Long Term Outcomes of Colon Polyps with High Grade Dysplasia after Endoscopic Resection

Jia-Jang Chang
Keelung Chang Gung Memorial Hospital https://orcid.org/0000-0003-3784-0014
Cheng-Hung Chien
Keelung Chang Gung Memorial Hospital of the CGMF
Shuo-Wei Chen
Keelung Chang Gung Memorial Hospital of the CGMF
Li-Wei Chen
Keelung Chang Gung Memorial Hospital of the CGMF
Ching-Jung Liu
Keelung Chang Gung Memorial Hospital of the CGMF
Cho-Li Yen (✉ cholіyen55@cgmh.org.tw)

Research article

Keywords: Colonoscopy, Colon polyp, High grade dysplasia, Surveillance

Posted Date: July 8th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-39348/v1

Version of Record: A version of this preprint was published on November 10th, 2020. See the published version at https://doi.org/10.1186/s12876-020-01499-2.

Abstract

Background

The clinical characteristics of patients with high-grade dysplasia (HGD) in colon polyps at baseline colonoscopy in relation to the risk of recurrent colonic adenomas have been unclear. We conducted this hospital- based cohort study recruiting patients who had undergone polypectomy at screening colonoscopy to assess the risk factors of recurrent colonic adenomas.

Methods

11,565 subjects had undergone screening colonoscopic examinations between September 1998 and August 2007. The patients who had HGD in colon polyps and had undergone surveillance colonoscopy were eligible.

Results

A total of 211 patients were recruited. The rates of metachronous adenomas and advanced adenomas at surveillance colonoscopy were 58% and 20%, respectively, during the mean follow-up period of 5.5 ± 1.8 (3–12) years. On univariate logistic regression analysis, the number of adenomas ≥ 3 at baseline colonoscopy was strongly associated with the rates of overall recurrence, multiple recurrence, advanced recurrence, proximal recurrence, and distal adenoma recurrence with odds ratios of 4.32 (2.06–9.04 95%CI), 3.47 (1.67–7.22 95%CI), 2.55 (1.11–5.89 95%CI), 2.46 (1.16–5.22 95%CI), 2.89 (1.44–5.78 95%CI), respectively. On multivariate analysis, male gender [P = 0.010; OR 3.09(1.32–7.25 95% CI)] and number of adenomas ≥ 3 [P = 0.002; OR 3.08(1.52–6.24 95%CI)] at index colonoscopy were significantly associated with recurrent advanced adenomas.

Conclusions

Recurrence of colonic adenomas at surveillance colonoscopy is common in patients who had undergone polypectomy for colon adenomas with HGD at baseline colonoscopy. The risk of developing future advanced adenomas is associated with the number of colon adenomas and male gender.

Background

Colorectal cancer (CRC) is the third leading cause of cancer-related death in Taiwan [1]. CRCs were found to originate from the initially benign colon adenomas that followed an adenoma-carcinoma sequence. Colonoscopy and polypectomy interrupted this adenoma-carcinoma sequence and reduced the incidence of CRC [2–5]. The occurrence of CRC was also effectively prevented by detection and concomitant removal of advanced adenomas that were defined as adenomas greater than 10 mm, with high grade dysplasia

(HGD) or ≥ 20% villous component [6]. The rates of recurrent adenomas after polypectomy have been reported to be 29–58% five years after screening [5, 7]. Previous studies have suggested that the characteristics of adenomas at index colonoscopy are closely related to recurrence of adenomas. Some studies have shown that location, size, histological type, presence of atypia, and number of adenomas detected at the index colonoscopy were risk factors for adenoma recurrence [8–11].

Whether advanced adenomas (villous adenoma, severe dysplasia or adenoma size ≧ 10 mm) at index colonoscopy have a more aggressive behavior leading to a faster growth and an earlier recurrence than the normal counterparts are still unclear [11]. In the univariate analysis from the NCI Pooling Project, adenomas with HGD were shown to be strongly associated with the risk for advanced neoplasia during surveillance colonoscopy (OR, 1.77; 95% CI, 1.41–2.22) [11] but the result was not demonstrated by other studies. There were few studies addressing the long- term outcomes of patients with HGD in colon polyps after polypectomy at index colonoscopy [12, 13]. We therefore conducted this retrospective cohort study. The primary goals of this study were to find out the cumulative incidence rate of recurrent advanced neoplasia in patients with HGD at baseline screening colonoscopy and the association between baseline endoscopic characteristics and the subsequent risk of advanced neoplasia.

Methods

Patients selection

After obtaining approval from the Institutional Review Board of Keelung Chang Gung Memorial Hospital (IRB No. 104-6993D), an extensive chart review was undertaken to review the colonoscopic reports and pathology reports of 11,565 patients who had undergone consecutive colonoscopic examinations at the Chang Gung Memorial hospital (Keelung, Taiwan) between September 1998 and August 2007. Patients who had adenoma at screening and had undergone surveillance colonoscopic examinations were identified. Patients with HGD in colon adenomas were selected and reviewed for their eligibility.

