FIT (OC-Sensor) in May 2015. The FIT positivity threshold was set at 30 µg haemoglobin per gram (µg/g) faeces so that the positivity rate would be 4 to 5%. People with a positive FOBT were referred for colonoscopy.

**Colonoscopies**

All certified endoscopists participated in the programme. As usual in France, colonoscopies were performed by gastroenterologists, generally with sedation/anaesthesia provided by an anaesthetist. The ER technique was left to the endoscopists’ discretion. Endoscopists were considered “experts” if they had ER success rates of LPs ≥ 90% and were regularly referred patients from other endoscopists. All colonoscopy and pathology reports were prospectively collected as part of routine practice, along with all data concerning resected polyps. The result of each colonoscopy was classified according to the worst-prognosis lesion.

**Colorectal polyps**

The size of each polyp was determined in most cases according to the pathology report, or failing that, from the endoscopist’s evaluation recorded in the colonoscopy report. The pathological examination of detected polyps was performed as usual, almost always by community general pathologists. In situ
and intramucosal carcinomas (categories 4.2 and 4.4 in the revised Vienna classification) were classified as high-grade dysplasia [17]. T1 CRC (malignant polyp) was defined as carcinoma invading the submucosa through the muscularis mucosa, but not beyond (Vienna 5). T1 CRCs were considered superficial when submucosal invasion was ≤ 1000 microns and deep invasive when it was > 1000 microns. They were divided in T1 CRCs with low risk of lymph node metastasis (LNM), i.e. with submucosal invasion ≤ 1000 microns without lymphovascular involvement, tumour budding and poor differentiated component, and high-risk T1 CRCs in the other cases (> 1000 microns, lymphovascular involvement, tumour budding and/or poor differentiation) [3]. In case of several LPs in a single patient, the management of the worst-prognosis lesion was considered (per patient analysis). The colonoscopy and pathology reports of all malignant polyps were further analysed concerning the use of any Paris, Kudo or NICE classifications, the description of an optical suspicion of malignancy, the resection technique, the outcomes of resection (success, i.e. complete ER, or failure), the number of pieces (en bloc vs piecemeal resection), and the pathology risk factors for LNM. The proximal colon was defined as proximal to the splenic flexure, splenic flexure being excluded.

Statistical methods

Quantitative variables were expressed using mean and standard deviation (SD) while categorical variables were expressed as numbers and percentages with 95% confidence intervals (95% CI) using the binomial distribution. The Chi² test was used to test for statistical significance by comparisons of proportions. Student’s t test was used to compare difference in group means. All statistical tests were 2-sided. The significance threshold was set at 0.05. Statistical analysis was performed using Excel 2013 (Microsoft).

Ethical approval

Formal ethical approval was not required because it was considered a non-interventional study by the Est IV ethics committee (routinely collected data for the purposes of quality assurance within the screening programme).

RESULTS

Colonoscopies and polyps

A total of 13,633 colonoscopies were performed in 13,624 individuals by 102 endoscopists, including four experts (flow chart fig. 1). Overall, 22,933 polyps were removed (table 1). Among them, 1256 LPs
(5.5%) were managed in 1164 patients (mean age 63.3 years; SD 6.7; 67.7% men) and analysed by 38 pathologists. The positive predictive value (PPV) of FIT for LPs was 8.5% [95% CI 8.1-9.0] (fig 1). Their characteristics are presented in table 2. Most measured 20-29 mm (64.3%). Half were non-pedunculated (51.8%) and situated in the distal colon (52.4%). The overall rate of T1 CRCs was 8.5%.

It increased significantly with polyp size (p<0.001) (table 1), non-pedunculated shape (10.8% vs 6.1% for pedunculated polyps, p=0.003) and distal location (17.3% in rectum, 8.9% in sigmoid colon and 5.4% in left and proximal colon, p<0.001). In comparison with pedunculated LPs, non-pedunculated LPs were significantly larger, more often proximal, with high-grade dysplasia or malignancy, with morphological features suggestive of malignancy, and biopsied (table 2).

**Management of pedunculated polyps**

Overall, 563 individuals harboured pedunculated LPs. Among them, 10 (1.7%) had morphological features suggestive of malignancy, were actually pT1 CRCs, and were all managed surgically (fig 2a). Among the other 553 individuals, with LPs initially assessed as benign, 38 (6.9%) were managed surgically (fig 2b). They harboured 27 pT1 CRCs, so that the sensitivity and negative predictive value (NPV) of the optical diagnosis of T1 CRC were 27.0% [95% CI 12.7-41.3] and 95.1% [95% CI 93.3-96.9] (table 2).

**Management of non-pedunculated polyps**

Overall, 601 individuals harboured non-pedunculated LPs. Among them, 68 (11.3%) had morphological features suggestive of malignancy and 38 were actually T1 CRCs. Of them, 57 (83.8%) were finally managed surgically (fig 2c). Among the other 533 individuals, 168 (31.5%) were managed surgically (fig 2d). They harboured 32 T1 CRCs, so that the sensitivity and NPV of the optical diagnosis of T1 CRC were 54.3% [95% CI 42.6-66.0] and 94.0% [95% CI 92.0-96.0] (table 2).

