Evaluation of polypectomy quality indicators of large nonpedunculated colorectal polyps in a nonexpert, bowel cancer screening cohort

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GRAPHICAL ABSTRACT

Background and Aims: With the introduction of the national bowel cancer screening program, the detection of sessile and flat colonic lesions ≥20 mm in size, defined as large nonpedunculated colorectal polyps (LNPCPs), has increased. The aim of this study was to examine the quality of endoscopic treatment of LNPCPs in the Dutch screening program.

Methods: This investigation comprised 2 related, but separate, substudies (1 with a cross-sectional design and 1 with a longitudinal design). The first examined prevalence and characteristics of LNPCPs in data from the national Dutch screening cohort from February 2014 until January 2017. The second, with screening data from 5 endoscopy units in the Southern part of the Netherlands from February 2014 until August 2015, examined performance on important quality indicators (technical and clinical successes, recurrence rate, adverse event rate, and surgery referral rate). All patients were part of the national Dutch screening cohort.

Results: In the national cohort, an LNPCP was detected in 8% of participants. Technical and clinical success decreased with increasing LNPCP size, from 93% and 96% in 20- to 29-mm lesions to 85% and 86% in 30- to 39-mm lesions and to 74% and 81% in ≥40-mm lesions ($P < .001$; $P = .034$). The cumulative recurrence rate at 12 months increased with LNPCP size, from 9% to 22% and 26% in the respective size groups ($P = .095$). The adverse event rate was 5%. The overall surgical referral rate for noninvasive LNPCPs was 7%.

Conclusions: In this performance of 2 substudies, it was shown that quality parameters for endoscopic resection of large polyps in the Dutch screening cohort are not reached, especially in ≥30-mm polyps. Endoscopic resection of large polyps could benefit from additional training, quality monitoring, and centralization either within or between centers. (Gastrointest Endosc 2021;94:1085-95.)

(footnotes appear on last page of article)

One of the goals of the fecal immunochemical test (FIT)-based bowel cancer screening program (BCSP) is to prevent cancer by removing high-risk advanced colorectal neoplasia.[1] Large nonpedunculated colorectal polyps (LNPCPs), defined as sessile and flat colonic lesions ≥20 mm in size, are believed to be especially at risk of progression to cancer

and bear the risk of submucosal invasion, which increases with size. In addition, endoscopic resection is technically more challenging and associated with a higher risk of adverse events and recurrence.[2] With LNPCPs expected to account for a significant amount of care within screening programs, quality of care for these lesions is of great importance.

The Dutch BCSP is controlled on quality indicators such as the cecal intubation rate, Gloucester comfort scale, and adenoma detection rate to optimize the outcome of colonoscopy.[1,3] Until now, no performance indicators exist for the quality of polypectomy, whereas the need for such measures has been recognized in the field.[4,5] Quality of endoscopic care for LNPCPs can be described by 2 pillars: effectiveness of endoscopic resection, displayed by technical and clinical success rate, recurrence rate, performing surveillance colonoscopy, and referral to surgery, and safety of endoscopic care for LNPCPs, displayed by adverse event rate. Current evidence suggests there is still room for improvement regarding quality of endoscopic care for LNPCPs, because recurrence after EMR is significant,[6] compliance with surveillance guidelines is suboptimal,[7] and noninvasive LNPCPs are frequently referred for surgery.[8,9]

Although expert centers have reported their outcomes of EMRs performed on LNPCPs, little is known regarding these outcomes in a screening setting. In this performance of 2 substudies, we evaluated the quality of endoscopic care for LNPCPs in the Dutch BCSP. Main outcomes were technical and clinical success, recurrence rate, surveillance compliance, adverse event rate of endoscopic therapy, and surgery referral rate for LNPCPs.

METHODS

For this study, cross-sectional data of the Dutch screening registry were used to determine the LNPCP prevalence, supplemented by longitudinal, regional screening data for in-depth analysis. Within the Dutch BCSP, citizens aged 55 to 75 years are invited to perform a FIT once every 2 years. Participants with positive FIT results are invited for a screening colonoscopy. We included all screening colonoscopies performed from the onset of the screening program in February 2014 up to January 2017.[10] Nonscreening colonoscopies were excluded.

National registry

Within the national BCSP, endoscopists have to be certified for quality assurance purposes. Certification involves a minimum number of colonoscopies and polypectomies per year, achievement of predefined quality levels for colonoscopy (cecal intubation rate ≥90% and adenoma detection rate ≥20%), a mandatory e-learning module (including Paris classification practicing), and evaluation of polypectomy skills by live practice and videos.[3,11] Formal training in advanced polypectomy was nonexistent at that time. Registration of specific parameters is obligatory within the screening program. These parameters include colonoscopy characteristics (ie, Boston Bowel Preparation Score, cecal intubation rate, cecal withdrawal time, and inspection time) and endoscopic aspects of colorectal lesions (ie, size, location [proximal location was defined as proximal to the splenic flexure], Paris classification, predicted histology, and resection technique). These data are stored in a national information system, called ScreenIT.[10]

The national screening organization provided national screening data, consisting of the total number of index colonoscopies and the number of index colonoscopies with ≥1 LNPCP detected between February 2014 and January 2017. Of the latter, colonoscopy characteristics and endoscopic aspects were described. Conclusions regarding histology, as evaluated by accredited pathologists, were not available for individual polyps because of a lack of coupling of endoscopy reports and pathology data. Furthermore, because only index colonoscopies were collected within the national screening organization, endoscopic or surgical follow-up data were also not available.

