

## Clinical and molecular analysis of early invasive carcinoma of the colon and rectum: identification of predictor(s) of metastasis

K. Hirano, M. Mai, T. Minamoto

Early colorectal carcinoma is defined as a primary adenocarcinoma confined to the mucosa or submucosa (early invasive carcinoma, EIC), whether it has metastasized or not. Metastasis occurs in 10-15% of all EIC patients. The clinical management of EIC remains controversial, because the decision for endoscopic or local resection vs. radical bowel resection depends on the risk of metastasis. Lymph node metastasis was reported to correlate with such morphological factors as nonpolypoid growth pattern, poorly differentiated histological characteristics, depth of invasion, and lymph vessel involvement. However, prediction of metastasis on the basis of such morphological factors alone is difficult. Reliable risk factors susceptible to more objective determination are needed to assess the presence of metastasis and, in turn, make possible a more reasonable way of identifying the appropriate therapy. In order to place the choice of therapy (endoscopic resection or radical surgery) in early invasive carcinoma of colon and rectum on a more rational basis, this study sought to identify molecular predictor(s) of metastasis. Several morphological risk factors (histological type, degree of tumor invasion, lymphatic and venous invasion) and expression of p53 and p27 proteins in the primary tumor were compared in 80 patients with EIC, including 12 (15%) with metastasis and/or recurrence. Of the factors enumerated, deeper invasion of the submucosal layer, lymphatic/venous invasion, p53 overexpression, and decreased expression of p27 were significantly correlated with metastasis. The results also indicated that altered expression of p53 or p27 is independently relevant to metastasis of EIC. Analysis of these markers together with determination of the morphological risk factors could complement the identification of patients with metastasis on the basis of known morphological risk factors. Since the molecular factors can be assessed more objectively than the morphological parameters, they may strengthen the ability to identify EIC that has undergone, or will undergo, metastasis.

**Table 4. Relative influence of the morphological risk factors and altered expression of p53 and p27 proteins on metastasis in the patients with colorectal EIC**

Variables	Metastasis		Chi-square analysis
	Present	Absent	
Gross type (n=80)			
Type I (protruding)	6	44	NS
Type II (superficial)	6	24	p=0.33197
Histological type (n=80)			
Well differentiated	4	47	p=0.01744
Moderately differentiated	8	21	
Degree of invasion (n=80)			
Non-massive	1	38	p=0.00238
Massive	11	30	pc=0.00463
Lymphatic/venous invasion (n=80)			
Absent	5	60	p=0.00014
Present	7	8	
p53 overexpression (n=71)			
Absent	3	43	p=0.0046
Present	8	17	
p27 expression (n=66)			
High	2	38	p=0.00161
Low	9	17	pc=0.00486

Abbreviation: n, number of patients analyzed; NS, no significant difference; pc, p value adjusted by Yates' correction