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The indirect role of site distribution in high-grade dysplasia in adenomatous colorectal polyps

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ABSTRACT

Background: The appropriate application of Endoscopic modalities for polypectomy depends on the likelihood that the adenoma in question harbors invasive cancer. While prior studies have evaluated polyp size and morphology in assessing the risk of malignancy, in recent decay some authorities have paid more attention to dysplasia. All in all, the relative risk of cancer based on polyp distribution in correlation with dysplasia has not been statistically studied which is done in our study.

Methods and Materials: Between June 2001 and March 2004, the distribution of 130 adenomatous polyps was compared with synchronous invasive or in situ cancer. Factors such as Patient age, Patients gender, location of lesion, size of polyp, histological subtype of adenoma on biopsy, degree of dysplasia, synchronous cancer, color of polyp, and number of polyps were included in the data collection.

Results: Multivariate logistic regression test was used to evaluate the association between malignancy and various clinical variables. It revealed histological subtype, high grade of dysplasia and size to be independent predictor of malignancy. However; left-sided location and histological subtype to be independent risk factor for high-grade dysplasia.

Conclusion: Lesions greater than 1 cm in diameter with high-grade dysplasia after speleinc flexure should be managed as presumptive malignancies with segmental colon resection. In intermediate-risk lesions the physician should decide individually.

KEY WORDS: Adenomatous Polyp, Dysplasia, Colorectal Distribution

INTRODUCTION

Colorectal Cancer is the most important malignancies in Iran and the second most common cancer overall.[1]Most colorectal cancers are believed to arise from benign adenomatous polyps[2,3],and this concept regarding the adenoma-carcinoma sequence is the main reason for the preventing screening and removal of the adenomatous polyps using colonoscopy.[4] To this end, a great number of studies have focused on endoscopically or surgically removed adenomas, correlating different epidemiologic and pathologic features of the patient and the adenoma respectively with the finding of invasive cancer or future risk.[5]The two factors that have been repeatedly shown to be independent risk factors for malignancy include the size of the lesion and its histologic subtype of adenoma,with the risk of invasive cancer increasing with large, villous type growth. The aim of this study was thus to determine whether the distribution of adenomatous polyps with that of colorectal cancer. We therefore have examined the extent correlation between high-grade dysplasia on biopsies and their distribution has not been studied.

MATERIALS AND METHODS

From approximately 23329 biopsies performed at Milad Hospital Tehran, from Jun 2001 to March 2004, 156 consecutive patients who had undergone biopsy of a solitary adenoma or synchronous invasive or in situ colorectal carcinoma were reviewed. Patients were excluded from analysis if they had been previously diagnosed with familial adenomatous Polyposis or inflammatory bowel disease, or if correlation of the lesions on endoscopy and surgical resection could not be confirmed. All in all, 130 patients were included in our study.Factors such as patient age, patient gender, location of lesion, size of lesion, histologic subtype of adenoma on biopsy, degree of dysplasia on biopsy and resection, synchronous cancer, color of polyp and number of polyps were included in the data collection. Polyps were classified as tubular if they had 0% to 25% villous component, tubulovillous lesion if they contained 26% to 75%

villous component, and villous lesions if greater than 75% villous component. Dysplasia was divided into high grade or low grade based on the pathologist's interpretation. All pathology specimens received intradepartmental review. Univariate and multivariate logistic regression was used to evaluate the association between malignancy and various clinical variables.Variables included patient age (by decade), location of lesion and its position to speleinc flexure, size of lesion (< 10 mm, >= 10 mm), histologic subtype of adenoma on biopsy (tubular, tubulovillous, villous), and degree of dysplasia (low or high grade).However, color of polyps and clinical indications of colonoscopy were included in our study.

All variables were treated as unordered categorical variables.

RESULTS

Twenty-one of 130 patients (16.2%) were found to have adenocarcinoma on pathologic examination of the surgical specimen. The distribution of adenomatous polyps and general characteristics of adenomas and carcinomas presenting with polyps were summarized in table 1. However, the variety of polyps' color and colonoscopic indication were explained in table 2.