**Endoscopic management**

The overall success rate of ER of benign LPs was 82.7% [95% CI 80.3-84.9]: at initial colonoscopy (67.4%) or during a second procedure, performed by the same endoscopist (7.6%) or another one (7.8%). It was 95.2% [95% CI 93.4-97.1] for pedunculated LPs and 70.2% [95% CI 66.4-74.1] for non-pedunculated LPs (p<0.001) (table 2). It increased significantly from 78.3% in 2015-2016 to 85.9% in 2017-2018 (p=0.002). It varied from 0 to 100% according to the endoscopist (mean 68.2%, SD 29.9%, median 72.0%). It was 90 to 100% in 24.8% of endoscopists and < 80% in 58.4% of them. It was 91.3% for “expert endoscopists” (91.8% for first-line and 90.9% for referral colonoscopies). There was
no significant correlation between ER success rate of benign LPs and adenoma detection rate (ADR), mean number of adenomas per colonoscopy, proximal serrated lesion detection rate and annual colonoscopy volume of the endoscopist (data not shown; the overall ADR was 58.6%, from 28.6% to 78.6% depending on the endoscopist). By contrast, 30 endoscopists managing annually ≥ 4 LPs had an ER success rate significantly higher than those managing < 4 (80.6% vs 63.5%, p=0.01). Overall, 85 patients (7.3%) were referred to an expert endoscopist. Referral rate to another more experienced endoscopist varied from 0 to 100% depending on the endoscopist. Among 59 endoscopists having an ER success rate < 80%, 54.4% did not refer any patient (likewise for 70.6% of 17 endoscopists having an 80-90% ER success rate). ESD was performed in 16 cases (2.7% of non-pedunculated LPs) and hybrid technique in 6 cases (1.0%), for benign LPs in 21 cases (95.5%). ESD or hybrid technique were en bloc in 16 (72.7%) cases.

**Surgery**

The characteristics of patients and LPs managed surgically are presented in table 3, in comparison with those managed endoscopically. The reasons for surgery, from the outset or secondarily, are detailed in table 4.

**Malignant polyps**

Of 735 CRCs, 232 (31.6%) were T1 CRCs, 107 of them being LPs. The endoscopist described polyp morphology using one of Paris, Kudo or NICE classifications in 13.3% of the colonoscopy reports. Endoscopic biopsies were performed in 56.2% of cases, the result of which being: absence of neoplasia (3.4%), low-grade dysplasia (28.8%), high-grade dysplasia (27.1%), in situ carcinoma (17.0%) and invasive carcinoma (23.7%). LP location was marked in 32 (30%) cases, by tattooing in two cases and by clipping in 30 cases. An ER was performed in 53 (49.5%) cases, 60.4% for 20-29 mm T1 CRCs and 39.6% for ≥ 30 mm T1 CRCs (p = 0.04), 78.4% for pedunculated T1 CRCs and 34.3% for non-pedunculated T1 CRCs (p<0.001). ER was en bloc in 49.1% of cases. Stage of T1 CRC (high vs low risk) was not significantly different between those initially assessed as benign or malignant, whatever their shape.

The pathology report was complete, analysing all risk factors for LNM, in 56.6% of cases of ERs (Sm or Haggitt stage 79% (30% in case of surgery), differentiation degree 98%, lymphovascular invasion status 91%, tumour budding status 77%, deep margin status 94%). It was Sm1 or Haggitt 1 or 2 in 19 (45.2%) cases. The reason for classifying 31 non-pedunculated LPs as high-risk T1 CRCs was Sm > 1.
in 19 (61.3%) cases, deep resection margin involved or not evaluable in seven (22.6%), and other risk factors (poor differentiation, budding or lymphovascular invasion) in five (16.1%). Among 24 non-pedunculated T1 CRCs removed endoscopically, an EMR was performed in 23 cases and an ESD in one case optically suspicious for malignancy. ER was en bloc in eight (33.3%) cases. Of 70 non-pedunculated T1 CRCs, 11 (15.7%) were Sm1, six of them (two in the recto-sigmoid, three optically suspicious for malignancy) being low-risk and > 25 mm, candidates for ESD (0.5% of all patients, one of 57 [95% CI 27-156] non-pedunculated LPs > 25 mm). In all, ER was curative in 17 (15.9%; 95% CI 9.5-24.2) patients, three (4.3%; 95% CI 0.9-12.0) with non-pedunculated T1 CRCs and 14 (37.8%; 95% CI 22.5-55.2) with pedunculated ones. Overall, one (1.9%) patient had surgery because of doubt on R0 resection linked to uncertain pathology related to piecemeal EMR.

Comparison between FIT and gFOBT periods (table 5)

Despite a positivity rate during the FIT period twice that of the gFOBT period, the PPV of FIT for LPs was slightly but significantly higher than that of gFOBT (8.5% vs 7.7%, p=0.02). There was no significant difference in overall rates of endoscopic and surgical management between the two periods.

DISCUSSION

This is the first population- and community-based study about LPs to be published, and the first embedded in an organised CRC screening programme with FIT. Compared with current recommendations, our results indicate that there is a tremendous amount of room for improving community endoscopy practices for the diagnosis and management of LPs in the French CRC screening programme [3-6].

