Novel risk stratification for recurrence after endoscopic resection of advanced colorectal adenoma

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Background: Advanced colorectal adenoma (ACA) refers to adenomas with the following predictive characteristics: ≥1 cm in diameter, and/or villous component, and/or high-grade dysplasia. ACA has high risk of transforming to colorectal cancer, and the recurrence rate is relatively high.

Objective: To assess the outcomes of patients with ACA undergoing endoscopic resection and to identify risk factors for local recurrence and development of metachronous advanced neoplasm.

Design: Retrospective cohort study.

Setting: Tertiary care medical center.

Patients: From 2005 to 2011, the records of 3625 patients who underwent colonoscopic polypectomy at Seoul National University Hospital were retrospectively reviewed. Patients with synchronous colorectal cancers, inflammatory bowel disease, previous colorectal resection, loss to follow-up, and incomplete resection were excluded.

Intervention: Endoscopic resection for ACA.

Main Outcome Measurements: Local recurrence and metachronous advanced neoplasm.

Results: The study included 917 patients with 1206 ACAs. The median duration of follow-up was 28.5 months (interquartile range, 12.8-51.7). Independent risk factors for local recurrence included ACA with 2 or more predictive characteristics (adjusted hazard ratio [HR], 2.46; 95% confidence interval [CI], 1.11-5.48; $P = .027$) and piecemeal resection (adjusted HR, 6.96; 95% CI, 1.58-30.71; $P = .010$). Independent risk factors for metachronous advanced neoplasm were male gender (adjusted HR, 1.65; 95% CI, 1.02-2.65; $P = .041$), ≥3 adenomas (adjusted HR, 2.56; 95% CI, 1.72-3.82; $P < .001$), and ≥3 ACAs (adjusted HR, 1.44; 95% CI, 1.01-2.06; $P = .045$).

Limitations: Retrospective design.

Conclusion: ACAs with 2 or more predictive characteristics recurred locally at a higher rate than ACAs with 1 predictive characteristic. These results suggest that patients who are found to have ACAs with 2 or more predictive factors at index colonoscopy are at higher risk for local recurrence, and follow-up colonoscopy should be performed sooner. (Gastrointest Endosc 2015;81:655-64.)

Abbreviations: ACA, advanced colorectal adenoma; CI, confidence interval; CRC, colorectal cancer; ESD, endoscopic submucosal dissection; HR, hazard ratio; IQR, interquartile range; SNUH, Seoul National University Hospital.

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Colorectal cancer (CRC) is the third most common cancer in men and the second most common in women worldwide.[1] The prevalence of CRC is increasing rapidly because of the spread of Westernized diet and lifestyle, especially in Asia, Eastern Europe, and South America.[2] However, the prevalence and mortality rate of CRC are decreasing in the United States,[2] probably because of improved treatment and early detection as a result of successful surveillance.[3,4]

CRC is a typical cancer that follows an adenoma–carcinoma sequence.[5,6] Adenoma, a precancerous lesion, becomes CRC in 5 to 15 years.[5,7,8] Advanced colorectal adenoma (ACA) refers to colorectal adenomas with the following predictive characteristics: $\geq$1 cm in diameter, and/or villous component, and/or high-grade dysplasia.[9-11] ACA has a higher risk of developing into adenocarcinoma than non-ACA, and the recurrence rate of adenoma after endoscopic resection of ACA is high. The prevalence of metachronous advanced neoplasm in patients with ACA at the index colonoscopy was reported to be 20% to 26% at 5 years.[12-14] Hence, risk stratification followed by appropriate surveillance is essential for early detection of recurrence and reduction of cancer risk after the endoscopic resection of ACA.

Guidelines from the U.S. Multi-Society Task Force on Colorectal Cancer have recommended 3-year surveillance for patients with each predictive characteristic of ACAs.[15] Previous studies have shown recurrence rates of 6% to 10% at 3 years after removal of adenomas larger than 1 cm and concluded a 3-year follow-up is adequate.[9,14,16-19] By contrast, the risk of recurrence for 2 other characteristics, villous histology and high-grade dysplasia, has not been determined conclusively. The recurrence rate and risk factors for recurrence of adenoma are well known, but the risk factors for recurrence of ACA have not yet been determined. In addition, it has not been determined whether ACAs satisfying 2 or 3 characteristics have higher risk of recurrence after endoscopic resection than ACAs with only 1 characteristic. Therefore, the aim of this study was to assess the outcomes of patients with ACA undergoing endoscopic resection and identify risk factors for local recurrence and metachronous advanced neoplasm, with attention paid to risk based on the number of ACA predictive characteristics.

METHODS

Study population and ethical considerations

We retrospectively reviewed the medical records of 3625 patients who underwent colonoscopic polypectomy from January 2005 to December 2011 at Seoul National University Hospital (SNUH), a tertiary referral center in Korea. Patients found to have pathologic confirmation of ACA were enrolled in this study. The exclusion criteria were as follows: (1) patients with inadequate pathology reports; (2) patients with synchronous CRCs; (3) patients who underwent previous colorectal resection; (4) patients with hereditary CRCs, including familial adenomatous polyposis and hereditary nonpolyposis CRC; (5) patients with inflammatory bowel disease; (6) patients who did not undergo follow-up colonoscopy after endoscopic resection; and (7) patients who had incomplete resection of ACA.

The completeness of resection was judged by endoscopists. Complete resection was defined as no remaining adenomatous tissue after EMR or endoscopic submucosal dissection (ESD) based on endoscopic findings. Incomplete resection was defined as remaining macroscopic adenomatous tissue after EMR or ESD. If an endoscopic resection was considered to be an incomplete resection macroscopically, electrocauterization, additional EMR or surgery was performed for residual tissue removal. The study protocol was approved by the Institutional Review Board Committee at SNUH (IRB No. 1303-009-470).

Indications for and techniques of polypectomy

Colonoscopy was performed using a standard colonoscope (CF H260AL; Olympus, Tokyo, Japan). Generally, 4 L polyethylene glycol solution was used for bowel preparation. Colonoscopic polypectomy was conducted when patients showed adequate bowel preparation. EMR and ESD were performed for the resection of ACAs. ESD was indicated for large (>2 cm in diameter) polyps for which en bloc resection by snare EMR was difficult.[20] Piecemeal resection was also performed for large polyps for which en bloc resection was technically difficult.

The inject-and-cut technique was used for EMR. A submucosal injection (NM-4U-1; Olympus) using epinephrine diluted with saline solution containing indigo carmine was performed. When the polyp was elevated above the mucosa, it was enclosed and grasped by a wire snare (SD-12L/U-1; Olympus). A cutting and coagulating electrical current was used to resect the polyp. For ESD, the area surrounding the adenoma was marked using a needle knife (KD-1L; Olympus) with electrical coagulation (20 W, VIO 300D; Erbe, Tübingen, Germany). Epinephrine diluted with saline solution containing indigo carmine was injected into the area surrounding the adenoma. After elevation of the mucosa, the polyp was incised using the needle knife, and the submucosa was dissected using an insulated-tip electrosurgical knife. Any visible vessels or bleeding in the polypectomy sites were coagulated or clipped to prevent delayed bleeding after either EMR or ESD. All colonoscopic resections were performed by 16 board-certified endoscopists with experience of at least 200 colon polypectomies.

All polyps detected at the index colonoscopy were removed as thoroughly as possible. A small number of patients who could not have complete removal of polyps because of numerous polyps at the index colonoscopy underwent additional colonoscopy for polypectomy within 1 month.

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