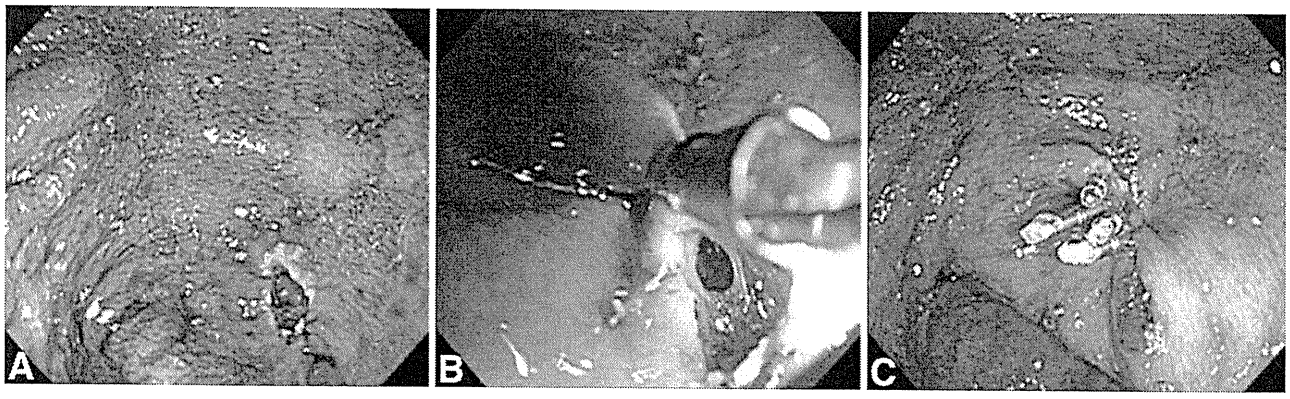

Figure 2. Colonoscopic clip closure of a small, linear perforation. **A,** A small, linear perforation is recognized after en bloc EMR of a cecal adenoma in a patient with ulcerative colitis being treated with steroids. **B,** The first clip is deployed, partially closing the tear. **C,** Completed closure is achieved with deployment of 4 clips. (Reproduced with permission from the ASGE)

MANAGEMENT

Until recently, surgery was the mainstay of treatment in the majority of patients, with nonoperative medical management in a select group (Fig. 1). Surgery is indicated in patients with large perforations, generalized peritonitis, or ongoing sepsis as well as in patients with concomitant pathology, such as a large sessile polyp, which is likely to be a carcinoma, unremitting colitis, or perforation complicating an obstructing colonic lesion. Other candidates for surgery include those whose conditions deteriorate with conservative management.[54] Surgery is associated with a significant morbidity (36%) and mortality (7%).[9] Conservative management may be undertaken in patients with asymptomatic perforations, those with localized peritonitis who improve clinically, and those with postpolypectomy coagulation syndrome.[53,55-57]

Endoscopic clips can be successful in the closure of colonoscopic perforations recognized during the colonoscopy. These clinical observations have been supported by a series of animal studies. Endoscopic closure is effective in creating a leak-proof seal of the perforation, healing of the perforation, preventing peritonitis, limiting peritoneal adhesions, and avoiding surgery.[47,58-70]

PREVENTION OF COLONOSCOPIC PERFORATION

Prevention is the most important factor in the management of colonic perforation. A number of precautions could be undertaken to avoid a perforation and complications arising from such an event.

Colon preparation

Poor bowel preparation. Defer colonoscopy in patients with poor bowel preparation to avoid the risk of fecal peritonitis.[9] In addition, deferring colonoscopy in these patients avoids the risk of colonic explosion from cautery-induced ignition of combustible gases.[71] A split-dose preparation of 4 L of polyethylene glycol solution or having the patient drink 2 to 3 liters of polyethylene glycol solution the morning of the procedure results in excellent preparation. Checking the color of the stools before each procedure and administering additional polyethylene glycol solution when necessary assures excellent preparation.[72,73]

Dry field. Suctioning of all the fluid and drying the operating field segment, along with upstream and downstream segments, prevent escape of luminal contents through a perforation. Moving the patient to the nondependent position so that the target lesion can be located may prevent fluid escape and peritonitis with perforation. Conscious sedation allows patient repositioning during the procedures.

Colonoscopy technique

A detailed review of the patient's demographics, comorbidities, and prior surgical procedures facilitates the risk assessment for colonoscopic perforation and selection of appropriate closure techniques, technologies, and precautions to prevent it (Fig. 3).

Fixed colon. Avoid excessive pushing of the colonoscope. Use of a smaller-caliber colonoscope along with careful tip deflection to negotiate the acute angles of a fixed colon in patients with adhesions from prior pelvic and abdominal surgeries is advised. Change of the patient's position, use of balloon-assisted endoscopy, use of a water immersion technique, or use of carbon dioxide insufflation also may be helpful.[74-79]

Redundant colon. Use of an enteroscope along with the application of abdominal compression at appropriate places, techniques to stiffen the endoscope further (deploying variable stiffness function, insertion of a biopsy forceps through the biopsy port, use of overtubes that lock and stiffen on demand), or holding the loops down (balloon-assisted endoscopy) may be effective.[80,81]

Prolonged procedures and failed procedures. Use of carbon dioxide, periodically venting the air out (by releasing the biopsy port cap), or intermittent suctioning may release the luminal pressure.