Table 1: Characteristic of adenomas and carcinomas presenting with a biopsy results

Age	Adenomatous polyps	43±14.77
	Synchronous malignancy	50±12.2
Sex	Male	70(53.8%)
	Female	60(46.2%)
Site Distribution	Ascending	36(27.7%)
	Transverse	2(1.5%)
	Descending	47(36.2%)
	Recto sigmoid	45(34.6%)
Histologic type	Tubular	75(57.7%)
	Tubulovillous	27(20.8%)
	Villous	28(21.5%)
Grade of Dysplasia	High	32(24.6%)
	Low	98(75.4%)
Morphology	Pedunculated	111(85.4%)
	Sessile	19(14.6%)
Size	<10mm	100(76.9%)
	>=10mm	30(23.1%)
Synchronous Malignancy	In situ or invasive	21(16.2%)
	Without invasion	109(83.8%)
Colonoscopic Indication	-Rectal Bleeding	86(66.2%)
	- Rectal Bleeding + Abdominal pain	20(15.4%)
	-Constipation	6(4.6%)
	-Mucous diarrhea	4(3.1%)
	-General abdominal pain	9(6.9%)
	-Weight loss	5(3.8%)
Color	Creamy	117(90%)
	Cream Brown	6(4.6%)
	Brown	3(2.3%)
	Gray	1(0.8%)
	Gray Brown	1(0.8%)
	Red	1(0.8%)
	White Brown	1(0.8%)

Table 2: Rate of Occult Malignancy in Benign Biopsy Group in Relation to Degree of Dysplasia, Size and Site distribution

Risk of Malignancy	Degree of Dysplasia	Size	Site Distribution	Rate of Malignancy
High	High	> = 1cm	After SF*	42.58% (9/21)
Intermediate	High	< 1cm	After SF	28.57% (6/21)
Low	Low	< 1cm	Before SF	0% (0/21)

In our study, high-grade dysplasia, villous histology, left-sided location, and increasing size were all features associated with an increased chance of malignancy. The rate of malignancy rose from 4.1% in biopsies showing low-grade dysplasia to 53.1% in biopsies revealing high-grade dysplasia. Likewise, the histology of the biopsy was predictive of malignancy with tubular, tubulovillous, and villous features corresponding, respectively, to a 2.7%, 22.2% and 44.4% risk of malignancy in the surgical specimen. Size of the lesion revealed an increase in malignancy risk with =< 1 cm and > 1 cm lesions harboring occult malignancy in 10 %, and 36.7% of cases, respectively.

On multivariate analysis, only size, degree of dysplasia, and histologic type of adenoma were independent predictors of a lesion harboring a malignancy. Odd ratios for adenomas grater than 1 cm compared with lesions that were less than 1 cm demonstrated a 3.6-fold increased. High grade of dysplasia on biopsy was associated with an 12.95-fold increased risk of occult cancer compared with low-grade lesions (95% confidence interval= 4.5 to 37.9).However, there was an 16.4-fold increased risk for villous component compared with tubular lesions (95% confidence interval= 4.8 to 83.6).Interestingly, on multivariate analysis, left-sided location and histologic type of adenoma were independent predictors of a lesion harboring a high-grade dysplasia. The shift to left was predictive of dysplasia with before and after speleinc flexure, respectively, to a 5.4%, 32.3%.Segregation of all studies lesions into three risk categories based on the location of adenoma, sized and dysplasia suggests the lowest risk tumors were always benign, whereas the highest risk tumors were almost malignant (Table 3).

We did not find any significant correlation between color, age, sex and malignancy.

