Prevalence of advanced histologic features in diminutive colon polyps

Nuretdin Suna[1], Aydın Şeref Köksal[2], Hakan Yıldız[1], Erkan Parlak[2], Ufuk Barış Kuzu[1], Mahmut Yüksel[1], Onur Aydınlı[1], Nesrin Turhan[3], Şükran Zişan Sakaoğulları[3], Zeki Mesut Yalınkılıç[1], Yasemin Özin[1], Nurgül Şaşmaz[1]

(1) Türkiye Yüksek İhtisas Hospital, [1]Department of Gastroenterology and [3]Pathology, Ankara, Turkey ; (2) Sakarya University Medical School, Department of Gastroenterology, Sakarya, Turkey.

Abstract

Background/Aims : **Accurate in vivo differentiation of colon polyp histology may serve to prevent the resection of diminutive hyperplastic polyps in the distal colon or the need for histologic assesment of diminutive polyps after resection. The clinical implementation of these strategies depends on the prevalence of advanced histologic findings among diminutive polyps. We aimed to determine the prevalence of advanced histologic features (villous features, high-grade dysplasia, and adenocarcinoma) in diminutive colon polyps and compare it to small and larger polyps.**

Patients/Methods : **The data of patients who had undergone elective colonoscopy at a tertiary-care referral center were retrospectively reviewed. The size, morphology, and location of all polyps were recorded. Polyps were divided into 3 groups according to their size : diminutive (≤ 5 mm), small (6-9 mm), and large (≥ 10 mm).**

Results : **A total of 7160 polyps in 3226 eligible patients were evaluated. The mean diameter of the polyps were 6.7 ± 4.9 mm. Histopathologic diagnosis were adenomatous in 4548 (63.5%) and non-adenomatous in 2612 (36.5%). Out of 7160 polyps, 4902 (68.5%) were diminutive (1-5 mm), 1360 (19%) were small (6-9 mm), and 898 (12.5%) large (≥ 10 mm) polyps. Among the diminutive polyps 2739 (55.9%) had adenomatous histology. There were 66 polyps (1.3%) with advanced histology in the diminutive group, 72 (5.2%) in the small group, 263 (29.2%) in the large polyp group. Diminutive polyps had a lower frequency of advanced histology compared to small and large polyps (p = 0.001). When the histology of the polyps were evaluated based on the size of the largest polyp the patient has, 2202 patients had polyp(s) ≤ 5 mm. The frequency of advanced histology was 2.2% in these patients.**

Conclusions : **The prevalence of advanced histology in diminutive polyps is quite low (1.3%) which supports the clinical implementation of discard, resect and discard strategies in diminutive polyps.** (Acta gastroenterol. belg., **2015**, 78, **287-291**).

Key words : colon, polyp, histology.

Introduction

Endoscopic polypectomy is the standart care for the treatment of all colon polyps. Once removed, the polyps are sent to pathology laboratory for histopathologic analysis in order to exclude the presence of invasive cancer and determine the future colonoscopy surveillance intervals. However, in recent years imaging technologies such as chromoendoscopy and electronic chromoendoscopy (NBI, FICE, I-Scan and autofluorescence) have revealed promising results for the real time assesment of colon polyp histology (1,2). Accurate in vivo differentiation between adenomatous and hyperplastic histology may serve to prevent the resection of diminutive hyperplastic polyps in the distal colon (discard strategy) or the need for histologic assesment of diminutive polyps after resection (resect and discard strategy) which decreases the duration, cost, and complications of colonoscopy.

The clinical implementation of discard, resect and discard strategies depends on multiple variables including the accuracy of electronic chromoendoscopy in prediction of in vivo adenomatous polyp histology and the prevalence of advanced histologic findings among diminutive polyps. American Society for Gastrointestinal Endoscopy (ASGE) recently developed a Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) statement defining the necessity of a ≥ 90% negative predictive value (when used with high confidence) of electronic chromoendoscopy for adenomatous histology and ≥ 90% agreement (when used with high confidence) in assignment of post-polypectomy surveillance intervals when compared with decisions based on pathology assessment of all identified polyps for application of discard, resect and discard strategies, respectively (3).

