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Multiple-marker reverse transcriptase-polymerase chain reaction study.

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**INTRODUCTION:** Lymph node status is a key factor for disease staging and is the main determinant for adjuvant therapy of colorectal cancer. The current staging procedure is unable to identify occult metastasis in lymph nodes, which is likely to be an important cause of treatment failure in some early-stage patients. The detection of occult metastasis could identify a patient subgroup at risk for disease relapse that would benefit from adjuvant therapy. The purpose of this study was to establish and test a multimarker reverse transcriptase-polymerase chain reaction assay for the molecular detection of occult metastases in lymph nodes. **METHODS:** Forty-four patients with colorectal cancer and 14 patients with benign bowel diseases undergoing colonic resection were enrolled in the study. Reverse transcriptase-polymerase chain reaction was used to detect expression of three epithelial markers, carcinoembryonic antigen, cytokeratin 20, and guanylyl cyclase C, in fresh colorectal lymph node tissue. **RESULTS:** Forty-six of 47 (97.9 percent) histologically positive lymph nodes were also positive by reverse transcriptase-polymerase chain reaction. Of 221 histologically negative nodes, 97 (43.9 percent) were positive for at least one of the three markers by reverse transcriptase-polymerase chain reaction: 24.9 percent for carcinoembryonic antigen, 16.7 percent for cytokeratin 20, and 24.9 percent for guanylyl cyclase C. Among these were 13 of 20 stage I and II cases, implying a staging shift to stage III by molecular diagnosis of occult metastasis. Fifty-nine additional nodes were found to be positive for occult metastases in 22 of 24 stage III and IV patients. **CONCLUSIONS:** These results indicate that occult metastases are detectable by reverse transcriptase-polymerase chain reaction in histologically negative lymph nodes from colorectal cancer. The use of a panel of three markers improves the specificity of the method.