Regional cohort

For evaluation of polypectomy quality indicators, follow-up data were needed of which the national cohort did not provide. Therefore, a prospective regional cohort of screening colonoscopies (part of the national registry) was used, containing the same parameters as the ScreenIT database. Patients were included if they had a screening colonoscopy between February 2014 and August 2015 in 1 of 5 endoscopy units in the Southern part of the Netherlands: Maastricht University Medical Center, Zuyderland Medical Center (2 locations), Maxima Medical Center Veldhoven, and Diagnostic Center Maastricht. None of these centers was a referral center. In addition to the colonoscopy parameters and polyp characteristics registered in the national cohort, data concerning patient characteristics (medical history and lifestyle factors), more detailed lesion characteristics (endoscopic, histopathologic), endoscopic or surgical therapy, and 3-year follow-up including surveillance endoscopies were collected. In contrast to the ScreenIT data, coupling of endoscopic to histopathologic findings at the patient and individual polyp level was warranted, providing the possibility of in-depth analysis.

The Medical Ethical Review Committee of the Maastricht University Medical Center (MEC 14-4-046) approved the study and waived the need for informed consent. The study is registered at the Dutch Trial Register (NTR4844).

Outcomes

The main outcomes were technical and clinical success, recurrence rate, surveillance compliance, adverse event rate, and surgery referral rate of LNPCPs. We calculated the size, morphology, site, and access (SMSA) score for every LNPCP,

with both easy and difficult accessibility, because this feature was not reported in our data. Hence, LNPCPs were categorized into SMSA score 3 (both calculated scores <12), SMSA scores 3 to 4 (lower score <12 and upper score ≥12) and SMSA score 4 lesions (both calculated scores ≥12).

Technical success was defined as a macroscopically complete resection during the first attempt, as judged by the endoscopist. Clinical success was defined as the absence of neoplasia 12 months after primary treatment. Clinical success included cases that never showed recurrence in these 12 months, but also cases that showed recurrence after 6 months, were treated successfully and showed no signs of neoplasia at the 12 month follow-up colonoscopy. Because of variation in surveillance intervals used in our regional cohort, we determined the recurrence rate after 6 and 12 months and after 3 years.

Recurrence was defined as all visible neoplastic tissue (size ≥1 mm) in and around (within 5 mm) the scar. The recurrence rate was calculated for all macroscopically complete, endoscopically resected LNPCPs and was cumulative (cumulative recurrence at 12 months included the lesions that showed recurrence at 12 months but also the lesions that showed recurrence at 6 months). In addition, recurrence rates after piecemeal and en-bloc EMR were determined after 12 months. Initial (macroscopically) complete resection was defined as complete resection of neoplastic tissue at the index colonoscopy without residual neoplastic tissue being present at the resection site.

Surveillance compliance was determined by comparing advised surveillance intervals with the recommended intervals in the applicable guidelines, namely the Dutch guideline colonoscopy surveillance[12] (2013) and the European Society for Gastroenterology postpolypectomy colonoscopy surveillance guideline[13] (2013). Surveillance intervals according to these guidelines were 4 to 6 months for piecemeal resection and 3 years for en-bloc R0 resection and serrated lesions.

Adverse events were divided into postpolypectomy syndrome (abdominal pain), direct postpolypectomy bleeding (identification of bleeding within 24 hours), delayed bleeding (symptoms of bleeding >24 hours after endoscopic therapy), and deep mural injury. Surgery referral rate was defined as the proportion of LNPCPs referred for surgery and was divided into primary and secondary surgery. Primary surgery was defined as surgical treatment without prior attempt at endoscopic resection. Secondary surgery was defined as surgery after prior endoscopic resection. Referral for surgery was performed without consultation of expert endoscopists.

Finally, experience and dedication of endoscopists was determined and association with technical success, and direct surgery referral was explored. Experienced endoscopists were defined as endoscopists with more than 10 years of experience, conforming to the definition used by Oka et al.[14] Dedicated endoscopists were defined as endoscopists who were executing advanced polypectomy programs in their center. Endoscopists were stratified according to their experience and dedication into 3 groups: nonexperienced, nondedicated endoscopists; an intermediate group, consisting of experienced, nondedicated endoscopists and nonexperienced, dedicated endoscopists; and experienced, dedicated endoscopists.

The performance on the different quality indicators within the Dutch screening program cohort was compared with benchmarks. These benchmarks were based on current evidence, including a systematic review evaluating endoscopic resection of large colorectal polyps, a systematic review evaluating local recurrence rates in large colorectal polyps, and the experience in the English BCSP.[2,6,15]

Furthermore, the prevalence, endoscopic appearance, and location of LNPCPs was evaluated. The prevalence of LNPCPs was calculated at the patient level and was defined as the proportion of patients presenting with 1 or more LNPCPs during index colonoscopy.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. (IBM Corp., Armonk, NY, USA). Baseline characteristics, recurrence rates, and surgical referral percentages were analyzed with descriptive statistics and are reported as proportions (%) for categorical variables and mean with standard deviation or median with interquartile range for numerical variables. To verify whether the regional cohort was a representative sample of the national cohort, the 1-sample t test was used for continuous measures and the χ^2 test for goodness of fit for categorical measures. One-way analysis of variance, Kruskal-Wallis, χ^2, or the Fisher exact test was used to compare groups within 1 cohort.