In this study we aimed to determine the prevalence of advanced histologic features (villous features, high-grade dysplasia, and adenocarcinoma) in diminutive colon polyps in order to determine whether it could support the clinical implementation of discard, resect and discard strategies.

Methods

Study design/setting

The study was a retrospective analysis of the data of patients who had undergone colonoscopy at Gastroenterology Department of Türkiye Yüksek İhtisas Hospital, a tertiary-care referral center, between 2007 and 2013. The study was approved by the Institutional Review Board.

Participants

The study group included patients who had undergone elective colonoscopy for screening, surveillance or

Correspondence to : Nuretdin Suna, M.D., Turkiye Yuksek Ihtisas Training and Research Hospital, Department of Gastroenterology, Atatürk Bulvarı Kızılay Sokak, No : 4, PC : 06100, Sıhhiye, Ankara, Turkey.
E-mail : nurettinsuna.44@hotmail.com

Submission date : 20/03/2015
Acceptance date : 12/05/2015

evaluation of symptoms. Exclusion criteria were history of inflammatory bowel disease, colectomy, colon cancer, or polyposis syndrome, use of antiplatelet or anticoagulant drugs that precluded removal of polyps, and refusal to undergo polypectomy. Patients with inadequate bowel preparation, in whom the cecum could not be reached or those who underwent polypectomy but the polyp could not be retrieved for histopathologic analysis were also excluded.

Colonoscopy procedure

Colonoscopies were performed by either gastroenterology attending physicians or gastroenterology fellows under the supervision of attending physicians. Commercially available standart definition colonoscopes (Olympus-PCF- Q260AL/I, Olympus-CF-Q260 DL/I, Fujinon EC-530WL), Evis Lucera CV-260SL video processor and high definition LCD monitor (OEV191H, Olympus Medical System Corp, Tokyo, Japan) were used. Most of the patients did not receive intravenous sedation or antispasmodics during colonoscopy.

The endoscopists screened the colon with standart definition white-light. Electronic or optic magnification were not used. If a polyp was detected during the examination, the size, morphology, and location of it was recorded. The size of the polyps were estimated by comparing it to the size of an open biopsy forceps or snare. Polyps were divided into three groups according to their size : diminutive (≤ 5 mm), small (6-9 mm), and large (≥ 10 mm). Morphology was classified according to Paris classification (4). Location of the polyps were estimated by depending on the anatomic landmarks. Finally all of the polyps were removed by either cold biopsy or snare electrocautery and send to pathology laboratory in separate specimen containers for histopathologic analysis.

Assesment of polyp histology

Polyp histology was determined by experienced pathologists. WHO classification was used for the histology. Advanced histology was defined as the presence of villous features in more than 25% of the glands, high-grade dysplasia or cancer. High grade dysplasia was defined as marked pseudostratification or stratification of neoplastic nuclei that extend toward to the luminal half of the cells and usually contain significant pleomorphism, increased mitotic activity, atypical mitoses, and marked loss of polarity.

Statistical analysis

Statistical analyses were performed by using the SPSS software version 18. Continuous variables were summarized by using means and standart deviation. Categorical variables were summarized by using percentages and 95% confidence intervals were calculated. Continuous variables were compared by using the Student t test if normally distributed and the Mann-Whitney U test if not normally distributed. Chi-square test or Fisher's exact test were used for the comparison of categorical variables when appropriate.