The patients with previous colon cancer or metachronous colon cancer at the index study, inflammatory bowel diseases (including Crohn's disease or ulcerative colitis), familial adenomatous polyposis (FAP), no surveillance total colonoscopy in three years after screening polypectomy, incomplete colonoscopy study, other systemic diseases causing death during surveillance studies were excluded.

A complete colon visualization was required for any patient who had undergone a colonoscopic examination at the colonoscopy unit of this hospital. For the patient who had colonic neoplastic lesions at colonoscopy, polypectomy was routinely performed with biopsy forceps (small lesions less than 5 mm), cold snare polypectomy, hot snare polypectomy or endoscopic submucosal resection. The gross appearance, size, histology, and location of the adenomas at baseline colonoscopy of the recurrence group were compared to that of the recurrence free group to illuminate the risk factors for future adenoma recurrence. The adenomas were categorized as protruding (0-Ip), subpedunculated (0-Ips), sessile (0-Is), lateral spreading (0-IIa) and depressed lesions (0-IIc) according to the Paris endoscopic classification of superficial neoplastic lesion [13]. The size, morphology and location of the adenomas were recorded in the

reports. The size of the adenomas was measured by an open biopsy forceps (diameter = 8 mm) or by a rule for the resected specimens. The locations of the adenomas were defined as proximal colon (caecum, ascending colon, hepatic flexure and transverse colon), distal colon (splenic flexure, descending colon, sigmoid colon and rectum).

The removed adenomas were obtained for pathologic examination. Advanced adenomas were defined as any adenoma greater than (≥) 10 mm, with villous or villotubular histology(≥ 20% villous component), or adenoma with high grade dysplasia (severe dysplasia or intramucosal carcinoma). The polyps were defined as tubular, tubulovillous, villous adenoma, or serrated polyp according to the histological characteristics.

A second look colonoscopy was performed 6 to 12 months after the index colonoscopy when the adenomas were removed by the piecemeal method or an incomplete resection was suspected. The patients who had undergone surveillance colonoscopy at least three years after the initial polypectomy were eligible for inclusion in this study. The clinical characteristics including gender, age, indication of colonoscopy, family history of colon cancer, tumor number, size, location and histology of the adenomas were analyzed in this study.

Continuous variables were expressed as mean ± standard deviation (mean ± SD) and categorical variables as frequencies or percentages. Independent t –test or chi-square test were used to compare the differences between all the patients with high grade dysplasia with different demographic characteristics (Table 1) and between recurrence and recurrence free groups (Table 2) as appropriate. Univariate logistic regression analysis was performed to obtain the odds ratios of all predictors for polyp recurrence (Table 3 and Table 4). Multivariate logistic regression analysis was performed to find out the risk ratios of any adenoma recurrence and advanced colorectal neoplasia recurrence base on baseline characteristics of patients and colon adenoma (Table 5). A p value < 0.05 was considered statistically significant and all calculations were two sided. All statistical analyses were performed using IBM SPSS 22.0 (IBM Inc., Armonk, New York).

Table 1
Baseline Characteristics of patients with HGD in adenomas

Characteristics	Number	%
Gender	M: 129	61.1%
	F: 82	38.9%
Family history of CRC §	11	5.2%
Stool OB positive§§	99	46.9%
Pedunculated(0-Ip) *	72	34.1%
Subpedunculated(0-Ips) *	97	46.0%
Sessile(0-Is) *	23	10.9%
Lateral spreading(0-IIa) *	18	8.5%
Depressed (0-IIc) *	1	0.5%
Tubular adenoma	154	73.0%
Tubulovillous/Villous adenoma	53	25.1%
Serrated adenoma	4	1.9%
Distal colon**	119	56.4%
Proximal colon***	28	13.3%
Both distal and proximal	64	30.3%

§ family history of CRC (first relatives). §§ positive fecal immunochemical test.

*The Paris endoscopic classification of superficial neoplastic lesion. ** Distal colon (splenic flexure, descending colon, sigmoid colon and rectum), ***Proximal colon (caecum, ascending colon, hepatic flexure and transverse colon),

Table 2
The clinical characteristics of 211 patients with or without adenoma recurrence

	Recurrence free (n = 88)	Recurrence(n = 123)	P value
Age, years	64.06 ± 11.87	63.89 ± 11.8	0.828
Size of polyp, cm	1.91 ± 1.11	1.83 ± 1.2	0.576
baseline polyp No.	1.68 ± 1.09	2.46 ± 1.57	0.03
Male gender	48 (54.5%)	81 (63.9%)	0.097
Morphology	35	37	0.201
Ip*	41	56	
0-Ips**	5	18	
0-Is***	7	11	
Lateral spreading (0-IIa)	0	1	
Depressed(0-IIc)			
Histology	60	95	0.284
tubular	27	26	
villous/villotubular	6	2	
serrated			
Location	54	65	0.706
Distal	14	14	
Proximal	20	44	
Both			
Ip* pdunculated. 0-Ip s** subpedunculated. 0-Is*** sessile			

