Advanced colorectal adenoma

KEYWORDS: Colorectal Neoplasms; Adenoma; Colonic Polyps

ABSTRACT
Colorectal cancer (CRC) arises from colorectal adenoma, through multistep process, accompanied by alterations of suppressor genes and oncogenes. The term "advanced colorectal adenoma" (ACA) describes colorectal polyps greater than 1 cm in diameter and/or villous component and/or severe dysplasia. ACA is present in 9.6% of asymptomatic patients (age range, 50 to 75 years) with or without distal neoplasia. Size is the most frequently studied characteristic of ACA. Advanced histology (severe dysplasia, carcinoma in situ, advanced carcinoma) was found in 6.1% and 2.0% patients with small and diminutive adenoma, respectively. Index ACA, especially recto-sigmoid ACA are marker for proximal, synchronous growth, advanced neoplasm (ACA or CRC), especially in older patients. The risk of metachronous adenomas is closely related to the pathology of initial adenomas (ACA) allowing identification of a high-risk group of adenoma patients for close surveillance after initial polypectomy.

INTRODUCTION
There is no doubt that the vast majority of colorectal cancers (CRC) arise from precursor lesions, benign adenomatous polyps or adenomas (1). Progression from adenoma to CRC is a multistep process, accompanied by alterations of several suppressor genes that result in abnormalities of cell regulation, and has a natural history of 10-15 years (2). The adenoma-carcinoma sequence postulates that adenomas contain dysplastic epithelium, which arises from mutations in different genes (3).

ADVANCED COLORECTAL ADENOMA
Confusion exists in the use of terms dysplasia and adenoma between West and East. In the West, protruded (polypoid) or slightly elevated noninvasive neoplastic lesions are called adenomas, while flat or depressed noninvasive lesions are called dysplasia. In the East, both described types of lesions are called adenomas and characterized as protruding, flat or depressed. Trend to use the terms polypoid and nonpolypoid adenomas is present now. Polypoid adenomas correspond to protruded polyps, but nonpolypoid adenomas include slightly elevated polyps and the flat or depressed areas of dysplasia (or adenoma) (3). The important indicators for progression from adenoma to carcinoma have been pathologic characteristics of the adenoma, such as larger size, villous (as opposed to tubular) histology, and severe (as opposed to mild to moderate) dysplasia (4-6).

Recently literature has adopted the term "advanced colorectal adenoma" (ACA) to describe colorectal polyps greater than 1 cm in diameter and/or villous component and/or severe dysplasia, features predicting an increased likelihood of malignant transformation (7,8). Advanced neoplasm was defined as CRC or previously described ACA (9). It is obvious that ACA are link in the chain from benign adenoma through malignant altered adenomas to advanced CRC (10). There is no satisfactory epidemiological data in literature about frequency of ACA in symptomatic and asymptomatic persons. ACA was present in 9.6% of asymptomatic patients (age range, 50 to 75 years) with or without distal neoplasia (11). Incidence rates for ACA at follow up flexible sigmoidoscopy 3 and 5 years, respectively, after negative examination were 0.9% and 1.1%, respectively (12). However, even large adenomas do not universally develop into carcinoma (13). In a study based on individuals living in the pre-colonoscopy era with polyps diameters of 1 cm or greater identified on barium enema who were not candidates or declined operative management, 4% developed colorectal carcinoma at 5 years, 7.4% at 10 years, and 12.4% at 20 years (14,15).

Of these three characteristics of advanced adenoma, the most frequently studied characteristic in epidemiological studies has been size (16,17). Size, proportion of villous histology, and degree of dysplasia are highly correlated with one another (17). Invasive colorectal carcinoma and carcinoma in situ are sometimes found in small tubular adenomas (18). The distribution of highly dysplastic adenomas by subsite is more highly correlated with that of carcinoma than that of villous or large adenomas (19,20). An analysis of 1878 small (6-10 mm) and diminutive (5 mm) colorectal polyps revealed advanced histology (severe dysplasia, carcinoma in situ, advanced carcinoma) in 6.1% and 2.0% respectively, indicating that at colonoscopy all colorectal polyps have to be removed (21). Urbanski et al. (22) found colorectal carcinoma in 15% of colorectal adenoma less than 10 mm. There are conflicting data in relation to proximal lesions in patients with distal advanced adenoma (10). Colonoscopy disclosed synchronous advanced and/or non-advanced neoplasm in 53.78% patients with ACA. ACA was the index lesions in 50% patients with synchronous advanced and/or non-advanced neoplasm, making a total of 26.89% patients with ACA. Advanced proximal adenoma was found in 16% patients with large distal adenoma (> 10mm). In patients with distal adenoma risk for proximal lesions increased with increasing age, size, and number of distal adenoma (23). The prevalence of advanced proximal neoplasm was similar among patients without tubular adenomas at sigmoidoscopy, those with tubular adenomas 1 cm in diameter, and those with tubular adenomas 1 cm in diameter or larger-prevalence, 5.3%, 5.5% and 5.6%, respectively. In the group of patients with distal tubulo-villous or villous adenoma, 12.1% had advanced proximal neoplasm. Patients with advanced distal histology and those older than 65 years are at increased risk for proximal advanced neoplasm (24). Schoen et al. found incidence of 5.9% proximal ACA in patients with recto-sigmoid ACA and it was greater percentage of proximal ACA compared with those with a non-advanced distal adenoma (2.9%, p<0.05) (25). Nagorni (10) reported synchronous proximal ACA (single or multiple), or associated proximal synchronous ACA and CRC, in 20.62% patients with distal recto-sigmoid ACA.

METACHRONOUS ADVANCED COLORECTAL ADENOMA
Metachronous adenomas are detected in 20.70.3% patients after polypectomy. Incidence of metachronous adenomas is greater after removing of multiple than single colorectal adenoma. Villous structure of adenoma is a predic-
tor for recurrence of adenoma (26). Nagomi (10) found 9.37% advanced metachronous adenoma 36-72 months after polypectomy of index ACA, as same as Fornasarig et al (27). All metachronous ACA were found in patients aged>60 years with three or more index advanced neoplasia. The risk of meachronous adenomas is closely related to the pathology of initial adenomas (ACA) allowing identification of a high-risk group of adenoma patients for close surveillance after initial polypectomy (28).

CONCLUSION

Index ACA, especially recto-sigmoid ACA are marker for proximal, synchronous growth, advanced neoplasim (AA or CRC), especially in older patients. Small colorectal polyp need complete colonoscopy and polypectomy and histological evaluation of all polyloid lesions. Metachronous ACA are not rare finding.

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