Results

Study population

A total of 18579 patients underwent colonoscopy within 6 years. Among them 4250 (22.8%) were excluded because of poor bowel preparation in 1371 (7.3%), colitis in 1085 (5.8%), history of colectomy in 840 (4.5%), colon cancer in 441 (2.3%), unability to reach cecum in 245 (1.3%), unability to retrieve the polyp for histopathologic analysis in 121 (0.6%), use of antiplatelet or anticoagulant drugs that precluded removal of polyps in 104 (%0.5), and polyposis syndrome in 43 (0.2%). The remaining 14329 patients constituted the study group. Among them 11103 (77.4%) had normal colonoscopy and 3226 (22.6%) (2024 male, 1184 female, mean age : 61 ± 18 years) had at least one colorectal polyp.

Characteristics of the polyps

Histology of the polyps

A total of 7160 polyps in 3226 eligible patients were evaluated. The mean diameter of the polyps were 6.7 ± 4.9 mm. Histopathologic diagnosis were adenomatous in 4548 (63.5%) and non-adenomatous in 2612 (36.5%). Seventy (1.5%) of the adenomatous polyps were serrated adenomas (68 sessile serrated adenomas and 2 traditional serrated adenomas). Among the adenomatous polyps 401 (8.8%) had advanced histology : 196 (2.7%) with HGD, 187 (2.6%) with villous features, and 18 with intramucosal cancer. Fourteen sessile serrated adenomas and 2 traditional serrated adenomas had low grade dysplasia. Of the non-adenomatous polyps, 1015 were hyperplastic (38.9%), 1040 had edematous colon mucosa (39.8%), 170 (6.5%) had normal mucosa, and 139 (5.3%) had non-specific changes (7.4%). The remaining 248 (9.4%) had other benign etiologies including lymphoid aggregates, lipoma, carcinoid, leiomyoma, pseudopolyp, regenerative changes, inflammatory changes, and colitis.

Histology of the polyps by lesion size and location

When the polyps were separated into three groups according to their size, 4902 (68.5%) were diminutive (1-5 mm), 1360 (19%) small (6-9 mm), and 898 (12.5%) were large (≥ 10 mm) polyps. The histopathologic diagnosis of the polyps based on their size is presented in Table 1. Among the 4902 diminutive polyps, 2739 (55.9%) were adenomatous. Diminutive polyps located in the rectosigmoid colon had significantly less adenomatous histology (37.2%) compared to those located proximal to sigmoid colon (69.9%) (p = 0.001) (Fig. 1).

Table 1. — **Histopathology of colon polyps by lesion size**

	≤ 5 mm (n = 4902)	6-9 mm (n = 1360)	< 10 mm (n = 6262)	≥ 10 mm (n = 898)
Neoplastic	2739 (55.9%)	1017 (74.8%)	3756 (59.9%)	792 (88.2%)
Tubular adenoma	2647 (54%)	982 (72.2%)	3629 (57.9%)	642 (71.4%)
Traditional serrated adenoma	57 (1.1%)	6 (0.4%)	63 (1%)	7 (0.7%)
Villous component	35 (%0.71)	28 (2%)	63 (1%)	124 (13.8%)
High-grade dysplasia	31 (0.63%)	43 (3.1%)	74 (1.1%)	122 (%13.5)
Cancer	0	1 (0.07%)	1 (0.02%)	17 (1.8%)
Any advanced histology	66 (1.3%)	72 (5.2%)	138 (2.2%)	263 (29.2%)
Non-neoplastic	2163 (44.1%)	343 (25.2%)	2506 (40%)	106 (11.8%)