$P \leq .05$ was considered statistically significant. Although there was multiple testing of outcome data arising from individual patients, no corrections to P-values were made because the purpose of the research was not to test any specific hypotheses about quality but to describe important measures of quality and to highlight any potential differences. Therefore, all P-values are presented uncorrected for multiple testing and should be taken as descriptive only. Notwithstanding, it should be noted that with any nominally significant P-value in this report, except for where $P < .001$, correction for multiple testing by the method of Bonferroni would have removed the significance from that finding.

In case of missing data, complete case analysis was performed. To assess performance differences between various centers in the regional cohort, leave-1-out cross-validation analyses were performed for main outcome measures.

RESULTS

Prevalence of LNPCPs in the screening cohort

Patient and polyp characteristics of both the national and regional screening cohort are provided in Tables 1

TABLE 1. Patient characteristics in the national and regional cohort

	National cohort		Regional cohort	
	2014-2017	2014-2015	2014-2015	*P* value*
Overall patient characteristics	(n = 124,155)	(n = 68,471)	(n = 3085)	
Age, y	67.4 ± 5.0	68.0 ± 4.8	68.2 ± 5.4	.001 *.098*
Gender, female	49,502 (40)	27,328 (40)	1229 (40)	.944
No. LNPCP patients (prevalence)	9772 (8)	5513 (8)	282 (9)	.011 *.034*
2014	1910 (8)	1910 (8)	156 (10)	
2015	3603 (8)	3603 (8)	123 (8)	
2016	3964 (8)			
2017 (until February)	295 (7)			
LNPCP patient characteristics	(n = 9772)	(n = 5624)	(n = 282)	
Mean age, y (standard deviation)	67.8 (5.0)	68.1 (4.7)	68.5 (5.1)	.006 *.149*
Gender, female	3520 (36)	1976 (35)	99 (35)	.755
American Society of Anesthesiologists classification				
I			129 (46)	
II			141 (50)	
III			12 (4)	
IV			0	

Values are mean ± standard deviation or n (%) unless otherwise defined.
LNPCP, Large nonpedunculated colorectal polyp.
**P* values correspond to the comparison of the national cohort (2014-2017) vs the regional cohort, except values in italic, which correspond to the statistical comparison between the national cohort 2014-2015 and the regional cohort 2014-2015.

and 2. In the national screening cohort, 124,155 patients underwent a colonoscopy after a positive FIT, and the prevalence of LNPCP patients was 8%. A total of 11,130 LNPCPs were found, of which 5788 (52%) were located in the proximal colon. The median size of LNPCPs was 25.0 mm (interquartile range, 20-35), and 2053 (18%) were ≥40 mm in size. This subgroup of LNPCPs (≥40 mm) was evenly distributed over the proximal and distal colon (1039 vs 1014; 51% vs 49%) but mainly located in the rectosigmoid (882/2053; 43%) and right-sided colon segment (873/2053; 43%).

Comparison of the national and regional cohort on patient, polyp, and colonoscopy characteristics confirmed that the regional cohort was a representative sample of the national cohort (Tables 1 and 2). Although there were statistically significant differences in LNPCP prevalence, size, and morphology, these small differences were not considered clinically relevant.

Technical success rate of endoscopic therapy

Both in the national and regional cohort, approximately 30% of the lesions were not resected during index colonoscopy. In the national cohort, 1189 of 6203 (19%) of the 20- to 29-mm LNPCPs were not resected during the initial colonoscopy, whereas this was 1096 of 2873 (38%) and 1047 of 2054 (51%) for 30- to 39-mm and ≥40-mm LNPCPs, respectively ($P < .001$).

In the regional cohort, endoscopic therapy was performed in 266 of 332 LNPCPs (80%) (Fig. 1). Most LNPCPs (242/266; 91%) were resected by EMR, whereas 21 of 266 (8%) were resected by hot snaring and 3 of 266 (1%) by endoscopic submucosal dissection. Technical success was achieved in 231 of 266 cases (87%; 95% confidence interval [CI], 82-91). Technical success rates were similar across the different centers (mean, 87%; leave-1-out-analysis range, 83%-89%). Technical success decreased with increasing LNPCP size, with 126 of 135 (93%) in 20- to 29-mm, 56 of 65 (86%) in 30- to 39-mm, and 49 of 66 (74%) in ≥40-mm LNPCPs ($P = .001$). Technical success was higher in LNPCPs that were resected during the first encounter (211/238; 89%) compared with LNPCPs that were resected in a second colonoscopy (20/28; 71%; $P = .018$). Reasons for technical failure were non-lifting of the lesion and/or difficult accessibility of the lesion. Technically failed cases were managed by referral to another center (n = 6), referral for surgery (n = 12), and endoscopic follow-up with resection of the residual neoplastic tissue during 1 or multiple follow-up colonoscopies (n = 17).