FIT is the CRC screening tool having the highest advanced neoplasia yield. The number of LPs detected annually by our FIT screening programme was 334, almost half (43.5%) of all LPs detected in Alsace, estimated at 769, as FIT-positive colonoscopies represented 8.3% of all colonoscopies, and assuming PPVs of 8.5% and 1% for FIT-positive and non-FIT colonoscopies, respectively [18,19]. The LP detection rate was 4.2 per 1000 persons screened with FIT, almost three times that of gFOBT screening (1.5 per 1000). Endoscopists had to manage an LP in one of every 12 FIT-positive patients referred for colonoscopy, i.e. 8 to 10 times more frequently than in colonoscopy screening programmes in Austria (1/94) or Poland (1/113) [18,19].
Our rate of ER of benign LPs was similar to those observed in the English Bowel Cancer Screening programme (BCSP) and in Brittany [10,11]. It was 46.9% at detection, intermediate between rates observed in the English BCSP (64.8%) and in non-BCSP patients (34.2%) (p=0.001) [20]. The ER rate for benign LPs was < 80% for almost 60% of our endoscopists. Even though ER rates have improved slightly in recent years in Alsace, they remain heterogeneous and lower in community-based studies than in expert series [8]. This leads to a non-negligible volume of surgeries for benign colorectal polyps [13,21], avoidable in 32% to 74% of cases if patients had been referred to expert endoscopists [14]. Surgery was definitely unwarranted in more than 60% of our benign LP patients, i.e. all those with pedunculated LPs and non-pedunculated LPs measuring 20 to 35 mm. It can even be reasonably stated that all surgeries performed for benign LPs are unwarranted in the absence of prior ER failure by an experienced endoscopist. Unfortunately, despite the higher morbidity-mortality rate of surgical resection [8,14], the majority (65.3%) of non-expert endoscopists referred their patients to a surgeon rather than to an experienced endoscopist. Moreover, screening programmes reports almost never mention the rate of referral to experienced endoscopists. It reached 7.3% in our FIT programme, more than five times higher than in Brittany (1.3%) [11].

The US guidelines “suggest measuring and reporting the proportion of patients referred to surgery for benign colorectal lesion management” [5]. This is a conditional recommendation, which means that “patient values and preferences might play a larger role than the existence or quality of evidence”. Yet, undoubtedly, almost all informed patients, caregivers, policy-makers and funders would consider surgery unacceptable for a benign LP that could be removed endoscopically in > 90% of cases by an experienced endoscopist. This would imply an assessment of individual endoscopist’s performance level. For this we would advise measuring the endoscopist’s ER rate for benign LPs. The rate of referral to surgery should not be used because it is actually a combination of two indicators: the ER rate and the rate of referral to an experienced endoscopist. Only the first indicator evaluates the endoscopist’s polypectomy competency, whereas the second one reflects the endoscopist’s behaviour when encountering an LP exceeding self-perceived LP ER competency. At the present time, this second indicator is too low, meaning that referral to experienced endoscopists has to be encouraged. By contrast, the proportion of patients referred to surgery for benign colorectal lesion management should be added to the existing quality indicators of CRC screening programmes, routinely measured and reported. This important parameter is almost never specified, but was 1.7% (95% CI 1.4-1.9)
overall (all sizes polyps) and 17.3% (95% CI 15.0-19.6) for LPs (4.8% for pedunculated LPs) in our FIT programme. It decreased significantly in Alsace for non-pedunculated LPs initially assessed as benign from 33.6% in 2015-16 to 24.0% in 2017-18 (p= 0.02), compared with the 34.3% in 2006-2009 in the English gFOBT BCSP [10]. There is today no established benchmark. The ER rate of benign LPs varied dramatically between endoscopists and was not correlated with ADR, proximal serrated lesion detection rate, or annual colonoscopy volume. Likewise, a previous study did not find any correlation between polypectomy competency and ADR or withdrawal time [22]. By contrast, the ER rate for endoscopists managing a high volume of LPs (≥ 4 per year) was 80.6%, significantly higher than that of low-volume endoscopists (63.5%, p=0.01). The existence of a volume threshold correlated with better outcomes is well demonstrated for other sophisticated interventional procedures, such as endoscopic retrograde cholangiopancreatography [23].

The ESGE and US guidelines recommend that “large sessile and laterally spreading or complex polyps should be removed by an appropriately trained and experienced endoscopist” [3,5]. Given the high incidence of LPs in FIT-positive colonoscopies (one in 12 colonoscopies) and the insufficient rate of referral to experienced endoscopists, one might wonder whether FIT-positive colonoscopies should be performed by accredited gastroenterologists only, as in English and Dutch BCSPs. Likewise, given the difficulties of interpretation, the moderate performances of community pathologists, and the decisional challenge, i.e. the indication (or not) for adjuvant surgery, endoscopically-removed T1 CRCs should be analysed, or at least reviewed, by gastrointestinal expert pathologists, as recommended by the ESGE [3].

The use of Paris, Kudo or NICE classifications was marginal in comparison with current guidelines [3-6]. However, given their moderate interobserver agreement among international Western experts, their use is questionable in daily practice [24]. The same is true for the optical diagnosis of malignancy, which should allow an optimal management of LPs based on personalised ER technique adapted to optical diagnosis of histology. Malignancy (i.e. sub-mucosal invasion) was suspected in only one half of non-pedunculated T1 CRCs and one-quarter of pedunculated ones. These results are better or similar to those obtained by screening-certified endoscopists in the Dutch BCSP (21.1% [25] and 39.1% [26]) and by Dutch expert endoscopists for non-pedunculated LPs (78.7%) [27]. In any case, we are far from the ideal situation where endoscopists would be able to predict accurately the absence of malignancy and perform EMR (piecemeal if necessary), to estimate a non-negligible risk of
superficial malignancy (non-granular pseudodepressed or granular nodular mixed type with macronodule) and perform en bloc EMR or ESD, and to diagnose deep invasive cancer to refer for surgery. For the moment, the NPV of optical diagnosis of T1 CRC was around 95%, enough to propose systematically an EMR for LPs without suspected malignancy. Likewise, for LPs with suspected malignancy, since the ER of high-risk T1 CRCs has no deleterious effect on long-term outcomes [28], EMR could be systematically attempted as first-line treatment, adapting the ultimate treatment to the pathology analysis of the resected specimen. Our results confirm that biopsy samples are far from sufficient to accurately diagnose LP malignancy and should not be used to choose the adequate resection technique. In any case, optical diagnosis of lymphovascular invasion, tumour budding and poor differentiation, which were the only reason for classifying LPs as high-risk T1 CRCs in 16% of cases, seems impossible. The usefulness of the CONECCCT table, a simple, mixed diagnostic and therapeutic classification system designed to improve histological prediction and choose the best therapeutic strategy for each lesion subtype, remains to be demonstrated [29].