Table 3
The impact of number and location of polyps at baseline on the recurrence of polyps at follow up colonoscopy

Recurrence	Distal colon polyps at baseline					Proximal colon polyps at baseline					
	< 3 adenomas* (51)		≧ 3 adenoma*(14)			< 3 adenomas*(26)			≧ 3 adenomas*(32)		
	%	OR	%	OR	p	%	OR	p	%	OR	p
Overall	49	1	93	13.42 (1.69-106.51)	0.04	55	1.23 (0.61–2.48)	0.558	71	2.41 (1.12–5.184)	0.024
Multiple	35	1	60	4.53 (1.45–14.19)	0.009	32	1.41 (0.66–3.04)	0.374	42	2.24 (1.05–4.79)	0.037
Distal	36	1	87	11.02 (2.33–52.17)	0.002	36	0.99 (0.48–2.05)	0.979	47	1.5753 (0.76–3.28)	0.224
Proximal	22	1	27	1.265 (0.36–4.45)	0.714	30	1.46 (0.67–3.33)	0.34	42	2.4026 (1.11–5.20)	0.026
Advanced	12	1	40	3.71 (1.10–12.50)	0.034	23	1.8769 (0.76–4.66)	0.175	29	2.2794 (0.93–5.56)	0.007

*( ) patient number. OR, odd ratio,; Overall = overall adenoma recurrence, Multiple = multiple adenoma recurrence

Distal = distal adenoma recurrence, Proximal = proximal adenoma recurrence, Advanced = advanced adenoma recurrence

Table 4
Baseline Clinical Characteristics and Risk Ratios for Recurrent Adenomas on Univariate Analysis

	Overall adenomas recurrence		Advanced adenomas recurrence	
	OR(95% CI)	P value	OR(95% CI)	P value
Age in years	1.00(0.98–1.03)	0.928	1.01(0.98–1.04)	0.441
Male gender (vs female)	1.75(0.99–3.06)	0.052	3.44(1.51–7.87)	0.003
Size of polyp (≥ 10 mm vs < 10 mm)	0.89(0.44–1.83)	0.758	0.95(0.40–2.26)	0.909
Adenoma number (≥ 3 vs < 3)	3.16(1.60–6.22)	0.001	2.45(1.22–4.93)	0.012
FH*(positive vs negative)	1.27(0.36–4.47)	0.713	0.38(0.05–3.02)	0.358
Stool OB** (Positive vs negative)	0.81(0.47–1.40)	0.448	1.10(0.56–2.15)	0.778
Pathology of polyps (Non-tubular vs tubular)	0.63(0.34–1.17)	0.143	0.94(0.44–2.02)	0.873
Location (Distal vs Proximal)	1.13(0.60–2.15)	0.707	0.49(0.34–1.02)	0.056
*positive family history of CRC(first relatives), ** positive fecal immunochemical test.				

Table 5
Baseline characteristics and risk ratios for recurrent adenomas on multivariate analysis

	Overall adenomas recurrence		Advanced adenomas recurrence	
	OR (95% CI)	P	OR(95%CI)	P
Age in years	0.99(0.97–1.02)	0.661	1.00(0.97–1.04)	0.795
Male vs female	1.59(0.87–2.90)	0.127	3.09(1.32–7.25)	0.010
Size ≥ 10 mm vs < 10 mm	0.76(0.35–1.65)	0.492	0.83(0.32–2.18)	0.704
Adenoma number ≥ 3 vs < 3	3.08(1.52–6.24)	0.002	2.11(1.00-4.43)	0.049
FH* positive vs negative	1.24(0.33–4.69)	0.755	0.45(0.05–3.84)	0.592
Stool OB** positive vs negative	0.90(0.50–1.62)	0.720	1.22(0.59–2.55)	0.611
Non-tubular vs tubular	0.59(0.30–1.34)	0.404	1.07(0.47–2.43)	0.871
Distal vs Proximal location	1.34(0.67–2.68)	0.746	0.52(0.23–1.156)	0.109
*:positive family history of CRC(first relatives); **: positive fecal immunochemical test.				

Results

Among 11,565 patients who had undergone colonoscopy examination, colon adenomas were found in 4149 patients (35.9%). Of these 4149 patients, 258 patients (6%) had advanced adenomas with HGD.

Forty-seven of 258 patients failed to complete surveillance colonoscopy and were excluded. Figure 1 shows the selection and exclusion results. A total of 211 patients were included for analysis. The mean age was 64 ± 12 years. The mean follow-up period was 5.5 ± 1.8 (3–12) years after index colonoscopy. 129 patients were male and 82 patients were female. 123 patients (58%) had recurrent adenomas at surveillance colonoscopy.