Recurrence after endoscopic therapy (regional cohort)

In 152 cases, follow-up colonoscopy was performed after initial macroscopically complete resection (included

TABLE 2. LNPCP lesion and colonoscopy characteristics in the national and regional (Limburg) cohort

	National cohort (n = 11,130)*	Regional cohort (n = 332)*	*P* value
LNPCP lesion characteristics			
Median size, mm (interquartile range)	25.0 (20-35)	30.0 (20-40)	.012
Proximal location	5788 (52)	175 (53)	.811
Location			.067
Colon	8297 (75)	262 (79)	
Cecum/ascending colon	4016 (36)	117 (35)	
Rectum	2833 (25)	70 (21)	
Morphology			.004
Sessile	8107 (73)	267 (80)	
Flat	2904 (26)	65 (20)	
Unknown	83 (1)	0	
Paris classification			
Is		267 (80)	
IIa		45 (14)	
IIa+c		7 (2)	
IIb		7 (2)	
IIc		5 (2)	
IIc+a		1 (.3)	
SMSA score			
SMSA 3		139 (42)	
SMSA 3/4		96 (29)	
SMSA 4		97 (29)	
Index colonoscopy characteristics			
Boston Bowel Preparation Scale ≥6	10,696 (96)	275/282 (98)	.235
Cecal intubation rate	10,903 (98)	274/282 (97)	.315
Mean cecal withdrawal time,† min (standard deviation)	29.7 (18.0)	28.4 (14.8)	.160
Treatment strategy index colonoscopy			.661
Snare resection (with coagulation)	7746 (70)	226 (68)	
Biopsy sampling/not removed	3347 (30)	94 (31)	
Other‡	37 (.3)	2 (1)	
Histopathologic outcome§			
Serrated polyps¶		29 (9)	
Adenoma, low-grade dysplasia		187 (59)	
Adenoma, high-grade dysplasia		48 (15)	
Submucosal invasion		55 (17)	
Histology of adenomas			
Tubular histology		113 (48)	
Tubulovillous histology		112 (48)	
Villous histology		10 (4)	

Values are n (%) unless otherwise defined.

LNPCP, Large nonpedunculated colorectal polyp; *SMSA*, size, morphology, site, and access of a lesion (reflects the complexity for endoscopic treatment).

*These numbers indicate the total amount of LNPCPs found. This differs from the number of LNPCP patients as shown in Table 1 because of multiple LNPCP lesions per patient in some cases.

†The cecal withdrawal time includes the procedure time.

‡Other treatment strategies include cold snaring, endoloop, or resection by biopsy sampling.

§In the national cohort, histopathology cannot be linked to specific lesions. In the regional cohort, 319 of 332 LNPCP lesions were evaluated by the pathologist (the remainder were lost during colonoscopy).

¶Serrated polyps include hyperplastic lesions (n = 11), sessile serrated adenomas (n = 15), and traditional serrated adenomas (n = 3).

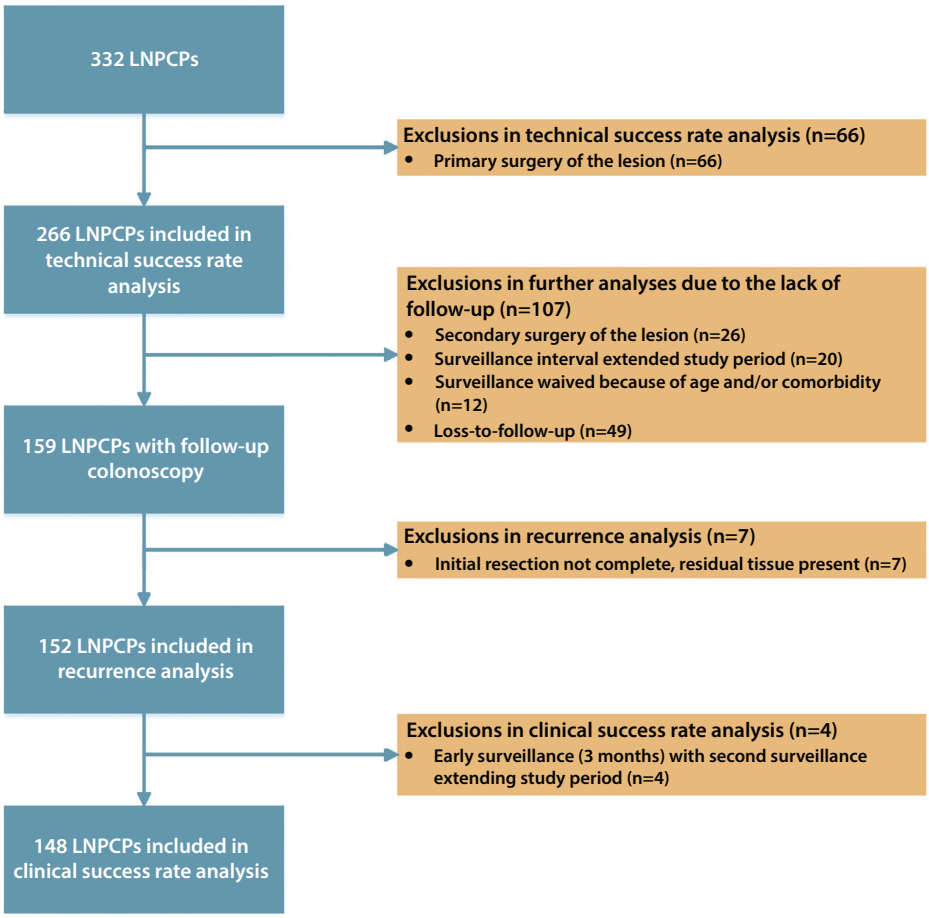

Figure 1. Flowchart of LNPCPs included in the quality indicator analyses in the regional bowel cancer screening program cohort. *LNPCP*, Large nonpedunculated colorectal polyp.

in recurrence analysis; Fig. 1). The cumulative recurrence rate in the regional cohort was 10% (15/152) after 6 months, 16% (24/152) after 12 months, and 19% (29/152) after 3 years (Fig. 2). After 12 months, the recurrence rate was 22% (21/94; 95% CI, 15-32) for piecemeal and 8% (3/38; 95% CI, 2-22) for en-bloc resection. The overall recurrence rate after 12 months increased with LNPCP size: 5 of 53 (9%) in 20- to 29-mm LNPCPs, 8 of 36 (22%) in 30- to 39-mm LNPCPs, and 11 of 43 (26%) in ≥40-mm LNPCPs ($P = .095$). No adjuvant treatment was performed to prevent recurrence.