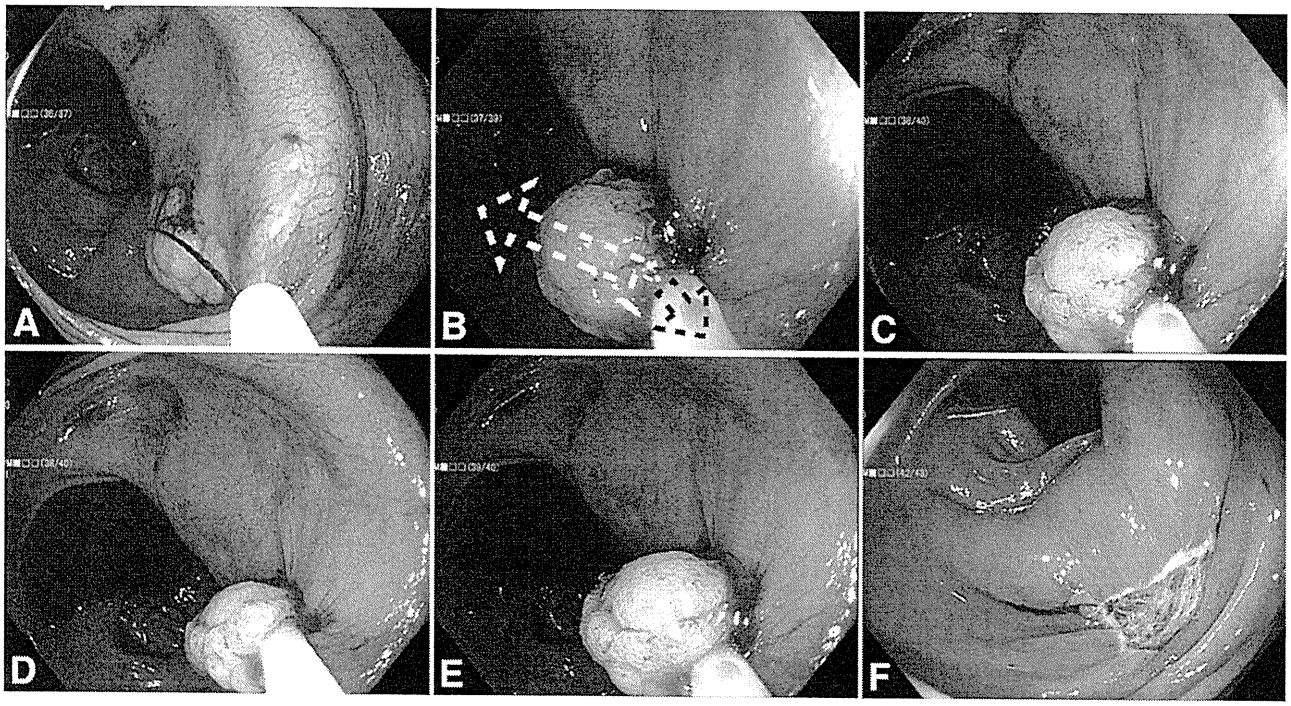

Figure 3. Prevention of perforation during EMR. **A,** A flat lesion after a submucosal injection of saline solution with a few drops of indigo carmine being captured with a stiff snare. **B,** After the snare was closed, the tip of the endoscope was moved to the left and upward (*white arrow*) while the snare was slightly pulled back (*black arrow*). **C,** The lesion after being tented away from its underlying muscularis propria. **D,** The endoscopist then asked the assistant to loosen the snare slightly, without loosening the lesion. **E,** The snare was closed snugly again. **F,** The lesion was resected.[92]

Small rectum. Avoid retroflexion in patients with small rectums.[82] Examine the rectal vault before endoscope withdrawal from the colon, because retroflexion-induced perforations could be identified and closed immediately with clips.[48,49,83-86]

Procedure note. Details of procedure duration, technical difficulties, and measures undertaken to overcome them should be noted to plan future endoscopies.

Management of lesions

Referral versus resection. It is important to decide whether it is better to refer to endoscopists with expertise in the endoscopic resection or undertake the resection if it could be done safely.[87,88]

Referral without biopsy. If a decision is made to refer, defer biopsies, because they cause submucosal fibrosis, which prevents subsequent adequate lifting and the ability to successfully resect the lesion. Avoid tattoo injection into the lesion because this leads to fibrosis in the submucosa.[89] Instead, inject it a fold away from the lesion.

Resection of diminutive polyps. Cold snare resection of diminutive polyps is safer than hot biopsy.[90,91]

Resection of pedunculated polyps. Apply a snare on the stalk of a pedunculated polyp away from the wall, and tent it up before cautery to limit transmural burn and perforation.

Resection of sessile and flat lesions. Ample injection of submucosal fluid to separate the lesion from the muscularis propria is critical to prevent thermal injury to the muscle.[32] The dynamic submucosal injection technique creates a large, submucosal cushion.[92] Piecemeal resection of large polyps (>2 cm) may limit deeper injury to the muscle compared with large, en bloc resections. Specific routine steps to prevent perforation during EMR have been described (Fig. 3).[93]

ESD of large, flat lesions. Accurate identification of the cutting plane is critical to avoiding perforation during ESD. Starting the submucosal dissection close to the mucosal layer and after the submucosal layer has been expanded and well-visualized allows dissection to be performed at the lower third or just above the muscle layer to avoid a perforation. When fibrosis is encountered, the short-type, small-caliber-tip, transparent hood is useful for exposing the muscularis propria.

ENDOSCOPIC MANAGEMENT OF COLONOSCOPIC PERFORATION

Endoscopic closure of colonic perforation has been successful, provided that the perforation is immediately recognized and closed without delay. This could be accomplished with a variety of devices. Through-the-scope clips have been used extensively over the last decade for endoscopic closure of colon perforations.[37,40,45,46,49,63,66-68,70,94-100] Recently, over-the-scope clips have been introduced in Europe and in the United