DISCUSSION

The presence or absence of invasive cancer is one of the most important determinants of appropriate management of a colonic adenoma. [6] Size, high-grade dysplasia, and histologic type were all found to be associated with an increased incidence with occult invasive cancer within an adenoma. [7, 8] A number of studies examining large numbers of resected polyps have demonstrated an association between these factors and the incidence of invasive cancer. (Table 3) We did find there is not the mutual under-

Table 3: Different studies in previous two decades in effective variable on malignancy

CountryYear	AuthorSample size	Dependent Variable	Histologic type	Size	Dysplasia	Shift to Lift
Japan(14)2004	Yamato M648	M	+	-	+	+
Spain(18)2004	Betes I.M1544	M(D→P)	+	+	+	+
USA(19)2004	Anderson Jc55	M(D→P)	+	+	+	NC
Italy(21)2004	Senore426	M(D→P)	+	+	+	NC
+USA(22)2003	Pinsky PF8802	M(D→P)	+	+	NC	NC
USA(23)2003	Lewis JD?	M(D→P)	NC	NC	-	NC
Taiwan(2)2002	Tze-Van f295	M	+	+	NC	NC
Switzerland(20)2001	Kulling D1681	M,D	+	+	+	+
Austria (24)2000	Hammer K834	M(D→P)	+	-	-	NC
Germany(25)2000	r.Scheiden225	M	NC	NC	NC	+
Switzerland(26)1999	Netzer P2272	M(D→P)	+	+	+	NC
Japan(27)1999	Yoichi735	M	NC	-	NC	+
USA(5)1999	Jerome M100	M	+	+	+	+
Italy(28)1997	Grassi A3951	M(>1cm)	+	+	+	+
Mexico(29)1996	Rocha R.JL.120	M	-	+	-	-
Spain(30)1995	Alonso100	M	+	-	+	-
Israel(31)1991	Pines A466	M	+	+	NC	+
Germany(19)1991	Nguyen NH907	D	+	+	→	+
USA(32)1991	Disario JA90	M	+	-	+	-
Italy(33)1990	Stolfi VM430	M	+	NC	+	-
USA(34)1990	Schuman BM52	M	NC	+	NC	-
USA(18)1990	O'Brien MJ3371	D	+	+	→	-
USA(35)1988	Stuls JP237	M	+	-	NC	-
1985(36)	Haggit RC129	M	-	NC	NC	+
Japan(17)1979	Shinya5786	M	+	+	NC	+
Our Study2005	130	M,D	+	+,-respectively	+	-,+respectively

M=Malignacy synchronously D=Dysplasia M (D→P) =Effect of distal malignancy on proximal lesions

-=negative effect +=Positive effect →=the studied variable NC= Not Consider

standing in all studies. The absence of such an association may be due to their selection of risk factors [9] or the environmental and genetic factors. [10]In Thailand, Rerknimitr showed that right-sided colorectal polyps were more risky than recto sigmoid. [12] Similarly, however, Yasser H. studied just site distribution between Hispanics and whites. [11] In our study, high-grade dysplasia on biopsy was a powerful predictor of the presence of invasive cancer in the resected specimens. Similar studies confirmed our conclusion. [5, 18, 20, 21, 27, 29]Directly, site distribution had a significant association with dysplasia. It means that left-sided polyps have the potential directly for high grade dysplasia indirectly for invasive or in situ cancer. Also, the role of Site distribution in some studies was mentioned. [5, 14, 17, 18, 20, 26, 28, 37] We believe this association is the first study to examine the ability of high-grade dysplasia and site distribution in an endoscopic biopsy to predict the presence of occult invasive or in situ cancer in adenomas of the colon.

CONCLUSION

Lesions less than 1 cm in diameter without high grade dysplasia located before speleinc flexure can be managed by endoscopic or laparoscopic resection when this expertise is available. Lesions greater than 1 cm in diameter with high-grade dysplasia after speleinc flexure should be managed as presumptive malignancies with segmental colon resection. In the remaining intermediate-risk lesions, treatment decisions will be predicted on the condition of the patient and the physician's treatment philosophy, but can be made with greater precision if the presence or absence of high-grade dysplasia in the biopsy specimen is taken into account.

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