Most recurrences at 12 months (22/24) were unifocal, smaller than 5 mm, and could be treated endoscopically. Six months after treatment of these recurrences, none showed additional recurrence. Two of 24 recurrences were interval carcinomas, treated surgically (Supplementary Table 1, available online at www.giejournal.org). Variation was seen between the centers regarding the recurrence rate (leave-1-out-analysis range, 4%-11% after en-bloc resection and 17%-24% after piecemeal resection) (Supplementary Table 2, available online at www.giejournal.org).

Clinical success rate of endoscopic therapy (regional cohort)

For clinical success rate analysis, 148 LNPCPs were included (Fig. 1). Clinical success was achieved in 129 of 148 cases (87%; 95% CI, 80-92). Clinical success decreased with increasing LNPCP size, with 61 of 65 (94%) in 20- to 29-mm, 33 of 39 (85%) in 30- to 39-mm, and 35 of 44 (80%) in ≥40-mm LNPCPs ($P = .078$). Clinical success was achieved in 115 of 133 LNPCPs (87%) resected during the first encounter and in 14 of 15 LNPCPs (93%) resected in a second colonoscopy ($P = .451$). In most cases, the reason for clinical failure was the absence of surveillance endoscopy and therefore no possibility to treat recurrence within the first 12 months. Again, variation between the centers was seen regarding the clinical success rate (mean, 87%; leave-1-out-analysis range, 85%-90%) (Supplementary Table 2).

Compliance with surveillance intervals (regional cohort)

In 210 of 332 cases, a surveillance interval was advised after endoscopic resection. The advised surveillance

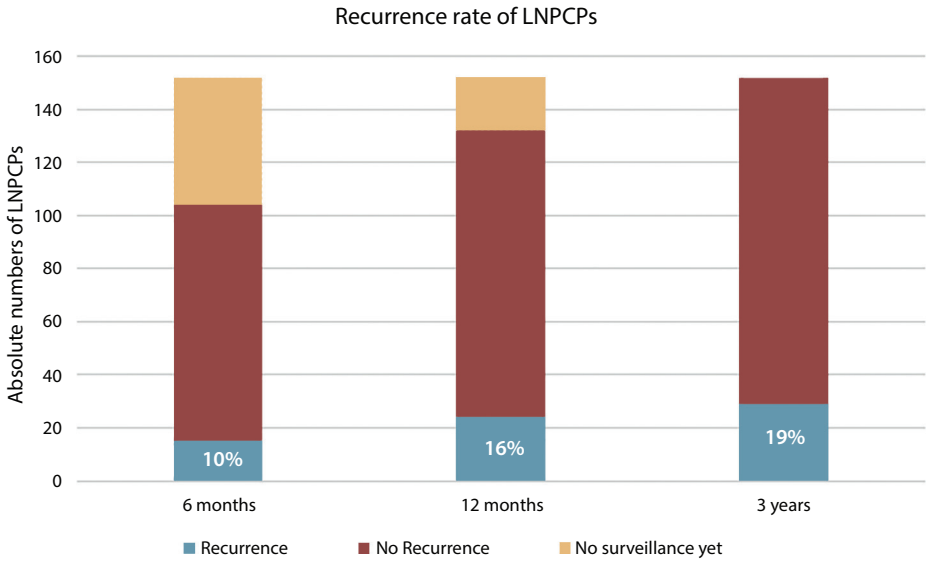

Figure 2. Recurrence rate of LNPCPs in the regional screening cohort. *LNPCP*, Large nonpedunculated colorectal polyp.

intervals are shown in Table 3. Compliance with surveillance guidelines was fulfilled in 85 of 115 (74%) piecemeal resected adenomatous LNPCPs and 19 of 47 (40%) en-bloc Rx/R1-resected adenomatous LNPCPs. In the other cases, the advised surveillance interval extended the recommended interval with more than 6 months. Compliance with surveillance intervals was 13 of 26 (50%) and 6 of 22 (27%) in en-bloc R0-resected adenomatous and serrated LNPCPs, respectively. In these groups, a large part of the LNPCPs was scheduled for earlier surveillance than the recommended 3 years.

Adverse events (regional cohort)

Adverse events occurred in 14 of 266 endoscopic procedures (5%; 95% CI, 3-9), all of which were resolved without surgery. Adverse events were postpolypectomy syndrome (1/266; .4%), direct postpolypectomy bleeding (3/266; 1%), and delayed bleeding (10/266; 4%). No deep mural injury occurred. An additional colonoscopy was performed in 5 direct and delayed bleeding cases (5/14; 36%), with clipping of the defect in 2 cases. The adverse event rate per size group was 5 of 161 (3%) in 20- to 29-mm LNPCPs, 3 of 85 (4%) in 30- to 39-mm LNPCPs, and 6 of 86 (7%) in ≥40-mm LNPCPs ($P = .366$).