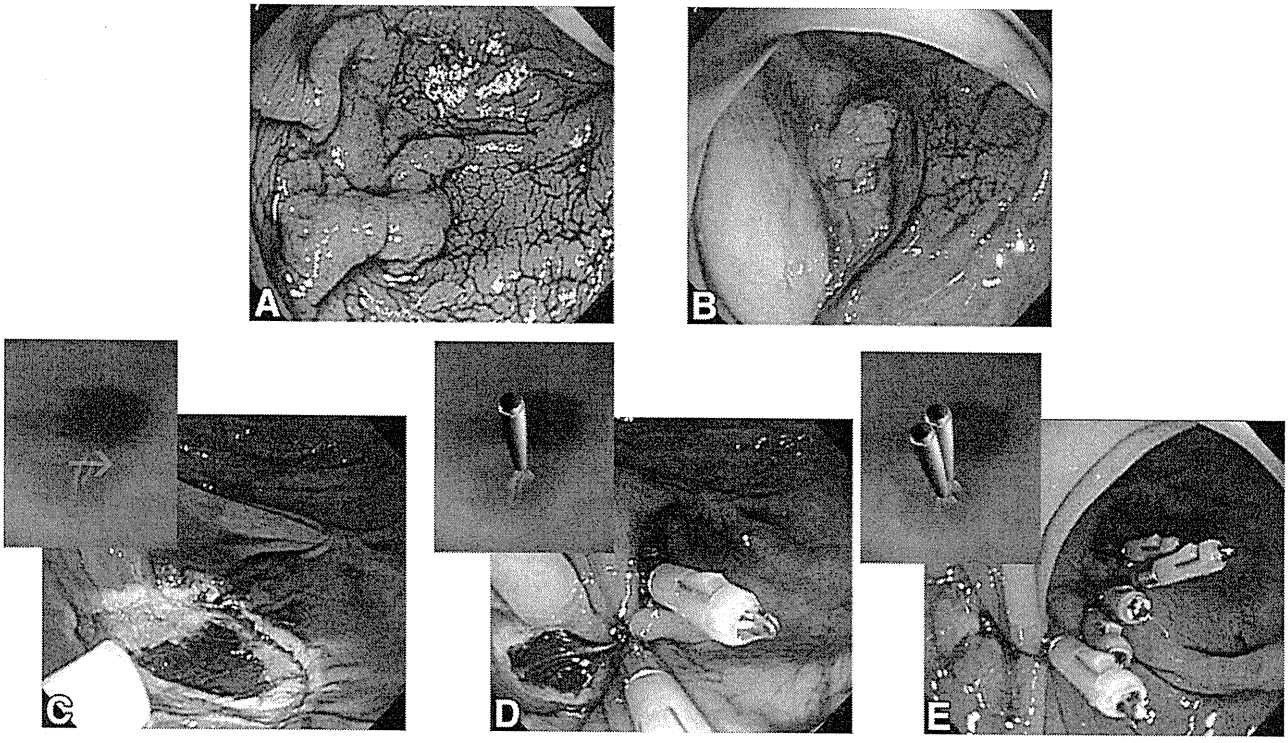

Figure 4. Colonoscopic clip closure of a perforation after EMR. **A, B, C,** EMR of a 2-cm, flat lesion with high-grade dysplasia resulted in a large linear perforation. **C, D, E,** This perforation was closed with clips starting at the top of the perforation and working downward. (Reproduced with permission from the ASGE)

States.[65,69,97,101-105] Suturing devices such as T-tags have been extensively investigated in animal models, especially in the closure of large, gaping perforations with everted edges that are not amenable to clip closure and closure of large defects after full-thickness resection of the colon, but these devices are not available in the market.[62,64,106,107] Both through-the-scope clips and over-the-scope clips produce results comparable to hand-sewn colostomy closure in terminal animal studies.[107,108] Through-the-scope clips can be deployed anywhere in the colon; hence they are ideal for immediate closure of perforations without leaving the site of perforation, thereby avoiding leakage of colon contents. Clips are useful in the closure of small (1 cm) nongaping perforations.[40,58-61,72] However, through-the-scope clips have been reported to be unsuccessful in the closure of large, gaping perforations with everted edges and defects after full-thickness resection, which might be closed with through-the-scope suturing devices such as T-tags.[62,107,109]

Emergency decompression of accumulated air in the peritoneum with a wide-bore needle is important to reduce respiratory compromise, to prevent circulatory decompensation, and to prevent air embolism in the portal venous system. Practical tips of the endoscopic management of colonic perforations are available through the American Society for Gastrointestinal Endoscopy Learning Center and as follows:

Through-the-scope clips

Clips can be used to close perforations immediately after their recognition during the colonoscopy. Both the endoscopist and assistant must be well-versed with the use of clips before undertaking endoscopic closure of perforations. Depending on the size and shape of the perforation, the following techniques can be used for closure of colonoscopic perforations and management of pneumoperitoneum (Figs. 3-6) (Videos 1-4, available online at www.giejournal.org. Reproduced with permission from the ASGE.).

Closure of a large perforation

Keeping the clip close to the end of the endoscope, with the hinge of the clip blades just outside the endoscope, allows the clip–endoscope to be maneuvered as a single unit. Open the clip and rotate the blades to align them at right angles to the defect. After engaging the lower blade to the lower edge of a transverse perforation, gently push the clip–endoscope unit while applying gentle suction to collapse the lumen so that as much tissue as possible from the opposite edge of the perforation can be grasped while the clip is slowly closed. For longitudinal perforations, apply the clip just above the upper end of a longitudinal perforation to pucker the edges below for easier application of subsequent clips, one below the other. Place additional clips from the top, down, in longitudinal perforations or left-to-right in circular perforations

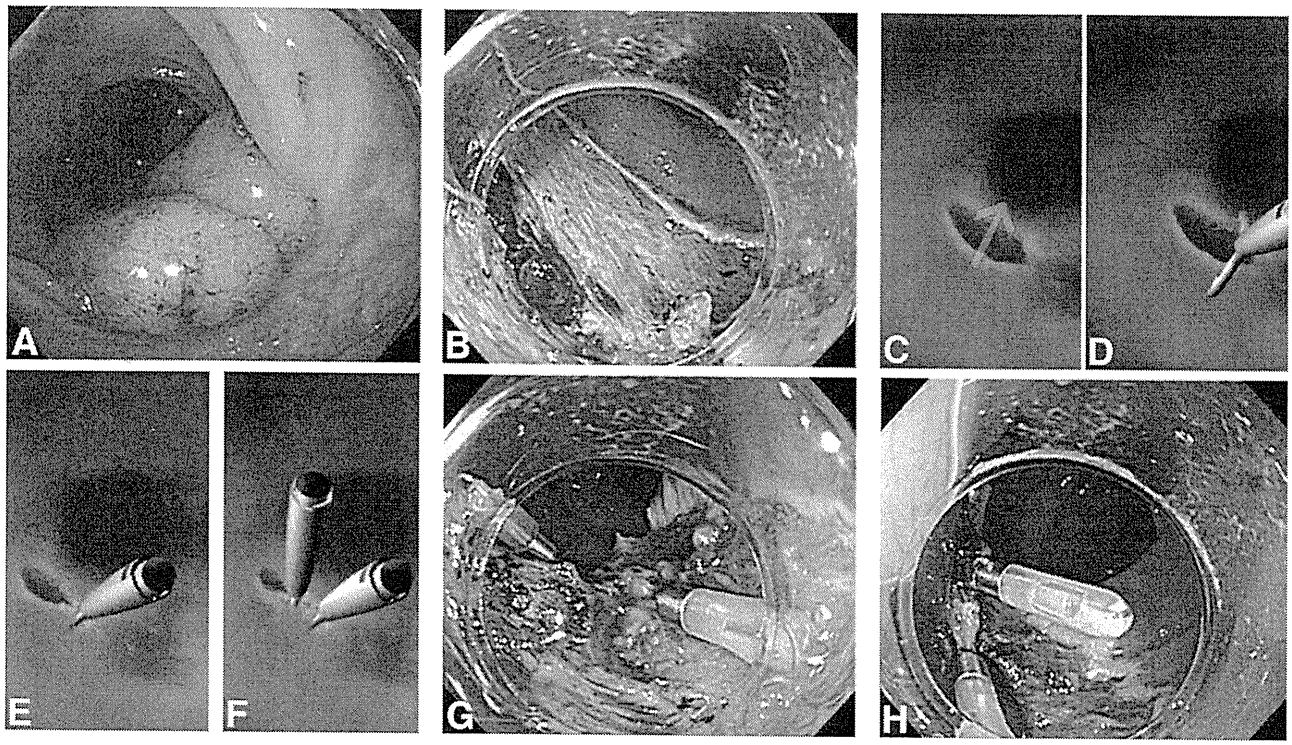

Figure 5. Colonoscopic clip closure of a perforation after endoscopic submucosal dissection (ESD). **A, B,** An unintended cut was made too deeply into the muscularis propria, resulting in a small linear perforation during ESD of a sessile lesion. **C-H,** The perforation as seen through a small-caliber tip transparent hood (ST hood). The perforation has been successfully closed by using 2 clips by approximating the lower edge to the upper edge of the perforation. (Reproduced with permission from the ASGE)