At most 0.5% of all LPs, one out of 57 non-pedunculated LPs, would have benefitted from ESD (six low-risk T1 CRCs ≥ 25 mm). Overall, our results bring further community-based evidence demonstrating the marginal role of ESD for colorectal lesions. The number of LPs needed to be treated by ESD to avoid one surgery was 16 in a review of ESDs performed in tertiary care centres [30]. In our study, the pathologist was unsure about the resection margin (R0) in only 1 of 53 (1.9%) LPs, leading to salvage surgery. In most cases, adjuvant surgery was motivated by histological LNM risk factors, such as Sm invasion > 1000 microns (61%), deep resection margin involved or not evaluable (23%), and/or lymphovascular invasion, tumour budding or poor differentiation (16%). ESD enables a more precise pathology diagnosis of the depth of invasion and the margin status than piecemeal EMR as there is less fragmentation and fewer cauterization artefacts. However, piecemeal EMR does not prevent all pathology diagnoses, although the exact rate of missed information due to piecemeal EMR is not known [31]. A randomised trial comparing piecemeal EMR and ESD is needed to determine whether the rates of T1 CRCs Sm1, R0, lymphovascular invasion and budding are different. It could be used to assess indirectly the histological information lost by piecemeal resection.

Today, ESD has a limited place for colorectal lesions, virtually nil for benign-appearing non-pedunculated LPs (one surgery avoided for 89 ESDs), and requires further evaluation for non-pedunculated LPs suspicious of malignancy (1 surgery avoided for 9 ESDs). Overall, we would state
that 1) endoscopists encountering LPs they are unable to remove endoscopically personally must refer their patients to experienced endoscopists, not to surgeons, and 2) experienced endoscopists should remove these LPs endoscopically using the ER method they do best, EMR, ESD or hybrid technique. The risk of malignancy was three-fold and two-fold higher for LPs located in the rectum and sigmoid respectively compared with the rest of the colon. This observation is in line with previous studies [32,33] and probably linked with the clinico-pathological and molecular differences between proximal, distal and rectal CRCs [34]. It suggests that appropriate treatment might be different between recto-sigmoid LPs and those in a more proximal location. For example, ESD could be initially restricted to rectal LPs (as suggested by the ESGE [4]), and eventually sigmoid LPs, while waiting for a demonstration of its interest in the rest of the colon.

Overall, 8.5% of our LPs were T1 CRCs (9.3% of them N1) and 15.9% of them were cured by ER, rates in line with those of other series (16.3% of 312 patients in a French population-based study [33,35]. These rates were significantly lower in pedunculated LPs (6.1%, 5.4% and 37.8%, respectively) than in non-pedunculated LPs (10.8%, 11.4% and 4.3%, respectively).

In addition to the fact that it was a large population- and community-based study and the first performed in an organised CRC screening programme with FIT, other strengths include that data were prospectively collected in a high-quality database. Our study is not without weaknesses. The main is the retrospective nature of the study. The size measurement was approximate in most cases, so that a few LPs measuring around 20 mm could have been wrongly included or excluded in the study. We had no information about subtypes of laterally spreading tumours and use of advanced endoscopic imaging, such as Narrow Band Imaging (NBI). The ER technique could be analysed for malignant polyps only. We did not assess the performances of the optical diagnosis between low-risk and high-risk T1 CRCs, and between superficial and deep invasive T1 CRCs. The Sm stage was almost never specified by pathologists in case of surgery, so that it was impossible to compare the invasiveness of T1 CRCs between those removed endoscopically and surgically. There was no centralised histological reviewing of T1 CRCs. The adverse events of both endoscopic and surgical treatments have not yet been analysed. Nevertheless, this analysis in a population- and community-based setting is of utmost interest for transparent information of invited populations, caregivers and funders and will be the subject of a separate article. In any case, the higher morbidity and mortality of surgery over endoscopy...
is now well demonstrated [10,11,14]. Last, we did not analyse late follow-up and the occurrence of residual or recurrent neoplasia.

**Conclusion**

In the French CRC screening programme with FIT, only three out of four LPs were cured endoscopically, four out of five benign LPs and one out of six malignant LPs. Polypectomy competency was notably endoscopist dependent, correlated with LP size, but not with colonoscopy volume and detection ability. Between 60% and 90% of surgeries could have been avoided if endoscopists with low LP resection volumes and/or lesser polypectomy competency had referred their patients with LPs they considered unresectable to experienced endoscopists instead of surgeons. The benefit offered by ESD for the management of colorectal LPs is marginal in a population-based community-based setting, estimated at one surgery avoided for 57 ESDs performed.