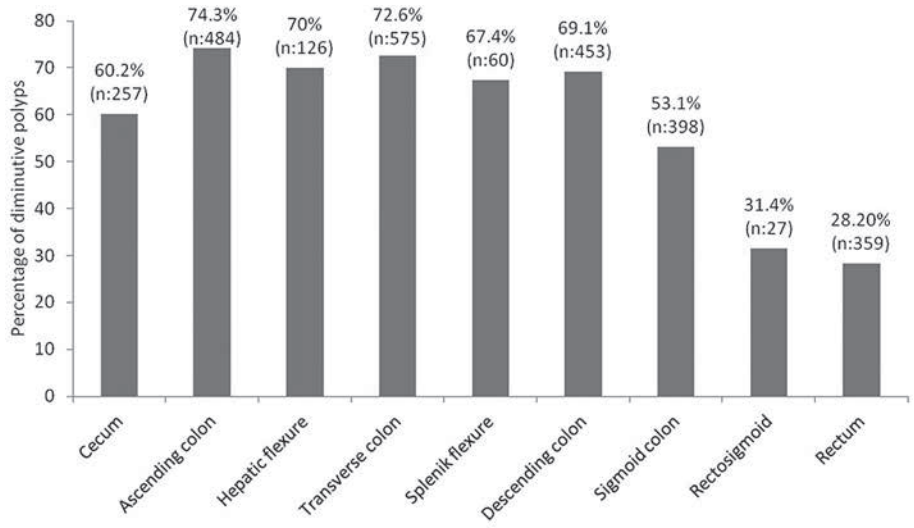

Fig. 1. — Prevalence of adenomatous histology in diminutive polyps by location

Prevalence of advanced histology by lesion size and location

There were 66 polyps (1.3%) with advanced histology in the diminutive group : 35 (0.71%) with villous features, 31 (0.63%) with HGD (Figs. 2, 3) and 11 (0.2%) with villous features +HGD. Of the small polyps, 72 (5.2%) had advanced histology : 43 (3.1%) with HGD, 28 (2%) with villous features, 1 (0.07%) with invasive cancer, and 10 (0.7%) with villous features +HGD. In the large polyp group, 263 (29.2%) had advanced histology : 124 (13.8%) with villous features, 122 (13.5%) with HGD, 17 (1.8%) with invasive cancer, and 46 (4.6%) with villous features +HGD.

The locations of the diminutive polyps harboring advanced histology are presented in Figure 4. Dimunitive polyps in the hepatic flexure had the highest prevalence of advanced histology (2.7%) followed by those in the transverse colon (2%), cecum (1.3%), ascending colon (1.2%), splenic flexure (1.1%), descending colon (1.1%), rectum (0.7%), and sigmoid colon (0.5%). Diminutive polyps located proximal to the sigmoid colon had more advanced histology (1.1%) than those located in the sigmoid colon and rectum (0.3%) ($p = 0.001$).

Diminutive polyps had significantly less villous features (0.7%) and HGD (0.63%) than small (2.1% and 3.1%, respectively) and large polyps (13.8% and 13.5 %, respectively) ($p = 0.001$ for both). Polyps < 10 mm had significantly lower frequency of villous features (1%) and HGD (1.1%) compared to those ≥ 10 mm (13.8% and 13.5%, respectively) ($p = 0.001$). Diminutive polyps had significantly lower frequency of advanced histology (1.3%) than small (5.2%) and large polyps (29.2%) ($p = 0.001$). Polyps < 10 mm had significantly lower frequency of advanced features (2.2%) compared to those ≥ 10 mm (29.2%) ($p = 0.001$).

When the histology of the polyps were evaluated based on the size of the largest polyp the patient has, 2202 patients had polyp(s) ≤ 5 mm, 636 had polyps