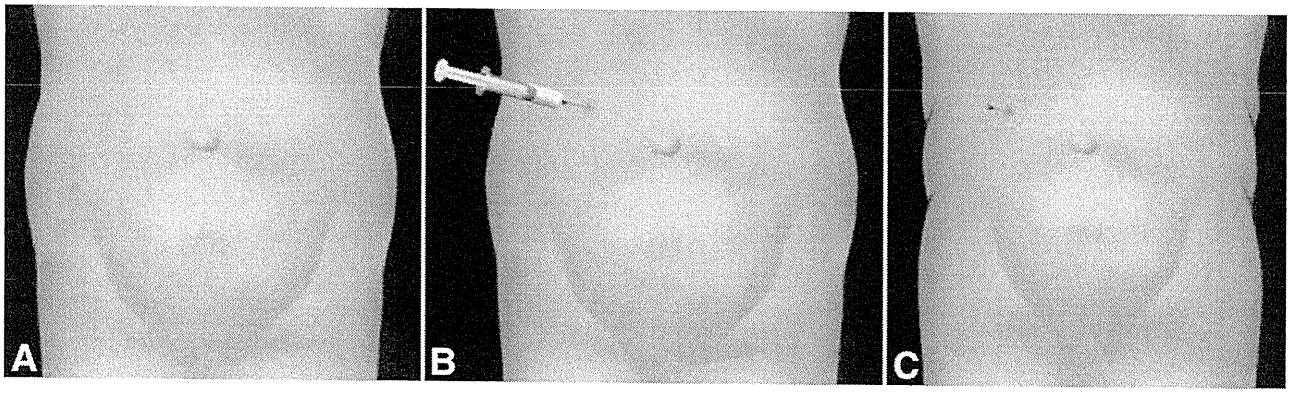

Figure 6. Needle decompression of tension pneumoperitoneum. (Reproduced with permission from the ASGE)

after satisfactory application of the first clip, which is the most critical component of closure. It is important to confirm satisfactory approximation of the edges before deployment of the clip. Perforations that are difficult to close with clips can potentially be closed with a loop-snare.[51]

Closure of small perforations during ESD

Instead of immediate closure of the perforation, it is important to continue ESD in order to make enough space to apply endoscopic clips. If endoscopic clips are hastily applied immediately after the recognition of the perforation, the clips may interfere with further ESD. After successful clip closure of the perforation, ESD can be continued at the earliest opportunity and the lesion removed during the same session. Finally, the resection bed after en bloc resection should be checked carefully, and additional clips should be applied accordingly.

What should be avoided during clipping

Panic. Be calm and steady once you recognize a perforation. Be patient while applying a clip because a clip misplaced to one edge of the perforation could lead to difficulty in applying additional clips for satisfactory closure.

Long shots. Keep the endoscope close to the site of perforation and avoid deploying clips from a distance

away, because long shots will interfere with precise delivery of the clips.

Stretching of the colon. Too much pushing of the clip against the wall limits grasping of the tissue and approximation of the edges of the perforation. Once the blades of the clip are placed across the perforation, gentle suction, instead of pushing the clip, allows the tissue to come into the blades to allow better closure. Avoid air insufflation, because it can worsen pneumoperitoneum.

Over-the-scope clips

Recently, the over-the-scope clip was introduced into the market, and preliminary reports are encouraging. Conceptually, the technique is similar to using a band ligation device, which has been reported as successful.[110] For this procedure, suction the perforation margins with or without the aid of a device to pull the edges into the cap, then deploy the clip, which creates a leak-proof seal.[97,111]

Management after endoscopic closure

A team approach involving surgeons in the management of the patients immediately after endoscopic closure of perforations is critical. The patient should have nothing by mouth and begin therapy with broad-spectrum intravenous antibiotics and hydration. Closely monitor all patients for signs of peritoneal irritation. Resume oral intake as soon as pain and fever resolve, appetite and bowel function return, and laboratory test signs of inflammation such as leukocytosis and elevated C-reactive peptide levels return to normal. If there is any deterioration, surgery should be undertaken.

SUMMARY

Colonoscopic perforation is a serious complication of colonoscopy. Its prevention is the best treatment strategy, although when it occurs and is immediately recognized, endoscopic clip closure can be very useful to manage select cases. It is emphasized that endoscopists need to have the necessary knowledge, ability, equipment, and team required to close the perforations safely.