Surgery for LNPCPs (regional cohort)

Of the 332 LNPCPs in the regional cohort, 92 were treated by surgery. Characteristics of these lesions are shown in Table 4. Nine LNPCPs (3%) were referred for local excision by transanal endoscopic microsurgery (referral for transanal endoscopic microsurgery instead of EMR/endoscopic submucosal dissection was based on local experience and availability), and another 15 LNPCPs were surgically resected because of a synchronous malignant colorectal lesion, which needed major surgical treatment (these 15 lesions were captured within the surgical specimen; the synchronous malignant lesions were not part of the group of 332 LNPCPs). These cases were excluded from the surgery referral rate analysis, leaving 68 LNPCPs (20%) referred for major surgery. Primary surgery was performed in 51 cases (15%) and secondary surgery in 17 cases (5%).

Primary surgery was performed because of suspicion of submucosal invasive cancer (SMIC) in 18 of 51 cases (35%), of which 16 (89%) showed SMIC in the surgical specimen. In 33 of 51 cases (65%, 10% of the total number of LNPCPs) there was no suspicion for SMIC during endoscopy, and the referral reason was "endoscopic unresectable or inaccessible," not further specified (all being SMSA score 3 or 4 lesions). Most (22/33; 67%) of these nonsuspicious, complex lesions were ≥30 mm, and 17 of 33 (52%) were located proximally. Of the 33 lesions, 12 (36%) showed SMIC in the surgical specimen. Accordingly, the overall primary surgery referral rate for noninvasive LNPCPs was 23 of 332 (7%; 95% CI, 5-10).

Secondary surgery was performed because of SMIC in 13 of 17 cases (77%) and because of nonlifting of noninvasive LNPCPs in the other 4 cases (24%). Leave-1-out analysis showed clear variation between centers in the surgery referral rate for noninvasive LNPCPs (mean, 7%; leave-1-out-analysis range, 4%-10%), especially for proximal lesions (mean, 52%; leave-1-out-analysis range, 33%-56%) (Supplementary Table 2).

TABLE 3. Advised surveillance intervals after endoscopic resection of large nonpedunculated colorectal polyps in the regional bowel cancer screening program cohort

	Adenomas (n = 188)			
	Piecemeal EMR (n = 115)	Rx/R1 en-bloc EMR (n = 47)	R0 en-bloc EMR (n = 26)	Serrated lesions (n = 22)
3-6 mo	85 (74)	19 (40)	6 (23)	7 (32)
1 y	19 (17)	7 (15)	5 (19)	4 (18)
3 y	11 (10)	12 (26)	13 (50)	6 (27)
5 y	0 (0)	9 (19)	2 (8)	5 (23)

Values are n (%). Lesions were included with available pathology assessment and advised surveillance interval.
Blue indicates too early, red indicates too late, and orange indicates appropriate surveillance interval recommendations (based on Dutch guideline colonoscopy surveillance[12] and European Society for Gastroenterology guideline[13]).

TABLE 4. Lesion characteristics of primary surgically, secondary surgically, and endoscopically treated large nonpedunculated colorectal polyps

	Overall (n = 332)	Primary surgery (n = 66)*	Secondary surgery (n = 26)*	Endoscopic treatment (n = 240)	*P* value
Median size, mm (interquartile range)	30.0 (20-40)	30 (20-40)	28 (20-50)	25 (20-35)	.171
Proximal location	175 (53)	30 (46)	11 (42)	134 (56)	.117
Location					.148
Colon	262 (79)	52 (79)	19 (73)	191 (80)	
Cecum/ascending colon	117 (35)	24 (36)	6 (23)	87 (36)	
Rectum	70 (21)	14 (21)	7 (27)	49 (20)	
Morphology					.023
Sessile	267 (80)	46 (70)	24 (92)	197 (82)	
Flat	65 (20)	20 (30)	2 (8)	43 (18)	
SMSA score					.079
SMSA 3	139 (42)	22 (33)	13 (50)	106 (44)	
SMSA -3/4	96 (29)	21 (32)	3 (12)	70 (29)	
SMSA 4	97 (29)	23 (35)	10 (38)	64 (27)	
Villous component	122 (38)	19 (29)	5 (19)	98 (41)	.031
Dysplasia					<.001
No dysplasia	30 (9)	2 (3	2 (8)	20 (8)	
Low-grade dysplasia	199 (60)	20 (30)	6 (23)	179 (75)	
High-grade dysplasia	48 (15)	14 (21)	4 (15)	29 (12)	
Carcinoma	55 (17)	30 (45)	14 (54)	12 (5)	

Values are n (%) unless otherwise defined.
SMSA, Size, morphology, site, and access of a lesion (reflects the complexity for endoscopic treatment).
*These groups not only include lesions referred for major surgery, but also include lesions referred for transanal endoscopic microsurgery and lesions referred for surgery because of a synchronous lesion.