There was no statistical difference between the recurrence and recurrence free group in terms of gross appearance, histologic finding, location, and size of adenomas at baseline colonoscopy (Table 2). The number of polyps at index colonoscopy was associated with future adenoma recurrence (P = 0.03)

A subgroup analysis for the impact of polyp number and location of polyp on the recurrence of polyps showed that patients who had adenoma number ≥ 3 were associated with a greater risk of metachronous adenoma recurrence (Table 3). For the distal colon polyps with number ≥ 3 at the index colonoscopy, the rates of overall recurrence, multiple recurrence, distal colon recurrence, proximal colon recurrence and advanced adenomas recurrence were 93%, 60%, 87%, 27% and 40%, respectively. In contrast, for the distally located polyps with number < 3, the overall recurrence rate, multiple recurrence rate, distal colon recurrence rate, proximal colon recurrence rate and advanced adenomas recurrence rate were 49%, 35%, 36%, 22% and 12%, respectively. For the adenomas located at the proximal colon at index colonoscopy, a similar odds ratio was also observed in the group of adenomas ≥ 3 in number but not in the group with the number < 3 (Table 3). The odds ratios for the overall recurrence, multiple recurrence, distal recurrence, proximal recurrence and advanced adenoma recurrence of adenomas ≥ 3 in number and < 3 in number were 13.42 (1.69-106.51), 4.53 (1.45–14.19), 11.02(2.33–52.17), 1.26 (0.36–4.45), and 3.71 (1.10–12.50), respectively (Table 3).

On univariate logistic regression analysis, the number of adenomas greater than 3 at the baseline colonoscopic examination was strongly associated with risks of overall recurrence, multiple recurrence, advanced recurrence, proximal recurrence, and distal adenoma recurrence (Table 4) with odds ratios of 4.32(2.06–9.04 95%CI), 3.47(1.67–7.22 95%CI), 2.55(1.11–5.89 95%CI), 2.46(1.16–5.22 95%CI), 2.89(1.44–5.78 95%CI), respectively. The clinical features of size, pathologic characteristics, or location of adenomas were not associated with the risk of overall recurrence, multiple recurrence, proximal recurrence, distal recurrence or advanced adenoma recurrence (Table 4). The multivariate logistic regression analysis revealed that the polyp number greater than 3 was associated with the risks of overall polyp recurrence [P = 0.002; OR 3.08(1.52–6.24 95%CI)] and advanced polyp recurrence during surveillances [P = 0.49; OR 2.11(1.00-4.43 95%CI). The male gender [P = 0.010; OR 3.09(1.32–7.25 95% CI)] was also associated with advanced polyp recurrence (Table 5). Of 211 patients who had undergone surveillance colonoscopy, 43 patients (20%) developed recurrent advanced colon polyps, but no one developed interval colorectal adenocarcinoma.

Discussion

The rates of developing metachronous adenoma and advanced adenoma after polypectomy for colon polyps with HGD were 58% and 20%, respectively, in the current study. The clinical features of age, gender, stool occult blood positivity, size of polyp, morphology, pathology and location of polyps were not different between the patients who had developed recurrent adenomas and those who had not.

The odds ratios of developing metachronous adenoma and advanced adenoma were 4.32 (2.06–9.04 95% CI) and 2.55(1.11–5.89 95% CI), respectively, when comparing subjects with polyp number ≥ 3 and ≤ 2 at the index colonoscopy.

There was no metachronous adenocarcinoma observed during the period of this cohort. The incidence rate of adenomas was 35.9% in our patients who had undergone screening colonoscopy. The rate is higher than that of the Western population of 20% [14] and 8.13 to16.5% of Taiwanese and Chinese ethnic groups, respectively [15–17], because our study subjects were mostly referred on account of positivity for stool occult blood or symptomatic of gastrointestinal disorders.

The reported reduction rates of colon cancer after polypectomy were around 50–80% and the occurrence of interval cancers was located mostly in the right colon [18–20]. The reason accounting for higher recurrent rates of interval carcinoma in the right colon included incomplete colonoscopy study due to poor endoscopic technique [21], incomplete removal of the polyps [22], difficulty in visualization of smaller adenomas in the right colon [23–24], or sessile serrated adenoma in the proximal colon.

At screening colonoscopy, the prevalence of polyps with HGD was 2.2% (258/11565) in our patients, which is slightly lower than that of 3.5% in the general population of Chinese ethnic [26]. There was no interval cancer during the follow up period in the current study, because we performed the second look colonoscopy 6 to 12 months after piecemeal resection for advanced polyps or suspected incomplete resection to ensure complete resection of polyps and to decrease the rate of undetected adenomas at the index colonoscopies, as has been suggested by some endoscopists in treatment using the piecemeal method [25–26]. Recurrent adenomas after polypectomy were reported to be about 36 to 64% within 2 to 6 years [12, 27–30]. In the current study, the overall recurrence rate of metachronous adenomatous polyps was 58%, which is similar to that of 64% in Toll's study [12]. The rate of recurrent advanced adenomas was 20% in the current study which is lower than that of 40% in Toll's report.

HGD in adenoma was considered following the adenoma-adenocarcinoma sequence and a precursor of adenocarcinoma [31]. However, the risk of future advanced adenomas in relation to HGD at index colonoscopy was reported to be small and variable.