REFERENCES

1. Yoshikane H, Hidano H, Sakakibara A, et al. Endoscopic repair by clipping of iatrogenic colonic perforation. Gastrointest Endosc 1997;46:464-6.
2. Viiala CH, Zimmerman M, Cullen DJ, et al. Complication rates of colonoscopy in an Australian teaching hospital environment. Intern Med J 2003;33:355-9.
3. Anderson ML, Pasha TM, Leighton JA. Endoscopic perforation of the colon: lessons from a 10-year study. Am J Gastroenterol 2000;95:3418-22.
4. Rathgaber SW, Wick TM. Colonoscopy completion and complication rates in a community gastroenterology practice. Gastrointest Endosc 2006;64:556-62.
5. Regula J, Rupinski M, Kraszewska E, et al. Colonoscopy in colorectal-cancer screening for detection of advanced neoplasia. N Engl J Med 2006;355:1863-72.
6. Gatto NM, Frucht H, Sundararajan V, et al. Risk of perforation after colonoscopy and sigmoidoscopy: a population-based study. J Natl Cancer Inst 2003;95:230-6.
7. Levin TR, Zhao W, Conell C, et al. Complications of colonoscopy in an integrated health care delivery system. Ann Intern Med 2006;145:880-6.
8. Rabeneck L, Paszat LF, Hilsden RJ, et al. Bleeding and perforation after outpatient colonoscopy and their risk factors in usual clinical practice. Gastroenterology 2008;135:1899-906, 906 e1.
9. Iqbal CW, Cullinane DC, Schiller HJ, et al. Surgical management and outcomes of 165 colonoscopic perforations from a single institution. Arch Surg 2008;143:701-6; discussion 6-7.
10. Singh H, Penfold RB, DeCoster C, et al. Colonoscopy and its complications across a Canadian regional health authority. Gastrointest Endosc 2009;69:665-71.
11. Lorenzo-Zuniga V, de Vega VM, Domenech E, et al. Endoscopist experience as a risk factor for colonoscopic complications. Colorectal Dis 2010;12:e273-7.
12. Lohsiriwat V, Sujarittanakarn S, Akaraviputh T, et al. What are the risk factors of colonoscopic perforation? BMC Gastroenterol 2009;9:71.
13. Wadas DD, Sanowski RA. Complications of the hot biopsy forceps technique. Gastrointest Endosc 1988;34:32-7.
14. Heldwein W, Dollhopf M, Rösch T, et al. The Munich Polypectomy Study (MUPS): prospective analysis of complications and risk factors in 4000 colonic snare polypectomies. Endoscopy 2005;37:1116-22.
15. Iishi H, Tatsuta M, Iseki K, et al. Endoscopic piecemeal resection with submucosal saline injection of large sessile colorectal polyps. Gastrointest Endosc 2000;51:697-700.
16. Tanaka S, Haruma K, Oka S, et al. Clinicopathologic features and endoscopic treatment of superficially spreading colorectal neoplasms larger than 20 mm. Gastrointest Endosc 2001;54:62-6.
17. Ahmad NA, Kochman ML, Long WB, et al. Efficacy, safety, and clinical outcomes of endoscopic mucosal resection: a study of 101 cases. Gastrointest Endosc 2002;55:390-6.
18. Bergmann U, Beger HG. Endoscopic mucosal resection for advanced non-polypoid colorectal adenoma and early stage carcinoma. Surg Endosc 2003;17:475-9.
19. Higaki S, Hashimoto S, Harada K, et al. Long-term follow-up of large flat colorectal tumors resected endoscopically. Endoscopy 2003;35:845-9.
20. Tung SY, Wu CS. Clinical outcome of endoscopically removed early colorectal cancer. J Gastroenterol Hepatol 2003;18:1175-9.
21. Tamura S, Nakajo K, Yokoyama Y, et al. Evaluation of endoscopic mucosal resection for laterally spreading rectal tumors. Endoscopy 2004;36:306-12.
22. Hurlstone DP, Sanders DS, Cross SS, et al. Colonoscopic resection of lateral spreading tumours: a prospective analysis of endoscopic mucosal resection. Gut 2004;53:1334-9.
23. Conio M, Repici A, Demarquay JF, et al. EMR of large sessile colorectal polyps. Gastrointest Endosc 2004;60:234-41.
24. Hurlstone DP, Cross SS, Drew K, et al. An evaluation of colorectal endoscopic mucosal resection using high-magnification chromoscopic colonoscopy: a prospective study of 1000 colonoscopies. Endoscopy 2004;36:491-8.
25. Su MY, Hsu CM, Ho YP, et al. Endoscopic mucosal resection for colonic non-polypoid neoplasms. Am J Gastroenterol 2005;100:2174-9.
26. Katsinelos P, Kountouras J, Paroutoglou G, et al. Endoscopic mucosal resection of large sessile colorectal polyps with submucosal injection of hypertonic 50 percent dextrose-epinephrine solution. Dis Colon Rectum 2006;49:1384-92.
27. Bories E, Pesenti C, Monges G, et al. Endoscopic mucosal resection for advanced sessile adenoma and early-stage colorectal carcinoma. Endoscopy 2006;38:231-5.
28. Jameel JK, Pillinger SH, Moncur P, et al. Endoscopic mucosal resection (EMR) in the management of large colo-rectal polyps. Colorectal Dis 2006;8:497-500.