Endoscopist experience in the regional screening cohort

In the regional 332 LNPCP cases, 24 endoscopists were involved. Fifteen (63%) had more than 10 years of experience, and 9 (38%) were dedicated to advanced polypectomy programs in their center. The direct surgery referral and technical success rates were, respectively, 51% and 71% for nonexperienced, nondedicated endoscopists, 17% and 88% for intermediate group endoscopists, and 8% and 90% for experienced, dedicated endoscopists ($P < .001$ and $P = .064$, respectively). Direct surgery referral rates and technical success rates for experienced versus nonexperienced and dedicated versus nondedicated endoscopists are shown in Supplementary Tables 3 and 4 (available online at www.giejournal.org).

DISCUSSION

In this performance of 2 substudies, the prevalence and outcomes of LNPCP polypectomy within the BCSP were analyzed. An LNPCP prevalence of 8% was observed.

Technical and clinical success rates for endoscopic resection were 87% (95% CI, 82-91) and 87% (95% CI, 80-92), respectively. Cumulative recurrence rates after 12 months were 22% (95% CI, 15-32) after piecemeal resection and 8% (95% CI, 2-22) after en-bloc resection, and adverse events occurred in 5% of cases (95% CI, 3-9). The primary surgery referral rate for noninvasive LNPCPs was 7% (95% CI, 5-10).

The prevalence of LNPCPs of 8% found in our study is in line with other large cohorts[16-18] but is higher compared with an English BCSP cohort. It should be taken into account that in the English BCSP cohort, preselection occurred.[15]

Although quality indicators for colonoscopy are widely implemented, increasing awareness has highlighted the need for quality indicators for polypectomy to further optimize screening programs.[4,5,19] The measured quality outcomes for (large) polypectomy in this study were technical success, recurrence rate, and clinical success and showed room for improvement. The technical success rate in our regional cohort (87%) is lower than reported in expert centers (95%) and a meta-analysis (96%; 95% CI, 96-97).[2,20] The clinical success rate in our cohort (87%) is also lower than reported in the English BCSP (94%) and expert centers (96%).[15,21] These differences might be explained by the fact that we observed a decrease in success rates with increasing LNPCP size. Sidhu et al[22] described technical success rates of 99% in SMSA score 2 lesions in expert centers, decreasing to 93% in SMSA score 4 lesions, in which SMSA refers to the size, morphology, site, and access of a lesion and reflects the complexity of a colorectal lesion with regard to endoscopic treatment. In contrast, we showed a decreased technical success rate to 74% in ≥40-mm lesions. Although the resection of 20- to 29-mm lesions in the Dutch BCSP is of sufficient quality, the gap in quality between expert centers and BCSP endoscopists clearly widens from ≥30-mm-sized LNPCPs. This emphasizes that the level of experience in endoscopic resection of LNPCPs is important for success.[14,23]

To increase exposure, centralization within or between centers should therefore be considered, and additional training should be implemented in clinical practice. Furthermore, implementation of quality monitoring on endoscopic resection could improve the outcomes on quality parameters and reduce practice variation. The lower clinical success rate in our study can partially be explained by noncompliance with surveillance guidelines. Not performing surveillance after 6 months influences the clinical success rate because of lack of opportunity to treat possible recurrences early. This stresses the importance of compliance with surveillance guidelines, of which we, in line with current evidence,[7] have shown that there is still substantial noncompliance.

The cumulative recurrence rates of 22% for piecemeal and 8% for en-bloc resection after 12 months are similar to recurrence rates described in large polypectomy cohorts (15%-31% piecemeal, 3%-6% en bloc) and meta-analyses (20% piecemeal [95% CI, 16-25], 3% en bloc [95% CI, 2-5]).[2,6,14,21,24,25] However, expert centers recently reported lower recurrence rates of 4.0% to 5.4% after adjustment of endoscopic treatment strategies.[26] This illustrates that recurrence rates in the Dutch BCSP can still be significantly improved by further ameliorating resection techniques. Detailed analysis showed that recurrence rates increased significantly with lesion size in our cohort, with a clear difference between 20- to 29-mm and ≥30-mm lesions (from 9% to 22%). Here, a clear difference in recurrence rates between the BCSP cohort and expert centers is illustrated, given the fact that reported recurrence rates in expert centers are 7% for SMSA score 2 lesions, 9% for SMSA score 3 lesions, and only increased to 24% in SMSA score 4 lesions.[22] Again, this confirms the need for additional training and monitoring on quality parameters for polypectomy and stresses the item to consider centralization of treatment of ≥30-mm lesions.

Safety of endoscopic resection in the screening program was high, which is in line with current evidence.[2,15] The adverse event rate was only 5%.

Although the primary surgery referral rate for noninvasive LNPCPs (7%) is lower than previously described,[2,15] a Dutch study on benign rectal polyps showed significant referral for major surgery, whereas 73% of cases were assessed as "probably feasible" for endoscopic therapy.[9] Furthermore, Vermeer et al[8] showed that a large amount of benign lesions were referred for major surgery because of complexity, without reassessment for endoscopic resection by an advanced endoscopy center. Additionally, de Neree tot Babberich et al[27] showed that predominantly large lesions in the proximal colon were referred for surgery, whereas risk of malignancy in proximal lesions was smaller than in distal lesions. A similar observation was made in our study. Therefore, current evidence suggests that despite emerging endoscopic techniques, the shift from surgical to endoscopic treatment of large colorectal polyps is lingering, and a significant number of noninvasive LNPCPs are still referred for surgery. This may also be an important quality measure because surgery has higher morbidity compared with endoscopic resection.[28]

Furthermore, our data support the assumption that experienced and dedicated endoscopists have higher success rates in advanced polypectomy and are less likely to refer large polyps for surgery than nonexperienced and nondedicated endoscopists. This again stresses the importance of additional training, consultation with dedicated experts, and centralization of care for large colorectal polyps.