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FIGURES

Figure 1: Flow Chart

Figure 2a: Management of pedunculated large polyps optically suspicious for malignancy (per patient analysis)

Figure 2b: Management of pedunculated large polyps optically assessed as benign (per patient analysis)

Figure 2c: Management of non-pedunculated large polyps optically suspicious for malignancy (per patient analysis)

Figure 2d: Management of non-pedunculated large polyps optically assessed as benign (per patient analysis)
REFERENCES

1 Ferlay J, Colombet M, Soerjomataram I, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. *Eur J Cancer* 2018;103:356-87.

2 Rex DK, Boland CR, Dominitz JA, et al. Colorectal Cancer Screening: Recommendations for Physicians and Patients From the U.S. Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2017;153:307-323.

3 Ferlitsch M, Moss A, Hassan C, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy* 2017;49:270-297.

4 Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2015;47:829-54.

5 Kaltenbach T, Anderson JC, Burke CA, et al. Endoscopic Removal of Colorectal Lesions—Recommendations by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2020;158:1095-1129.

6 Rutter MD, Chattree A, Barbour JA, et al. British Society of Gastroenterology/Association of Coloproctologists of Great Britain and Ireland guidelines for the management of large non-pedunculated colorectal polyps. *Gut* 2015;64:1847-73.

7 Belderbos TD, Leenders M, Moons LM, et al. Local recurrence after endoscopic mucosal resection of nonpedunculated colorectal lesions: systematic review and meta-analysis. *Endoscopy* 2014;46:388-402.

8 Hassan C, Repici A, Sharma P, et al. Efficacy and safety of endoscopic resection of large colorectal polyps: a systematic review and meta-analysis. *Gut* 2016;65:806-20.

9 Russo P, Barbeiro S, Awadie H, et al. Management of colorectal laterally spreading tumors: a systematic review and meta-analysis. *Endosc Int Open* 2019;7:E239-E259.

10 Lee TJ, Rees CJ, Nickerson C, et al. Management of complex colonic polyps in the English Bowel Cancer Screening Programme. *Br J Surg* 2013;100:1633-9.

11 Le Roy F, Manfredi S, Hamonic S, et al. Frequency of and risk factors for the surgical resection of non-malignant colorectal polyps: a population-based study. *Endoscopy* 2016;48:263-70.
12 Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. *Gastrointest Endosc* 2015;81:31-53.

13 Peery AF, Cools KS, Strassle PD, et al. Increasing Rates of Surgery for Patients With Nonmalignant Colorectal Polyps in the United States. *Gastroenterology* 2018;154:1352-1360.

14 de Neree Tot Babberich MPM, Bronzwaer MES, Andriessen JO, et al. Outcomes of surgical resections for benign colon polyps: a systematic review. *Endoscopy* 2019;51:961-72.

15 Denis B, Ruetsch M, Strentz P, et al. Short-term outcomes of the first round of a pilot colorectal cancer screening programme with guaiac based faecal occult blood test. *Gut* 2007;56:1579-84.

16 Denis B, Gendre I, Perrin P. Participation in four rounds of a French colorectal cancer screening programme with guaiac faecal occult blood test: a population-based open cohort study. *J Med Screen* 2015;22:76-82.

17 Dixon MF. Gastrointestinal epithelial neoplasia: Vienna revisited. *Gut* 2002;51:130-131.

18 Ferlitsch M, Reinhart K, Pramhas S, et al. Sex-specific prevalence of adenomas, advanced adenomas, and colorectal cancer in individuals undergoing screening colonoscopy. *JAMA* 2011 28;306:1352-8.

19 Wieszczy P, Kaminski MF, Franczyk R, et al. Colorectal Cancer Incidence and Mortality After Removal of Adenomas During Screening Colonoscopies. *Gastroenterology* 2020;158:875-883.

20 Dattani M, Crane S, Battersby NJ, et al. Variations in the management of significant polyps and early colorectal cancer: results from a multicentre observational study of 383 patients. *Colorectal Dis* 2018;20:1088-96.

21 Bronzwaer MES, Koens L, Bemelman WA, et al. Volume of surgery for benign colorectal polyps in the last 11 years. *Gastrointest Endosc* 2018;87:552-561.

22 Duloy AM, Kaltenbach TR, Keswani RN. Assessing colon polypectomy competency and its association with established quality metrics. *Gastrointest Endosc* 2018;87:635-644.

23 Keswani RN, Qumseya BJ, O'Dwyer LC, Wani S. Association Between Endoscopist and Center Endoscopic Retrograde Cholangiopancreatography Volume With Procedure Success and Adverse Outcomes: A Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol* 2017;15:1866-1875.

24 van Doorn SC, Hazewinkel Y, East JE, et al. Polyp morphology: an interobserver evaluation for the Paris classification among international experts. *Am J Gastroenterol* 2015;110:180-7.
25 Meulen LWT, van de Wetering AJP, Debeuf MPH, et al. Optical diagnosis of T1 CRCs and treatment consequences in the Dutch CRC screening programme. *Gut* 2020 Jan 14. [Epub ahead of print]

26 Vleugels JLA, Koens L, Dijkgraaf MGW, et al. Suboptimal endoscopic cancer recognition in colorectal lesions in a national bowel screening programme. *Gut*. 2019 Dec 10. [Epub ahead of print]

27 Backes Y, Schwartz MP, Ter Borg F, et al. Multicentre prospective evaluation of real-time optical diagnosis of T1 colorectal cancer in large non-pedunculated colorectal polyps using narrow band imaging (the OPTICAL study). *Gut* 2019;68:271-279.

28 Overwater A, Kessels K, Elias SG, et al. Endoscopic resection of high-risk T1 colorectal carcinoma prior to surgical resection has no adverse effect on long-term outcomes. *Gut* 2018;67:284-290.