29. Arebi N, Swain D, Suzuki N, et al. Endoscopic mucosal resection of 161 cases of large sessile or flat colorectal polyps. Scand J Gastroenterol 2007;42:859-66.
30. Wei SC, Chang YT, Shieh MJ, et al. The clinical and endoscopic characteristics, treatment, and long-term prognosis of early colorectal cancer in Taiwan. Dis Colon Rectum 2007;50:856-60.
31. Kaltenbach T, Friedland S, Maheshwari A, et al. Short- and long-term outcomes of standardized EMR of nonpolypoid (flat and depressed) colorectal lesions ≥ 1 cm (with video). Gastrointest Endosc 2007;65: 857-65.
32. Deyhle P, Largiadèr F, Jenny S, et al. A method for endoscopic electroresection of sessile colonic polyps. Endoscopy 1973;5:38-40.
33. Fujishiro M, Yahagi N, Nakamura M, et al. Endoscopic submucosal dissection for rectal epithelial neoplasia. Endoscopy 2006;38:493-7.
34. Onozato Y, Ishihara H, Iizuka H, et al. Endoscopic submucosal dissection for early gastric cancers and large flat adenomas. Endoscopy 2006; 38:980-6.
35. Tanaka S, Oka S, Kaneko I, et al. Endoscopic submucosal dissection for colorectal neoplasia: possibility of standardization. Gastrointest Endosc 2007;66:100-7.
36. Tamegai Y, Saito Y, Masaki N, et al. Endoscopic submucosal dissection: a safe technique for colorectal tumors. Endoscopy 2007;39:418-22.
37. Saito Y, Uraoka T, Matsuda T, et al. Endoscopic treatment of large superficial colorectal tumors: a case series of 200 endoscopic submucosal dissections (with video). Gastrointest Endosc 2007;66:966-73.
38. Hurlstone DP, Atkinson R, Sanders DS, et al. Achieving R0 resection in the colorectum using endoscopic submucosal dissection. Br J Surg 2007;94:1536-42.
39. Fujishiro M, Yahagi N, Kakushima N, et al. Outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms in 200 consecutive cases. Clin Gastroenterol Hepatol 2007;5:678-83; quiz 45.
40. Saito Y, Uraoka T, Yamaguchi Y, et al. A prospective, multicenter study of 1111 colorectal endoscopic submucosal dissections (with video). Gastrointest Endosc 2010;72:1217-25.
41. Toyonaga T, Man IM, Morita Y, et al. The new resources of treatment for early stage colorectal tumors: EMR with small incision and simplified endoscopic submucosal dissection. Dig Endosc 2009;21(suppl 1): S31-7.
42. Toyonaga T, Man-i M, Fujita T, et al. Retrospective study of technical aspects and complications of endoscopic submucosal dissection for laterally spreading tumors of the colorectum. Endoscopy 2010;42:714-22.
43. Rabeneck L, Saskin R, Paszat LF. Onset and clinical course of bleeding and perforation after outpatient colonoscopy: a population-based study. Gastrointest Endosc 2011;73:520-3.
44. Saito Y, Matsuda T, Kikuchi T, et al. Successful endoscopic closure of colonic perforations requiring abdominal decompression after endoscopic mucosal resection and endoscopic submucosal dissection for early colon cancer. Digestive Endosc 2007;19:S34-9.
45. Swan MP, Bourke MJ, Moss A, et al. The target sign: an endoscopic marker for the resection of the muscularis propria and potential perforation during colonic endoscopic mucosal resection. Gastrointest Endosc 2010;73:79-85.
46. Albuquerque W, Moreira E, Arantes V, et al. Endoscopic repair of a large colonoscopic perforation with clips. Surg Endosc 2008;22:2072-4.
47. Sileri P, Del Vecchio Blanco G, Benavoli D, et al. Iatrogenic rectal perforation during operative colonoscopy: closure with endoluminal clips. JSLS 2009;13:69-72.
48. Quallick MR, Brown WR. Rectal perforation during colonoscopic retroflexion: a large, prospective experience in an academic center. Gastrointest Endosc 2009;69:960-3.
49. Katsinelos P, Kountouras J, Chatzimavroudis G, et al. Endoscopic closure of a large iatrogenic rectal perforation using endoloop/clips technique. Acta Gastroenterol Belg 2009;72:357-9.
50. Fu WP, Quah HM, Eu KW. Traumatic rectal perforation presenting as necrotising fasciitis of the lower limb. Singapore Med J 2009;50:e270-3.
51. Mocciaro F, Curcio G, Tarantino I, et al. Tulip bundle technique and fibrin glue injection: unusual treatment of colonic perforation. World J Gastroenterol 2011;17:1088-90.
52. Ignjatovic M, Jovic J. Tension pneumothorax, pneumoretroperitoneum, and subcutaneous emphysema after colonoscopic polypectomy: a case report and review of the literature. Langenbecks Arch Surg 2009;394:185-9.
53. Kim DH, Pickhardt PJ, Taylor AJ, et al. Imaging evaluation of complications at optical colonoscopy. Curr Probl Diagn Radiol 2008;37:165-77.
54. Damore LJ, 2nd, Rantis PC, Vernava AM, 3rd, et al. Colonoscopic perforations: etiology, diagnosis, and management. Dis Colon Rectum 1996; 39:1308-14.
55. Luigiano C, Consolo P, Scaffidi MG, et al. Endoscopic mucosal resection for large and giant sessile and flat colorectal polyps: a single-center experience with long-term follow-up. Endoscopy 2009;41:829-35.
56. Waye JD. Management of complications of colonoscopic polypectomy. Gastroenterologist 1993;1:158-64.
57. Fatima H, Rex DK. Minimizing endoscopic complications: colonoscopic polypectomy. Gastrointest Endosc Clin N Am 2007;17:145-56, viii.
58. Raju GS, Pham B, Xiao SY, et al. A pilot study of endoscopic closure of colonic perforations with endoclips in a swine model. Gastrointest Endosc 2005;62:791-5.
59. Raju GS, Ahmed I, Brining D, et al. Endoluminal closure of large perforations of colon with clips in a porcine model (with video). Gastrointest Endosc 2006;64:640-6.
60. Raju GS, Ahmed I, Xiao SY, et al. Controlled trial of immediate endoluminal closure of colon perforations in a porcine model by use of a novel clip device (with videos). Gastrointest Endosc 2006;64:989-97.
61. Raju GS, Ahmed I, Shibukawa G, et al. Endoluminal clip closure of a circular full-thickness colon resection in a porcine model (with videos). Gastrointest Endosc 2007;65:503-9.
62. Raju GS, Shibukawa G, Ahmed I, et al. Endoluminal suturing may overcome the limitations of clip closure of a gaping wide colon perforation (with videos). Gastrointest Endosc 2007;65:906-11.
63. Taku K, Sano Y, Fu KI, et al. Iatrogenic perforation associated with therapeutic colonoscopy: a multicenter study in Japan. J Gastroenterol Hepatol 2007;22:1409-14.
64. Raju GS, Fritscher-Ravens A, Rothstein RI, et al. Endoscopic closure of colon perforation compared to surgery in a porcine model: a randomized controlled trial (with videos). Gastrointest Endosc 2008;68:324-32.
65. Schurr MO, Hartmann C, Ho CN, et al. An over-the-scope clip (OTSC) system for closure of iatrogenic colon perforations: results of an experimental survival study in pigs. Endoscopy 2008;40:584-8.
66. Kang HY, Kang HW, Kim SG, et al. Incidence and management of colonoscopic perforations in Korea. Digestion 2008;78:218-23.
67. Magdeburg R, Collet P, Post S, et al. Endoclipping of iatrogenic colonic perforation to avoid surgery. Surg Endosc 2008;22:1500-4.
68. Trecca A, Gaj F, Gagliardi G. Our experience with endoscopic repair of large colonoscopic perforations and review of the literature. Tech Coloproctol 2008;12:315-21; discussion 22.
69. von Renteln D, Schmidt A, Vassiliou MC, et al. Endoscopic closure of large colonic perforations using an over-the-scope clip: a randomized controlled porcine study. Endoscopy 2009;41:481-6.
70. Yang DH, Byeon JS, Lee KH, et al. Is endoscopic closure with clips effective for both diagnostic and therapeutic colonoscopy-associated bowel perforation? Surg Endosc 2010 24:1177-85.
71. Manner H, Plum N, Pech O, et al. Colon explosion during argon plasma coagulation. Gastrointest Endosc 2008;67:1123-7.
72. Saito Y, Fukuzawa M, Matsuda T, et al. Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection. Surg Endosc 2010;24:343-52.
73. Kim HN, Raju GS. Bowel preparation and colonoscopy technique to detect non-polypoid colorectal neoplasms. Gastrointest Endosc Clin N Am 2010;20:437-48.