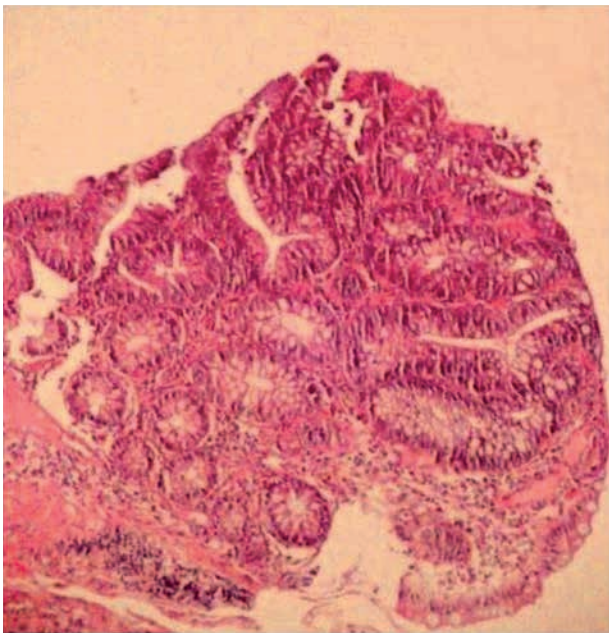

Fig. 2. — High grade dysplasia in a diminutive polyp (HE ×100).

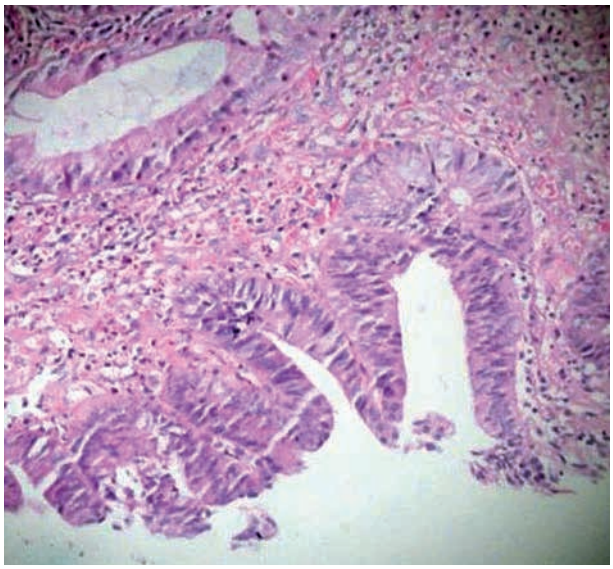

Fig. 3. — High grade dysplasia in a diminutive polyp (HE ×100).

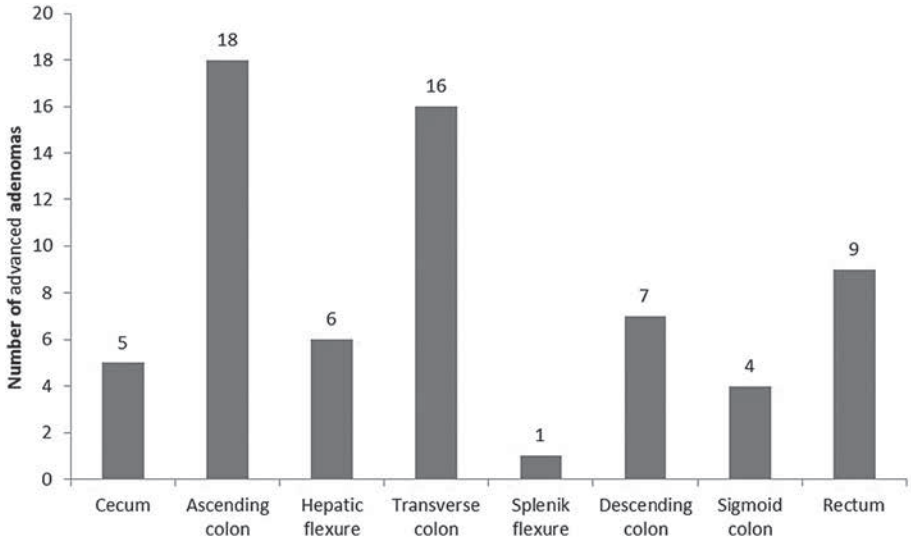

Fig. 4. — Distribution of diminutive polyps with advanced histology by location

6-9 mm, and 388 had ≥ 10 mm polyps. The frequency of advanced histology was in 2.2%, 9.7%, and 42.5% in these patients, respectively.