29 Fabritius M, Gonzalez JM, Becq A, et al. A simplified table using validated diagnostic criteria is effective to improve characterization of colorectal polyps: the CONECCT teaching program. *Endosc Int Open* 2019;7:E1197-E1206.

30 Fuccio L, Repici A, Hassan C, et al. Why attempt en bloc resection of non-pedunculated colorectal adenomas? A systematic review of the prevalence of superficial submucosal invasive cancer after endoscopic submucosal dissection. *Gut* 2018;67:1464-1474.

31 Pioche M, Rivory J, Jacques J. Colorectal endoscopic submucosal dissection for all LSTs: histological information loss due to piecemeal EMR is no longer acceptable. *Endosc Int Open* 2019;7:E1195-E1196.

32 Burgess NG, Hourigan LF, Zanati SA, et al. Risk Stratification for Covert Invasive Cancer Among Patients Referred for Colonic Endoscopic Mucosal Resection: A Large Multicenter Cohort. Gastroenterology 2017;153:732-742.

33 Bogie RMM, Veldman MHJ, Snijders LARS, et al. Endoscopic subtypes of colorectal laterally spreading tumors (LSTs) and the risk of submucosal invasion: a meta-analysis. *Endoscopy* 2018;50:263-282.

34 Li FY, Lai MD. Colorectal cancer, one entity or three. *J Zhejiang Univ Sci B* 2009;10:219-29.

35 Barel F, Cariou M, Saliou P, et al. Histopathological factors help to predict lymph node metastases more efficiently than extra-nodal recurrences in submucosa invading pT1 colorectal cancer. *Sci Rep* 2019;9:8342.
| Polyp size (mm) | 0-9    | 10-19  | 20-29  | 30-39  | ≥ 40   |
|----------------|--------|--------|--------|--------|--------|
| Total number (%) | 17140 (74.7) | 4537 (19.8) | 807 (3.5) | 287 (1.3) | 162 (0.7) |
| Number of malignant polyps (%) | 15 (0.1) | 97 (2.1) | 53 (6.6) | 27 (9.4) | 27 (16.7) |
Table 2: Characteristic features and management of large polyps during the faecal immunochemical test period

| POLYP CHARACTERISTICS | Pedunculated | Non-pedunculated | p   |
|-----------------------|--------------|------------------|-----|
|                       | number (%)   | number (%)       |     |
| POLYP CHARACTERISTICS | 606 (48.2)   | 650 (51.8)       |     |
| Size                  | <0.001       |                  |     |
| 20 – 29 mm            | 484 (79.9)   | 324 (49.8)       |     |
| 30 – 39 mm            | 96 (15.8)    | 190 (29.2)       |     |
| >= 40 mm              | 26 (4.3)     | 136 (20.9)       |     |
| Location *            | <0.001       |                  |     |
| Rectum                | 63 (10.4)    | 116 (17.9)       |     |
| Distal colon          | 473 (78.0)   | 184 (28.4)       |     |
| Proximal colon        | 70 (11.6)    | 348 (53.7)       |     |
| Histology             | <0.001       |                  |     |
| Conventional adenoma  | 595 (98.2)   | 603 (92.8)       |     |
| Sessile serrated adenoma/polyp | 2 (0.3)   | 27 (4.2)       |     |
| Hyperplastic          | 2 (0.3)      | 4 (0.6)          |     |
| Non-adenomatous non-serrated | 7 (1.2) | 16 (2.5)       |     |
| Dysplasia             | <0.001       |                  |     |
| T1 CRC                | 37 (6.1)     | 70 (10.8)        |     |
| Low-risk T1 CRC       | 10 (27.0)    | 9 (12.9)         |     |
| **High-risk T1 CRC** | 22 (59.5) | 31 (44.3) |
|----------------------|-----------|-----------|
| **Unknown T1 CRC**   | 5 (13.5)  | 30 (42.9) |
| **High grade – pTis**| 154 (25.4)| 200 (30.8) |
| **Low grade**        | 408 (67.3)| 355 (54.6) |
| **No dysplasia**     | 7 (1.2)   | 25 (3.8)  |
| **Suspicious for T1 CRC** | 10 (1.7) | 71 (10.9) | <0.001 |

**Optical diagnosis of T1 CRC**

| **Sensitivity % [95% CI]** | 27.0 [12.7-41.3] | 54.3 [42.6-66.0] |
|-----------------------------|-------------------|------------------|
| **Specificity % [95% CI]**  | 100 [100-100]     | 94.4 [92.4-96.3] |
| **PPV % [95% CI]**          | 100 [100-100]     | 55.9 [44.1-67.7] |
| **NPV % [95% CI]**          | 95.1 [93.3-96.9]  | 94.0 [92.0-96.0] |

**Biopsy sample during colonoscopy**

|                  | 8 (21.6) | 51 (72.9) | <0.001 |
|------------------|----------|-----------|--------|

**PATIENT MANAGEMENT**

|                  | 563 (48.4) | 601 (51.6) |
|------------------|------------|------------|
| Individuals with benign large polyps | 526 (49.8) | 531 (50.2) |
| Individuals with T1 CRCs             | 37 (34.6)  | 70 (65.4)  |

**Endoscopic resection 1st attempt n (%)**

|                  | 474 (84.2) | 252 (41.9) | <0.001 |
|------------------|------------|------------|--------|

**Endoscopic resection 2nd attempt n (%)**

|                  | 41 (7.3)   | 124 (20.6) | <0.001 |
|------------------|------------|------------|--------|