In the meta-analysis study of Saini [32], the patients with HGD in polyps had a relative risk of advanced adenomas of 1.84 (95% CI 1.06–3.19) compared to those who had no HGD. Some other studies including a randomized controlled trial revealed no association of HGD with subsequent advanced adenomas during surveillance colonoscopy [33–36].

Two meta-analyses [37–38] have also shown that the presence of HGD had a small association with the risk of future advanced adenomas. On the multivariate analysis in these studies, the presence of HGD did not confer recurrence of metachronous adenomas. Most of the advanced adenomas are ≥ 1 cm [39]. However, if the adenomas with HGD can be removed completely, the risk for metachronous recurrence is probably dependent on the number of colon polyps and male gender as shown in this study. The rationale is also applicable to the association of villous histology of the resected adenomas with the risk of recurrent advanced adenomas. A cohort study had shown that the presence of villous adenomas at baseline colonoscopy had a relative risk of 1.8 of future adenomas [33]. Two other studies including one meta-analysis and a pooled analysis had found no association of villous histology with future adenomas [32, 14], which is in accordance with the present study result. The size of colonic adenomas has been shown to be closely related to the histological features of HGD and invasive cancer [40]. HGD in histology or prominent villous component was seen in 87.5% of large polyps (≥ 1 cm) [95% CI = 86–89.4]) [41]. The risk of recurrent advanced adenomas was shown to be corresponding with the size of polyps at index colonoscopy. In Martinez's study [14], with polyp size of 0.5 cm as the reference group, the adenoma size of 1.0 to 1.9 cm or ≥ 2.0 cm at the baseline colonoscopy had a relative risk of 2.3 and 3.0, respectively, of recurrent advanced adenomas. There were four other studies showing an increase of relative risk of recurrent advanced adenomas in colonic adenomas greater than 1 cm at base-line [22, 32, 34–36]. The relative risk of polyps with HGD at baseline was 6.87 (95% CI 2.61–18.07) of interval advanced neoplasia in Lieberman's study, in which 6 among 11 patients who had recurrent cancers or high-grade dysplasia were found in the portion of colon where the polyps were resected [22]. In the current study, the size of adenomas greater than 1 cm does not increase the risk of advanced adenomas on surveillance colonoscopy, which is in line with Saini's meta-analysis [32]. Incomplete removal or missed adenomas [21–22] might account for the contradictory observations.

The number of adenomas ≥ 3 has been shown to increase the risk of recurrent advanced adenomas. The relative risk was between 1.5 and 5.0 [22, 32, 34–36] with one adenoma as the reference group. The current study in concert with the previous studies has found odds ratios of 2.45(1.22–4.93) on univariate analysis and 2.11(1.00-4.43) on multivariate analysis, respectively, when comparing adenoma number ≥ 3 to adenoma number ≤ 2. Male gender is also associated with advanced adenoma recurrence in his study with an odds ratio of 3.09, which is consistent with Zhang's study that reported male gender and the number of adenoma ≥ 3 had high risk of advanced adenoma recurrence [17].

The natural history of colonic adenomas is still elusive. Two longitudinal follow up studies for small polyps (6–9 mm) using computed tomography showed the tumor progress rates of 22% [42] and 35% [43] during the follow up periods of 8 and 3 years, respectively. Advanced histology was seen in 47% of progressing polyps [43], which is similar to the rate of 40% in our patients with the baseline adenoma number ≥ 3. The high incidence rate of recurrent adenomas and advanced adenomas in patients with multiple adenomas is hard to explain solely on incomplete resection of adenomas. The multiple small polyps that were not detected on optical colonoscopy at baseline might have progressed slowly with time and became detectable on surveillance colonoscopy. The multiplicity or polyclonicity in patients with adenoma number ≥ 3 in number is a reasonable explanation but a longer observation with other non-

invasive study modalities such as computed tomography or capsule endoscopy to detect missed adenomas may be required to elucidate the natural history of recurrent adenomas. The surveillance recommended by the United States Preventive Services Task Force (USPSTF) was 3 years after removal of advanced adenoma, traditional serrated adenoma, or advanced sessile serrate adenoma [44]. The European guidelines [45] recommended a more aggressive surveillance at 1 year for high risk polyps (≥ 20 mm). In the treatment with piecemeal resection, Walsh et al revealed a rate of 14% polyp recurrence after at least one negative examination, and the rate of CRC development was 17% in 65 patients with large flat polyps [46]. A second look examination for patients who underwent piecemeal resection or suspected incomplete resection may be warranted.

The current study had some limitations. We did not take into account the impact of diet change or life style change such as abstinence of smoking, alcohol drinking and the reduction of body mass index after polypectomy, as which might have some influences on the recurrence of adenomas or advanced adenomas [47–48]. The current study did not include the low risk patients as control group and the surveillance time of patients recruited was not the same. This might influence the rate of recurrent adenomas.

Conclusions

In conclusion, colon polyps recurrence is common in the patients with high grade dysplasia at index colonoscopy. The number of polyps greater than 3 (≥ 3) and male gender have a higher risk for future occurrence of adenomas and advanced adenomas.