Discussion

In this study we retrospectively analysed the data of patients who had undergone elective colonoscopy for screening, surveillance or evaluation of symptoms and found no cancer and a low rate of (1.3%) advanced histological features in 4902 diminutive (≤ 5 mm) colorectal polyps.

Colorectal cancer risk is related to the size of a polyp which clearly increases in adenomatous polyps larger than 10 mm in size. Clarifying the cancer risk in smaller polyps, which constitute the majority of all, is important for determining the optimal interval of colorectal cancer screening with computed tomography colonography and clinical application of discard, resect and discard strategies based on in vivo differentiation of colon polyp histology by imaging technologies such as chromoendoscopy and electronic chromoendoscopy. ASGE recently stated that realtime endoscopic assessment of the histology of the colorectal polyps by electronic chromoendos-

copy should have a ≥ 90% negative predictive value for predicting adenomatous histology and ≥ 90% agreement in assignment of post-polypectomy surveillance intervals for application of discard, resect and discard strategies in dimunitive colorectal polyps (3). Electronic choromoendoscopy have a limited role in predicting the presence or absence of advanced histological features. Therefore the safety and cost effectivity of these strategies depend on the prevalence of adenomatous histology and advanced histological features in diminutive polyps. Although there is not an established threshold level, lower prevalence rates increase the safety and cost effectivity.

Four large screening series revealed a 49-64% prevalence rates of adenomatous histology in diminutive polyps (6-9). Those in the distal colon may have lower prevalence of adenomatous histology because of increased frequency of tiny hyperplastic lesions in this area (10). Our results were compatible with those in the literature and revealed 55.9% and 37.2% prevalence rates of adenomatous histology in diminutive colorectal polyps located throughout the colon and in the distal colon, respectively. Rex *et al*. retrospectively reviewed a database including 8798 diminutive polyps and revealed a 0.87% advanced histology among them (9). Lieberman *et al*. reported 1.7% advanced histology in 3744 diminutive polyps (6). A metaanalysis including 4 large series through 2009 revealed that 0.9% of patients with diminutive only lesions had an advanced adenoma (11). Later on retrospective analysis of data from 3 prospective clinical trials revealed a 0.5% prevalence rate of advanced histology in 1620 diminutive polyps (8). A recently published study reported a 1.3% prevalence rate of advanced histology in 10816 diminutive polyps (12). Although the prevalence of advanced histological features in diminutive polyps is very low in these studies, there are some other studies which have reported higher rates such as 2.7% in 1305 polyps and even 10% in 1025 polyps (5,13). The latter study was based on direct measurement of polyp size by certified pathologists and explained the lower rates of advanced histology in other studies with possible overestimation of polyp size by endoscopy which leads to interpretation of diminutive polyps as small polyps. In our study we found a 1.3% rate of advanced histology in diminutive polyps which was compatible with the ones reporting lower rates. In our study we defined advanced adenoma as the presence of villous features in more than 25% of the glands therefore our results may be underestimating the results of studies defining advanced histology as the presence of any villous component.

The limitations of our study were its retrospective desing and high number of endoscopists participating in the study. Endoscopic estimation of polyp size may not be accurate as reported by Schoen *et al*. who found an inaccurate estimation in 20% of the time, with a tendency to overestimate polyp size (14). On the other hand the study has 4920 diminutive polyps and is one of the largest cohorts.

In conclusion, the prevalence of advanced histology in diminutive polyps is quite low (1.3%) which supports the clinical implementation of discard, resect and discard strategies in diminutive polyps.