**Same endoscopist**

|                  | 22 (3.9)   | 58 (9.7)   | <0.001 |
|------------------|------------|------------|--------|

**Other and expert endoscopist**

|                  | 19 (3.4)   | 66 (11.0)  | <0.001 |
|------------------|------------|------------|--------|

**Endoscopic resection (overall)**

|                  | 515 (91.5) | 376 (62.6) | <0.001 |
|------------------|------------|------------|--------|
| Category                                      | Value 1 | Value 2 | p-value |
|-----------------------------------------------|---------|---------|---------|
| Benign large polyps                           | 501 (95.2) | 373 (70.2) | <0.001 |
| T1 CRCs                                       | 14 (37.8) | 3 (4.3) | <0.001 |
| **En bloc endoscopic resection for T1 CRC**   | 18 (48.6) | 8 (11.4) | <0.001 |
| Surgery from outset                           | 32 (5.7) | 202 (33.6) | <0.001 |
| **Adjuvant surgery for high-risk T1 CRC**     | 15 (40.5) | 21 (30.0) | 0.3 |
| Surgery (overall)                             | 48 (8.5) | 225 (37.4) | <0.001 |

* Two missing data

CRC: colorectal cancer; NPV: negative predictive value; PPV: positive predictive value;
**Table 3**: Characteristics of patients and large polyps classified by final therapeutic modality (faecal immunochemical test period)

|                       | Endoscopy | Surgery | p   |
|-----------------------|-----------|---------|-----|
|                       | n (%)     | n (%)   |     |
| **Population**        |           |         |     |
| Number                | 891       | 273     | -   |
| Mean age (SD) years   | 63.0 (6.8) | 64.6 (6.2) | <0.001 |
| Men                   | 606 (68.0) | 182 (66.7) | 0.7  |
| **Polyps**            |           |         |     |
| Mean size (SD) mm     | 26.0 (7.7) | 33.72 (12.1) | <0.001 |
| Location              |           |         | <0.001 |
| Rectum                | 130 (14.6) | 44 (16.2) |     |
| Sigmoid               | 437 (49.1) | 63 (23.1) |     |
| Left and proximal colon | 323 (36.3) | 165 (60.7) |     |
| **Morphology**        |           |         | <0.001 |
| Pedunculated          | 515 (57.8) | 48 (17.6) |     |
| Non-pedunculated      | 376 (42.2) | 225 (82.4) |     |
| **Histology**         |           |         | 0.02 |
| Conventional adenoma  | 857 (96.2) | 261 (95.6) |     |
| Category                                | Count 1 | Count 2 |
|-----------------------------------------|---------|---------|
| Sessile serrated adenoma/polyp          | 21 (2.3)| 2 (0.7) |
| Non-serrated non-adenomatous            | 13 (1.5)| 10 (3.7)|

**Dysplasia**

| Category                        | Count 1 | Count 2 |
|---------------------------------|---------|---------|
| T1 high-risk CRC                | 5 (0.6) | 49 (17.9)|
| T1 low-risk CRC                 | 11 (1.2)| 7 (2.6) |
| T1 unknown risk CRC             | 1 (0.1) | 34 (12.5)|
| High-grade dysplasia            | 227 (25.5)| 105 (38.5)|
| Low-grade dysplasia             | 627 (70.4)| 74 (27.1)|
| Non-dysplastic                  | 20 (2.2) | 4 (1.5) |
**Table 4**: Reasons for surgery during the faecal immunochemical test period

|                          | Total      | Pedunculated | Non-pedunculated | p     |
|--------------------------|------------|--------------|------------------|-------|
| **From the outset**      | 202 (17.4) | 29 (5.2)     | 173 (28.8)       | <0.001|
| T1 CRC suspicion         | 51 (25.2)  | 5 (17.2)     | 46 (26.6)        | 0.3   |
| ER failure               | 8 (4.0)    | 0 (0)        | 8 (4.6)          | 0.2   |
| ER not attempted         | 142 (70.3) | 24 (82.8)    | 118 (68.2)       | 0.1   |
| Polyposis                | 1 (0.5)    | 0 (0)        | 1 (0.6)          | 0.7   |
| **Secondary**            | 71 (6.1)   | 19 (3.4)     | 52 (8.7)         | <0.001|
| Adjuvant surgery         | 39 (54.9)  | 16 (84.2)    | 23 (44.2)        | <0.01 |
| ER failure               | 29 (40.9)  | 3 (15.8)     | 26 (50.0)        | <0.01 |
| ER complication          | 3 (4.2)    | 0 (0)        | 3 (5.8)          | 0.5   |
| **Total surgery**        | 273 (23.5) | 48 (8.5)     | 225 (37.4)       | <0.001|

CRC: colorectal cancer; ER: endoscopic resection
Table 5: Presentation and management of large polyps during the two guaiac-based faecal occult blood test and faecal immunochemical test screening programmes

|                           | gFOBT 2007-2014 | FIT 2015-2019 | p     |
|---------------------------|-----------------|---------------|-------|
| **Population and colonoscopy results** |                 |               |       |
| Positivity rate           | 2.1%            | 4.6%          | < 0.001 |
| Colonoscopies n           | 13,952          | 13,624        | -     |
| Mean age (SD) years       | 62.0 (7.0)      | 62.5 (7.0)    | <0.001 |
| Men n (%)                 | 7764 (55.6)     | 8150 (59.8)   | <0.001 |
| Number of polyps (n per colonoscopy) | 14,410 (1.0)  | 22,933 (1.7) | -     |
| LPs n (%)                 | 1186 (8.2)      | 1256 (5.5)    | <0.001 |
| Positive predictive value for LPs | 1081/13952 (7.7)| 1164/13624 (8.5)| <0.001 |
| Number needed to endoscope to detect one LP | 12.9 | 11.7 | - |
| LP detection rate         | 1.5/1000 screened | 4.2/1000 screened | <0.001 |
| LPs' mean size (SD) mm    | 27.0 (9.7)      | 27.5 (9.3)    | 0.2   |
| T1 CRCs n (%)             | 113/1186 (9.5)  | 107/1256(8.5) | 0.1   |