Declarations

Ethics approval and consent to participate

The study received approval from the Institutional Review Board of Keelung Chang Gung Memorial Hospital (IRB No. 104-6993D),

Informed consent was not required, because this study involved chart reviewing of colonoscopy reports and pathology report.

Consent for publication

Not applicable

Availability of data and material

The data of colonoscopy reports and pathology reports between September 1998 and August 2007 can be available from the electronic medical record at the Chang Gung Memorial hospital (Keelung, Taiwan) between September 1998 and August 2007.

The datasets generated and/or analysed during the current study are not publicly available due the hospital's principle and the right of privacy of patients but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests"

Funding:

The study is an original research supported by a research grant from the Chang Gung Memorial Hospital CMRPG2303

There was no other funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript

Authors Contribution

JJC study design, analysis and drafting of manuscript.

SWC, LWC, CJ L provision of clinical data

CHC provision of clinical data, analysis and interpreted the data

CLY data collection, study design and revision of the manuscript.

All authors read and approved the final manuscript.

Acknowledgements

The authors like to thank Dr. Kuo-Su Chen for providing statistical analysis and assistance

References

1. Chiang CJ, Lo WC, Yang YW, You SL, Chen CJ, Lai MS, et al. Incidence and survival of adult cancer patients in Taiwan, 2002–2012. J Formos Med Assoc. 2016 Dec;115(12):1076–88.
2. Winawer SJ, Zauber AG, O'Brien MJ, et al. Randomized comparison of surveillance intervals after colonoscopic removal of newly diagnosed adenomatous polyps: the National Polyp Study Work group. N Engl J Med. 1993;328:901–6.
3. Zauber AG, Winawer SJ, O'Brien MJ, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancerdeaths. N Engl J Med. 2012;366:687–96.
4. Brenner H, Stock C, Hoffmeister M, et al. Effect of screening sigmoidoscopy and screening colonoscopy on colorectal cancer incidence and mortality: systematic review and meta-analysis of randomised controlled trials and observational studies. BMJ. 2014;348:g2467.

5. Five-Year Analysis of the Prevention of
Arber N, Spicak J, Rácz I, et al. Five-Year Analysis of the Prevention of.
6. Colorectal S. Adenomatous Polyps Trial Am J Gastroenterol 2011.
7. 106.:1135–1146.
8. Brenner H, Hoffmeister M, Stegmaier C, et al. Risk of progression of advanced adenomas to colorectal cancer by age and sex: estimates based on 840,149 screening colonoscopies. Gut. 2007;56:1585–9.
9. Jianmin Tian, MD, and Anil B
Hannah L, Miller MD, Rupa Mukherjee MD. Jianmin Tian, MD, and Anil B.
10. Nagar MD. Colonoscopy Surveillance After Polypectomy May be Extended.
11. Beyond Five Years. J Clin Gastroenterol. 2010;44:e162–6.
12. Nusko G, Mansmann U, Kirchner T, Hahn EG, et al. Risk related surveillance following colorectal polypectomy. Gut. 2002;51:424–8.
13. Noshirwani KC, van Stolk RU, Rybicki LA, Beck GJ, et al. Adenoma size and number are predictive of adenoma recurrence: implications for surveillance colonoscopy. Gastrointest Endosc. 2000;51:433–7.
14. van Stolk RU, Beck GJ, Baron JA, et al. Adenoma characteristics at first colonoscopy as predictors of adenoma recurrence and characteristics at follow-up. The Polyp Prevention Study Group. Gastroenterology. 1998;115:13–8.
15. Martinez ME, Sampliner R, Marshall JR, et al. Adenoma characteristics as risk factors for recurrence of advanced adenomas. Gastroenterology. 2001;120:1077–83.
16. Toll AD, Fabius D, Hyslop T, et al. Prognostic significance of high-grade dysplasia in colorectal adenomas. Colorectal Dis. 2011;13:370–3.
17. The Paris endoscopic. classification of superficial neoplastic lesions: esophagus.
18. stomach, and colon November 30 to December 1. 2002 Gastrointest Endosc 2002; 58: 6 (SUPPL):S5-S43.
19. Martínez ME, Baron JA, Lieberman DA, Schatzkin A, Lanza E, Winawer SJ, et al. A pooled analysis of advanced colorectal neoplasia diagnoses after colonoscopic polypectomy. Gastroenterology. 2009;136:832–41.
20. Sung JJ, Chan FK, Leung WK, et al. Screening for colorectal cancer in Chinese: comparison of fecal occult blood test, flexible sigmoidoscopy, and colonoscopy. Gastroenterology. 2003;124(3):608–14.
21. Liu HH, Wu MC, Peng Y, Wu MS, et al. Prevalence of advanced colonic polyps in asymptomatic Chinese. World J Gastroenterol. 2005;11(30):4731–4.
22. Zhang LM, Liu YL, Zhu YM, et al. Analysis of colonic adenomas recurrence after adenoma removes. Int J Clin Exp Med. 2016;9(11):21234–42.
23. Low risk of colorectal cancer and advanced
Brenner H, Haug U, Arndt V, et al. Low risk of colorectal cancer and advanced.
24. adenomas more than 10 years after negative colonoscopy. Gastroenterology.
25. 2010.;138:870–876.