Several limitations of our study should be acknowledged. First, we assumed the regional cohort to be a representative sample of the national cohort. Given the limited data from the national cohort, this assumption

and extrapolation of results should be made with caution. However, we have shown that the 2 cohorts match on important parameters in this study. Second, recurrence rates may have been underestimated because of the limited compliance with surveillance guidelines. Follow-up colonoscopy was performed in only 67% of cases, of which most were performed within 12 months. In addition, the lesions without follow-up mainly consisted of en-bloc resected 20- to 29-mm lesions, influencing the recurrence rate only minimally. Furthermore, determining recurrence rates at 12 months for en-bloc resection may also have led to an under- or overestimation, because not all patients within this group underwent a surveillance colonoscopy within 12 months because the surveillance guidelines advise follow-up after 3 years for these resections. Variance in surveillance intervals may also have caused bias in clinical success analysis at 12 months. Third, the accessibility portion of the SMSA score was not described in our cohort. Therefore, SMSA score was calculated with both easy and difficult accessibility. Although we did not find any associations between SMSA score and recurrence rate or surgery referral rate, it should be noted that we could not draw any conclusions regarding the value of the SMSA score based on this cohort because exact accessibility per lesion was unknown. Fourth, the level of training of endoscopists participating in our study is not measured systematically, quality of resection is not retrievable, and it is unknown whether recent insights have already been implemented in clinical practice. However, all endoscopists have followed the national bowel cancer screening training program and have been certified for screening colonoscopies. Finally, our study showed variation between centers that unfortunately could not be further investigated at the national level. To gain more insight in the quality of polypectomy and variation between centers at the national level, the national ScreenIT registry should be optimized for evaluation purposes and quality indicators for polypectomy should be included.

In conclusion, in this Dutch screening program cohort it was shown that quality parameters for endoscopic resection of LNPCPs are not reached, especially in $\geq$30-mm polyps. Endoscopic resection of large polyps could benefit from additional training, quality monitoring, and centralization, either within or between centers.

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Abbreviations: BCSP, bowel cancer screening program; FIT, fecal immunochemical test; LNPCP, large nonpedunculated colorectal polyp; SMIC, submucosal invasive cancer; SMSA, size, morphology, site, and access.

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SUPPLEMENTARY TABLE 1. Characteristics of interval cancers

	Interval cancer no. 1	Interval cancer no. 2
Initial lesion		
Size	20 mm	50 mm
Morphology	Sessile	Sessile
Location	Rectum	Ascending colon
Type of resection	En-bloc EMR	Piecemeal EMR
Pathology	T1N0M0 adenocarcinoma Resection margin .1 mm Kikuchi sm2 No lymphovascular invasion	Tubulovillous adenoma High-grade dysplasia
Interval cancer		
Time to diagnosis	6 mo	3 y Loss-to-follow-up (surveillance at 6 mo was not performed)
Diagnosed by	Endoscopy	Endoscopy
Indication	Surveillance	Symptomatic iron deficiency
Treatment	Transanal endoscopic microsurgery	Major surgery
Pathology	T2N0M0 adenocarcinoma R0 resection	T2N0M0 No lymphovascular invasion
Sequel	Wait and see at patient's request 1 y later: metastasized disease	—

EMR, Endoscopic mucosal resection; —, no additional follow-up within study period.

SUPPLEMENTARY TABLE 2. Results of leave-1-out analyses

Outcome measure	Total	Leave-1-out analysis no. 1	Leave-1-out analysis no. 2	Leave-1-out analysis no. 3	Leave-1-out analysis no. 4	Leave-1-out analysis no. 5
Technical success	86.8 (82.0-90.5)	88.1	83.2	86.1	86.8	88.6
Cumulative recurrence at 12 mo						
Piecemeal	22.3 (14.7-32.3)	22.8	16.7	23.9	24.4	21.8
En bloc	7.9 (2.1-22.5)	7.9	4.0	11.1	8.6	8.3
Clinical success	87.2 (80.4-91.9)	87.0	89.5	84.8	86.3	88.3
Primary surgery referral rate	6.9 (4.5-10.4)	6.7	9.8	8.6	7.0	3.5
Proximal location of lesions referred because of complexity	51.5 (33.9-68.8)	53.8	55.2	55.6	51.9	33.3

Values are % (95% confidence interval) or %.

SUPPLEMENTARY TABLE 3. Direct surgery referral rate according to experience and dedication of endoscopists

	Nondedicated	Dedicated	Total
≤10 y of experience	25/49 (51%; 95% CI, 37-65)	19/93 (20%; 95% CI, 13-30)	142
>10 y of experience	15/106 (14%; 95% CI, 8-23)	7/84 (8%; 95% CI, 4-17)	190
Total	155	177	332

CI, Confidence interval.

SUPPLEMENTARY TABLE 4. Technical success rate according to experience and dedication of endoscopists

	Nondedicated	Dedicated	Total
≤10 y of experience	17/24 (71%; 95% CI, 49-87)	67/74 (91%; 95% CI, 81-96)	98
>10 y of experience	78/91 (86%; 95% CI, 76-92)	69/77 (90%; 95% CI, 80-95)	168
Total	115	151	266

CI, Confidence interval.