**Management**

| Number of individuals | 1081 | 1164 | - |

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Table and text continued...
|                                |     |     |    |
|--------------------------------|-----|-----|----|
| Individuals with benign LPs    | 968 | 1057|    |
| Individuals with T1 CRCs       | 103 | 107 |    |
| Endoscopic resection 1<sup>st</sup> attempt n (%) | 710 (65.7) | 726 (62.4) | 0.1 |
| Endoscopic resection 2<sup>nd</sup> attempt n (%) | 130 (12.0) | 165 (14.2) | 0.1 |
| Endoscopic resection (overall)  | 840 (77.7) | 891 (76.5) | 0.5 |
| Benign LPs                     | 806/968 (83.3) | 874/1057 (82.7) | 0.7 |
| T1 CRCs                        | 34/103 (33.0) | 17/107 (15.9) | <0.01 |
| Surgery from outset            | 202 (18.7) | 234 (20.1) | 0.4 |
| Adjuvant surgery for high-risk T1 CRC | 39 (3.6) | 36 (3.1) | 0.5 |
| Surgery (overall)              | 241 (22.3) | 273 (23.5) | 0.5 |

CRC: colorectal cancer; FIT: faecal immunochemical test; gFOBT: guaiac-based faecal occult blood test; LP: Large polyp; SD: standard deviation.
13,624 individuals FIT+ colonoscopy

- 4,143 (30.4%) normal
- 7,696 (56.5%) polyps < 20 mm
- 8,746 (64.2%) polyps
- 735 (5.4%) cancers
- 1,057 (7.7%)* polyps ≥ 20 mm
- 107 (0.8%) pT1 ≥ 20 mm
- 628 (4.6%) cancers (108 pT1 < 20 mm)
- 1,164 (8.5%) polyps ≥ 20 mm benign and malignant

* 7 individuals harbour a small cancer pT1 and a large benign polyp
1st colonoscopy n = 10 individuals

Endoscopic resection
- 1st endoscopist n = 4 (40%)
- 2nd expert n = 1 (10%)

Secondary surgery
- adjuvant n = 4 (40%)
- endoscopic failure n = 1 (10%)

Total endoscopic resection 0 individual (0%)

Surgery from outset n = 5 (50%)

Total surgery 10 individuals (100%)
- 10 malignant
- 0 benign

Histology
All pT1 N0 CRCs
- 6 Sm >1/Haggitt >1-2 or High-risk
- 4 Sm not specified
1st colonoscopy n = 553 individuals

Endoscopic resection n = 529 (95.7%)
- 1st endoscopist: n = 484 (87.5%)
- 2nd endoscopist: n = 45 (8.2%) (17 by expert)

Secondary surgery
- adjuvant n = 12 (2.2%)
- endoscopic failure n = 2 (0.4%)

Total endoscopic resection 515 individuals (93.1%)
- 14 malignant
- 501 benign

Histology
- 27 (4.9%) pT1 CRCs
- 10 Sm1/Haggitt 1-2 low-risk
- 16 Sm>1 or high-risk
- 1 Sm not specified
- 2 pN1 - 11 pN0 – 14 Nx
- 526 benign polyps

Surgery from outset n = 24 (4.3%)

Total surgery 38 individuals (6.9%)
- 13 malignant
- 25 benign
1st colonoscopy n = 68 individuals

Endoscopic resection n = 21 (30.9%)
- 1st endoscopist n = 4 (5.9%)
- 2nd endoscopist n = 17 (25.0%) (11 by expert)

Surgery from outset n = 47 (69.1%)

Secondary surgery
- adjuvant n = 6 (8.8%)
- endoscopic failure n = 4 (5.9%)

Total endoscopic resection 11 individuals (16.2%)
- 2 malignant
- 9 benign

Histology
38 (55.9%) pT1 CRCs
- 5 Sm1 low-risk
- 14 Sm>1 or high-risk (1 M1)
- 19 Sm not specified
- 5 pN1 - 30 pN0 - 3Nx
30 benign polyps

Total surgery 57 individuals (83.8%)
- 36 malignant
- 21 benign
1st colonoscopy n = 533 individuals

Endoscopic resection n = 407 (76.4%)
1st endoscopist n = 250 (46.9%)
2nd endoscopist n = 157 (29.5%) (65 by expert)

Surgery from outset n = 126 (23.6%)

Secondary surgery
- adjuvant n = 17 (3.2%)
- endoscopic failure n = 22 (4.1%)
- perforation n = 3 (0.6%)

Total endoscopic resection 365 individuals (68.5%)
- 1 malignant
- 364 benign

Histology
- 32 (6.0%) pT1 CRCs
- 4 Sm1 low-risk
- 17 Sm>1 or high-risk
- 11 Sm not specified
- 3 pN1 - 26 pN0 - 3 Nx
501 benign polyps

Total surgery 168 individuals (31.5%)
- 31 malignant
- 137 benign