26. Baxter NN, Goldwasser MA, Paszat LF, et al. Association of colonoscopy and death from colorectal cancer. Ann Intern Med. 2009;150:1–8.
27. Brenner H, Chang-Claude J, Seiler CM, et al. Interval cancers after negative colonoscopy: population-based case-control study. Gut. 2012;61:1576–82.
28. Lieberman DA, Weiss DG, Harford WV, et al. Five-year colon surveillance after screening colonoscopy. Gastroenterology. 2007;133:1077–85.
29. Bensen S, Mott LA, Dain B, Rothstein R, Baron J, et al. The colonoscopic miss rate and true one-year recurrence of colorectal neoplastic polyps: Polyp Prevention Study Group. Am J Gastroenterol. 1999;94:194–99.
30. Gupta S, Balasubramanian BA, Fu T, et al. Polyps with advanced neoplasia are smaller in the right than in the left colon: implications for colorectal cancer screening. Clin Gastroenterol Hepatol. 2012;10:1395–401.
31. Eckardt VF, Fuchs M, Kanzler G, Remmele W, Stienen U, et al. Follow-up of patients with colonic polyps containing severe atypia and invasive carcinoma. Compliance, recurrence, and survival. Cancer. 1988 Jun 15;61(12):2552–7.
32. Hofstad B, Vatn MH, Andersen SN, Huitfeldt HS, Rognum T, Larsen S, et al. Growth of colorectal polyps: redetection and evaluation of unresected polyps for a period of three years Gut 1996; 39:449–456.
33. Leung WK, Tang V, Lui PC, et al. Detection rates of proximal or large serrated polyps in Chinese patients undergoing screening colonoscopy. J Dig Dis. 2012;13(9):466–71.
34. Jorgensen OD, Kronborg O, Fenger C, et al. The Funen Adenoma Follow-up Study. Incidence and death from colorectal carcinoma in an adenoma surveillance program. Scand J Gastroenterol. 1993;28:869–74.
35. Schatzkin A, Lanza E, Corle D, et al Polyp Prevention Trial Study Group. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. N Engl J Med. 2000;342:1149–55.
36. Baron JA, Cole BF, Sandler RS, et al. A randomized trial of aspirin to prevent colorectal adenomas. N Engl J Med. 2003;348:891–9.
37. Robertson DJ, Greenberg ER, Beach M, et al. Colorectal cancer in patients under close colonoscopic surveillance. Gastroenterology. 2005;129:34–41.
38. Brenner H, Kloor M, Pox CP. Colorectal cancer. Lancet. 2014;383:1490–502.
39. Saini SD, Kim HM, Schoenfeld P. Incidence of advanced adenomas at surveillance colonoscopy in patients with a personal history of colon adenomas: a meta-analysis and systematic review. Gastrointest Endosc. 2006;64:614–26.
40. Bertario L, Russo A, Sala P, Pizzetti P, Ballardini Andreola S, Spinelli P. Predictors of metachronous colorectal neoplasms in sporadic adenoma patients. Int J Cancer. 2003;105:82–7.
41. Bonithon-Kopp C, Piard F, Fenger C, Cabeza E, O'Morain C, Kronborg O, et al. Colorectal adenoma characteristics as predictors of recurrence. Dis Colon Rectum. 2004;47:323–33.