74. Marshall JB. Use of a pediatric colonoscope improves the success of total colonoscopy in selected adult patients. Gastrointest Endosc 1996; 44:675-8.
75. Marshall JB, Perez RA, Madsen RW. Usefulness of a pediatric colonoscope for routine colonoscopy in women who have undergone hysterectomy. Gastrointest Endosc 2002;55:838-41.
76. Rex DK. Accessing proximal aspects of folds and flexures during colonoscopy: impact of a pediatric colonoscope with a short bending section. Am J Gastroenterol 2003;98:1504-7.
77. Horiuchi A, Nakayama Y, Kajiyama M, et al. Usefulness of a small-caliber, variable-stiffness colonoscope as a backup in patients with difficult or incomplete colonoscopy. Am J Gastroenterol 2004;99:1936-40.
78. May A, Nachbar L, Ell C. Push-and-pull enteroscopy using a single-balloon technique for difficult colonoscopy. Endoscopy 2006;38: 395-8.
79. Rex DK, Chen SC, Overhiser AJ. Colonoscopy technique in consecutive patients referred for prior incomplete colonoscopy. Clin Gastroenterol Hepatol 2007;5:879-83.
80. Moreels TG, Macken EJ, Roth B, et al. Cecal intubation rate with the double-balloon endoscope after incomplete conventional colonoscopy: a study in 45 patients. J Gastroenterol Hepatol 2010;25:80-3.
81. Lichtenstein GR, Park PD, Long WB, et al. Use of a push enteroscope improves ability to perform total colonoscopy in previously unsuccessful attempts at colonoscopy in adult patients. Am J Gastroenterol 1999;94:187-90.
82. Hough DM, Kuntz MA, Fidler JL, et al. Detection of occult colonic perforation before CT colonography after incomplete colonoscopy: perforation rate and use of a low-dose diagnostic scan before CO2 insufflation. AJR Am J Roentgenol 2008;191:1077-81.
83. Ahlawat SK, Charabaty A, Benjamin S. Rectal perforation caused by retroflexion maneuver during colonoscopy: closure with endoscopic clips. Gastrointest Endosc 2008;67:771-3.
84. Fu K, Ikematsu H, Sugito M, et al. Iatrogenic perforation of the colon following retroflexion maneuver. Endoscopy 2007;39(suppl 1):E175.
85. Bechtold ML, Hammad HT, Arif M, et al. Perforation upon retroflexion: an endoscopic complication and repair. Endoscopy 2009;41(suppl 2): E155-6.
86. Sullivan JL, Maxwell PJ, 4th, Kastenberg DM, et al. Rectal perforation by retroflexion of the colonoscope managed by endoclip closure. Am Surg 2010;76:108-10.
87. Voloyiannis T, Snyder MJ, Bailey RR, et al. Management of the difficult colon polyp referred for resection: resect or rescope? Dis Colon Rectum 2008;51:292-5.
88. Swan MP, Bourke MJ, Alexander S, et al. Large refractory colonic polyps: Is it time to change our practice? A prospective study of the clinical and economic impact of a tertiary referral colonic mucosal resection and polypectomy service (with videos). Gastrointest Endosc 2009;70: 1128-36.
89. Han KS, Sohn DK, Choi DH, et al. Prolongation of the period between biopsy and EMR can influence the nonlifting sign in endoscopically resectable colorectal cancers. Gastrointest Endosc 2008;67:97-102.
90. Tappero G, Gaia E, De Giuli P, et al. Cold snare excision of small colorectal polyps. Gastrointest Endosc 1992;38:310-3.
91. Uno Y, Obara K, Zheng P, et al. Cold snare excision is a safe method for diminutive colorectal polyps. Tohoku J Exp Med 1997;183:243-9.
92. Soetikno R, Kaltenbach T. Dynamic submucosal injection technique. Gastrointest Endosc Clin N Am 2010;20:497-502.
93. Soetikno R, Gotoda T, Nakanishi Y, et al. Endoscopic mucosal resection. Gastrointest Endosc 2003;57:567-79.
94. Yang DH, Byeon JS, Lee KH, et al. Is endoscopic closure with clips effective for both diagnostic and therapeutic colonoscopy-associated bowel perforation? Surg Endosc 2010;24:1177-85.
95. Niimi K, Fujishiro M, Kodashima S, et al. Long-term outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms. Endoscopy 2010;42:723-9.
96. Mangiavillano B, Viaggi P, Masci E. Endoscopic closure of acute iatrogenic perforations during diagnostic and therapeutic endoscopy in the gastrointestinal tract using metallic clips: a literature review. J Dig Dis 2010;11:12-8.
97. Parodi A, Repici A, Pedroni A, et al. Endoscopic management of GI perforations with a new over-the-scope clip device (with videos). Gastrointest Endosc 2010;72:881-6.
98. Barbagallo F, Castello G, Latteri S, et al. Successful endoscopic repair of an unusual colonic perforation following polypectomy using an endoclip device. World J Gastroenterol 2007;13:2889-91.
99. Aksoz K, Yoruk G, Buyrac Z, et al. Transanal endoscopic repair of rectal perforation with hemoclips. J Laparoendosc Adv Surg Tech A 2005;15: 170-2.
100. Mana F, De Vogelaere K, Urban D. Iatrogenic perforation of the colon during diagnostic colonoscopy: endoscopic treatment with clips. Gastrointest Endosc 2001;54:258-9.
101. Kirschniak A, Kratt T, Stuker D, et al. A new endoscopic over-the-scope clip system for treatment of lesions and bleeding in the GI tract: first clinical experiences. Gastrointest Endosc 2007;66:162-7.
102. von Renteln D, Denzer UW, Schachschal G, et al. Endoscopic closure of GI fistulae by using an over-the-scope clip (with videos). Gastrointest Endosc 2010;72:1289-96.
103. Voermans RP, Vergouwe F, Breedveld P, et al. Comparison of endoscopic closure modalities for standardized colonic perforations in a porcine colon model. Endoscopy 2011;43:217-22.
104. Seebach L, Bauerfeind P, Gubler C. "Sparing the surgeon": clinical experience with over-the-scope clips for gastrointestinal perforation. Endoscopy 2010;42:1108-11.
105. Kirschniak A, Subotova N, Zieker D, et al. The over-the-scope clip (OTSC) for the treatment of gastrointestinal bleeding, perforations, and fistulas. Surg Endosc 2011;25:2901-5.
106. Raju GS, Malhotra A, Ahmed I. Colonoscopic full-thickness resection of the colon in a porcine model as a prelude to endoscopic surgery of difficult colon polyps: a novel technique (with videos). Gastrointest Endosc 2009;70:159-65.
107. Agrawal D, Chak A, Champagne BJ, et al. Endoscopic mucosal resection with full-thickness closure for difficult polyps: a prospective clinical trial. Gastrointest Endosc 2010;71:1082-8.
108. Voermans RP, Vergouwe F, Breedveld P, et al. Comparison of endoscopic closure modalities for standardized colonic perforations in a porcine colon model. Endoscopy 2011;43:217-22.
109. von Renteln D, Schmidt A, Vassiliou MC, et al. Endoscopic full-thickness resection and defect closure in the colon. Gastrointest Endosc 2010;71: 1267-73.
110. Han JH, Park S, Youn S. Endoscopic closure of colon perforation with band ligation; salvage technique after endoclip failure. Clin Gastroenterol Hepatol 2011;9:e54-5.
111. Voermans RP, Deprez PH, Moine OL, et al. Endoscopic closure of iatrogenic perforations of the gastrointestinal tract using the over-the-scope-clip: a prospective multicenter human trial [abstract]. Gastrointest Endosc 2011;71:AB132.