References

1. RASTOGI A., EARLY D.S., GUPTA N., BANSAL A., SINGH V., ANSSTAS M., JONNALAGADDA S.S., HOVIS C.E., GADDAM S., WANI S.B., EDMUNDOWICZ S.A., SHARMA P. Randomized, controlled trial of standard-definition white-light, high-definition white-light, and narrow-band imaging colonoscopy for the detection of colon polyps and prediction of polyp histology. *Gastrointest. Endosc*., 2011, **74** : 593-602.
2. IGNJATOVIC A., EAST J.E., GUENTHER T., HOARE J., MORRIS J., RAGUNATH K., SHONDE A., SIMMONS J., SUZUKI N., THOMAS-GIBSON S., SAUNDERS B.P. What is the most reliable imaging modality for small colonic polyp characterization ? Study of white-light, autofluorescence, and narrow-band imaging. *Endoscopy*, 2011, **43** : 94-99.
3. REX DK., KAHI C., O'BRIEN M., LEVIN T.R., POHL H., RASTOGI A., BURGART L., IMPERIALE T., LADABAUM U., COHEN J., LIEBERMAN D.A. The American Society for Gastrointestinal Endoscopy PIVI (Preservation and Incooparation of Valuable Endoscopic Innovations) on real-time endoscopic assesment of the histology of diminutive colorectal polyps. *Gastrointest. Endosc*., 2011, **73** : 419-422.
4. The Paris endoscopic classification of superficial neoplastic lesions : esophagus, stomach, and colon : November 30 to December 1, 2002. *Gastrointest. Endosc*., 2003, **58** : S3-S43.
5. TSAI F.C., STRUM W.B. Prevalence of advanced adenomas in small and diminutive colon polyps using direct measurement of size. *Dig. Dis. Sci*., 2011, **56** : 2384-2388.
6. LIEBERMAN D., MORAVEC M., HOLUB J., EISEN G. Polyp size and advanced histology in patients undergoing colonoscopy screening : implications for CT colonography. *Gastroenterology*, 2008, **135** : 1100-1105.
7. PICKHARDT P.J., CHOI J.R., HWANG I., BUTLER J.A., PUCKETT M.L., HILDEBRANDT H.A., WONG R.K., NUGENT P.A., MYSLIWIEC P.A., SCHINDLER W.R. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *N. Engl. J. Med*., 2003, **349** : 2191-200.
8. GUPTA N., BANSAL A., EARLY D.S., JONNALAGADDA S., WANI S.B., EDMUNDOWICZ S.A., SHARMA P., RASTOGI A. Prevalence of advanced histological features in diminutive and small colon polyps. *Gastrointest. Endosc*., 2012, **75** : 1022-1030.
9. REX D.K., OVERHISER A.J., CHEN S.C., CUMMINGS O.W., ULBRIGHT T.M. Estimation of impact of American College of Radiology recommendations on CT colonography reporting for resection of high-risk adenoma findings. *Am. J. Gastroenterol*., 2009, **104** : 149-153.
10. HEWETT D.G., HUFFMAN M.E., REX D.K. Leaving distal colorectal hyperplastic polyps in place can be achieved with high accuracy by using narrow-band imaging : an observational study. *Gastrointest. Endosc*., 2012, **76** : 374-380.
11. HASSAN C., PICKHARDT P.J., KIM D.H., DI GIULIO E., ZULLO A., LAGHI A., REPICI A., IAFRATE F., OSBORN J., ANNIBALE B. Systematic review : distribution of advanced neoplasia according to polyp size at screening colonoscopy. *Aliment. Pharmacol. Ther*., 2010, **31** : 210-217.
12. CHIU H.M., CHANG L.C., SHUN C.T., WU M.S., WANG H.P. Current management of diminutive colorectal polyps in Taiwan. *Digestive Endoscopy*, 2014, **26** (Suppl. 2) : 64-67.
13. BUTTERLY L.F., CHASE M.P., POHL H., FIARMAN G.S. Prevalence of clinically important histology in small adenomas. *Clin. Gastroenterol. Hepatol*., 2006, **4** : 343-348.
14. SCHOEN R.E., GERBER L.D., MARGULIES C. The pathologic measurement of polyp size is preferable to the endoscopic estimate. *Gastrointest. Endosc*., 1997, **46** : 492-496.