42. Chung SJ, Kim YS, Yang SY, Song JH, Kim D, Park MJ, et al. Five-year risk for advanced colorectal neoplasia after initial colonoscopy according to the baseline risk stratification a prospective study in 2452 asymptomatic Koreans. Gut. 2011;60:1537–43.
43. van Heijningen EM, Lansdorp-Vogelaar I, Kuipers EJ, Dekker E, Lesterhuis W. Ter Borg F, etal. Features of adenoma and colonoscopy associated with recurrent colorectal neoplasia based on a large community-based study. Gastroenterology. 2013;144:1410–8.
44. de Jonge V, Sint Nicolaas J, van Leerdam ME, Kuipers EJ, Veldhuyzen van Zanten SJ, et al. Systematic literature review and pooled analyses of risk factors for finding adenomas at surveillance colonoscopy. Endoscopy. 2011;43:560–72.
45. Calderwood AH, Lasser KE, Roy HK, et al. Colon adenoma features and their impact on risk of future advanced adenomas and colorectal cancer. World J Gastrointest Oncol. 2016;8:826–34.
46. Sawhney MS, Dickstein J, Leclair J, Lembo C, Yee E, et al. Adenomas with high-grade dysplasia and early adenocarcinoma are more likely to be sessile in the proximal colon. Colorectal Dis. 2015;17(8):682–8.
47. Pickhardt PJ, Hain KS, Kim DH, et al. Low rates of cancer or high-grade dysplasia in colorectal polyps collected from computed tomography colonography screening. Clin Gastroenterol Hepatol. 2010;8:610–5.
48. Hassan C, Pickheadt PJ, Kim DH, et al. Systematic review: distribution of advanced neoplasia according to polyp size at screening colonoscopy. Aliment Pharmacol Ther. 2009;31:210–7.
49. Pickhardt PJ, Kim DH, Pooler BD, et al. Assessment of volumetric growth rates of small colorectal polyps with CT colonography: a longitudinal study of natural history. Lancet Oncol. 2013;14:711–20.
50. Tutein Nolthenius CJ, Boellaard TN, de Haan MC, et al et al. Evolution of screen-detected small (6–9 mm) polyps after a 3-year surveillance interval: assessment of growth with CT colonography compared with histopathology. Am J Gastroenterol. 2015;110:1682–90.
51. Lieberman DA, Rex DK, Winawer SJ, Giardiello FM, Johnson DA, Levin TR. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology. 2012;143:844–57.
52. Steele RJ, Pox C, Kuipers EJ, et al. European guidelines for quality assurance in colorectal cancer screening and diagnosis. Endoscopy 2012; 44 Suppl 3: SE 140–150.
53. Walsh RM, Ackroyd FW, Shellito PC. Endoscopic resection of large sessile colorectal polyps. Gastrointest Endosc. 1992;38:303–9.
54. Davenport JR, Su T, Zhao Z, et al. Modifiable lifestyle factors associated with risk of sessile serrated polyps, conventional adenomas and hyperplastic polyps. Gut. 2018;67:456–65.
55. Burnett-Hartman AN, Passarelli MN, Adams SV, et al. Differences in epidemiologic risk factors for colorectal adenomas and serrated polyps by lesion severity and anatomical site. Am J Epidemiol. 2013;177:625–37.

Figures

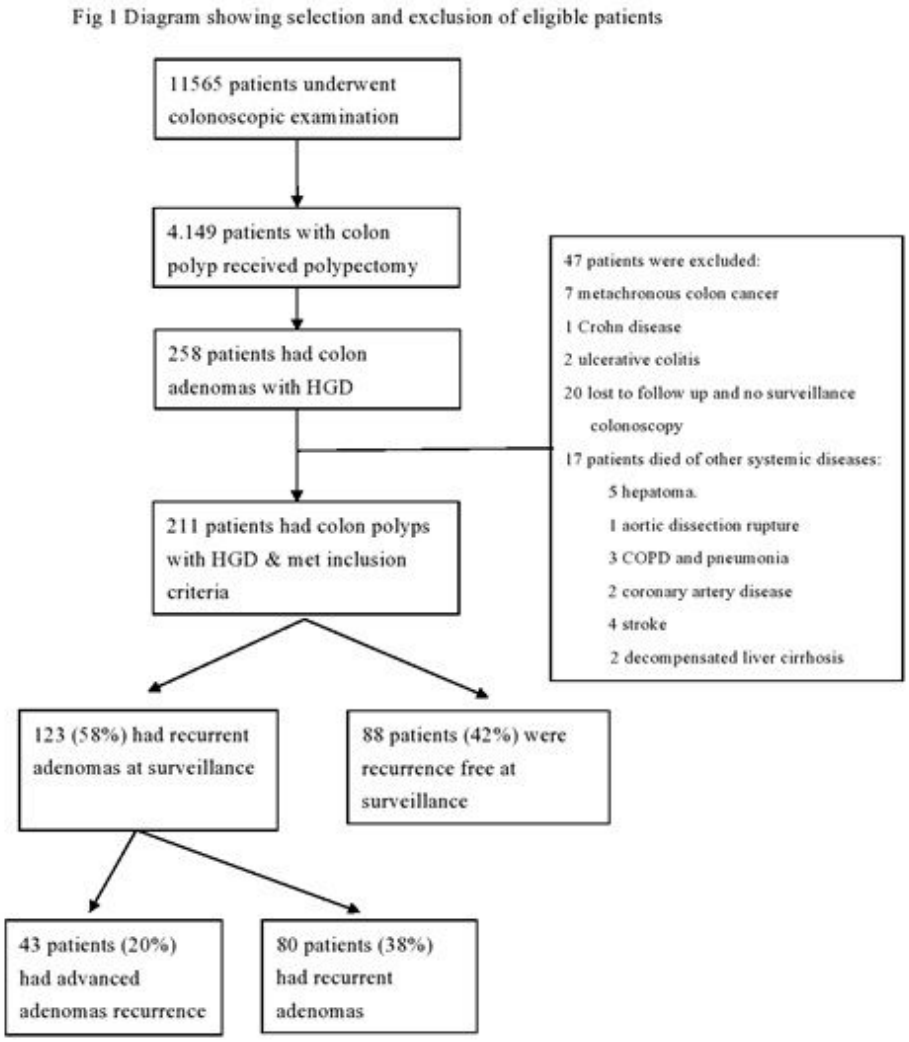

Figure 1

Diagram showing selection and exclusion of eligible patients