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Macroscopic estimation of submucosal invasion in the colon

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Colorectal cancer is the third most prevalent cause of cancer-related mortality in Japan, and the incidence of submucosal colorectal cancer is increasing. To reduce colorectal cancer mortality, however, early detection of colorectal cancer is required and adequate diagnosis of depth is needed. Current endoscopes provide high-resolution imaging that result in clear, vivid features of the detected lesions. In particular, when combined with image enhancement, high-magnification endoscopy can provide a detailed analysis of the morphologic architecture of the pit pattern and the capillary pattern in a simple and quick manner. Characteristic colonoscopic findings obtained by a combination of conventional colonoscopy, magnifying chromoendoscopy, and narrow-band imaging are useful for determining the depth of invasion of early-stage colorectal cancers, an essential factor in selecting a treatment modality.

Introduction

Colorectal cancer is the third most prevalent cause of cancer-related mortality in Japan, and the incidence of early invasive colorectal cancer (ie, submucosal cancer) is increasing. In the National Cancer Center patient population from 1962 to 1990, cancers confined to the submucosa accounted for 6.9% (162/2337) of all invasive cancers treated surgically. Between 1991 and 2009 the incidence of submucosal cancers increased to 17.5% (974/5572). The most likely reasons for this increased incidence include a greater recognition of early-stage lesions by Japanese endoscopists and the 1992 introduction of immunochemical fecal occult blood testing in Japan.

To reduce colorectal cancer mortality, not only is early detection of colorectal cancer required, but also adequate decision making (ie, depth diagnosis) is needed. Small colorectal neoplasms are believed to have a lower malignant potential than large ones, and several authors have reported that the malignant potential of early colorectal cancer increases with size.[1-3] However, evaluation for submucosal invasion requires more than just the measurement of the lesion size. Although this finding may be true for adenomatous lesions, the data for submucosal invasive cancers are conflicting.

Current endoscopes provide high-resolution imaging that results in clear, vivid, and detailed features of the detected lesions. In particular, when combined with image enhancement, high-magnification endoscopy can provide a detailed analysis of the morphologic architecture of mucosal crypt orifices (ie, pit pattern) and the microvascular architecture (capillary pattern, CP) in a simple and quick manner.[4-6] As such, magnifying chromoendoscopy and NBI with magni-

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fication have been shown to be effective for differentiating between colorectal neoplastic and nonneoplastic lesions and for determination of the depth invasion of colorectal cancers.[7-11] We highlight methods to assess the depth of invasion of early-stage colorectal cancers based on a review of the literature and endoscopic images.

Importance of estimating depth of submucosal invasion

Endoscopic mucosal resection is indicated to treat intramucosal colorectal cancers because the risk of lymph node metastasis is nil.[12,13] In contrast, surgery is indicated to treat submucosal invasive cancers because of the 6% to 12% risk of lymph node metastasis.[14-17]

Between 1998 and 2004, a total of 378 submucosal cancers (except pedunculated type lesions) were treated surgically at the National Cancer Center Hospital. We retrospectively analyzed clinicopathological features, incidence of lymph node metastasis, and risk factors for lymph node metastasis, such as depth of submucosal invasion ($\geq$1000 μm or $<$1000 μm), lymphovascular invasion, poorly differentiated adenocarcinoma, tumor size, and growth pattern (polypoid growth type/nonpolypoid growth type)[18] in all cases (Table 1).

The overall incidence of lymph node metastasis was 11.9% (45/378) and univariate analysis identified a strong relationship between lymph node metastasis and the following 3 factors: depth of submucosal invasion, lymphovascular invasion, and poorly differentiated adenocarcinoma. Therefore, the findings of deep submucosal invasion ($\geq$1000 μm) and/or lymphovascular invasion and/or poorly differentiated adenocarcinoma in an endoscopic mucosal resection specimen indicate the need to consider additional surgery with lymph node dissection.[19] Although lymphovascular invasion and poorly differentiated adenocarcinoma components are impossible to predict before resection, the vertical depth of invasion of submucosal cancers can be estimated based on the morphologic appearance at the time of endoscopy.

Estimation of submucosal invasion using conventional and magnifying colonoscopy

Conventional colonoscopy (including chromoendoscopy)

How to differentiate between mucosal/submucosal superficial and submucosal deep cancers?

New diagnostic modalities such as endoscopic ultrasonography using miniprobe and magnifying chromoendoscopy are reported to be useful for the depth diagnosis of early-stage colorectal cancers. However, these modalities are relatively expensive and time consuming. If invasion depth could be diagnosed using only conventional colonoscopy, it would be more cost-effective and convenient.

Saitoh et al reported that characteristic colonoscopic findings obtained by a combination of videocolonoscopy and chromoendoscopy are clinically useful for determining the invasion depth of depressed type colorectal cancers.[20] In this report, characteristic colonoscopic findings (ie, expansion appearance, deep depression surface, irregular bottom of depression surface, and folds converging toward the tumor) are needed for surgical operation. According to their results, the invasion depth of depressed type early colorectal cancers could be correctly determined in 58 of 64 lesions (91%). In our own large study involving 379 lesions (179 intramucosal cancers and 200 submucosal cancers), we analyzed the endoscopic features of submucosal deep invasion using a high-definition colonoscope.[21] Lesions were divided into 3 macroscopic subtypes (pedunculated type, sessile type, and superficial type) based on endoscopic findings. Eight endoscopic factors (tumor size, loss of lobulation, excavation, demarcated depressed area, stalk swelling, fullness, fold convergence, and pit pattern) were evaluated retrospectively for association with submucosal invasion and then compared with histopathologic results. In this report, the superficial type had a significantly higher frequency of submucosal deep invasion [52.4% (77/147) vs 24.6% (14/57) and 39.4% (69/175), P value < 0.05, respectively, for pedunculated and sessile types]. Moreover, "fullness: a bursting appearance due to expansive growth of the

Table 1 Risk factors for lymph node metastasis in patients with submucosal cancer

Variable	Lymph node metastasis (−)	Lymph node metastasis (+)	Univariate analysis (P value)	Multivariate analysis P value	Multivariate analysis Odds ratio	Multivariate analysis 95% Confidence interval
Submucosal invasion ($\geq$1000 μm/$<$1000 μm)	286/47	44/1	0.03	0.35	2.8	0.3–23.4
Lymphovascular invasion (ly/v) (+/−)	87/246	33/12	<0.0001	<0.0001	6.8	3.3–13.9
Poorly differentiated adenocarcinoma (por) (+/−)	45/288	13/32	<0.01	0.09	1.9	0.9–4.2
Tumor size ($\geq$20 mm/$<$20 mm)	163/170	20/25	NS	—	—	—
Growth pattern (polypoid growth/nonpolypoid growth)	173/160	28/17	NS	—	—	—

NS = nonsignificant.

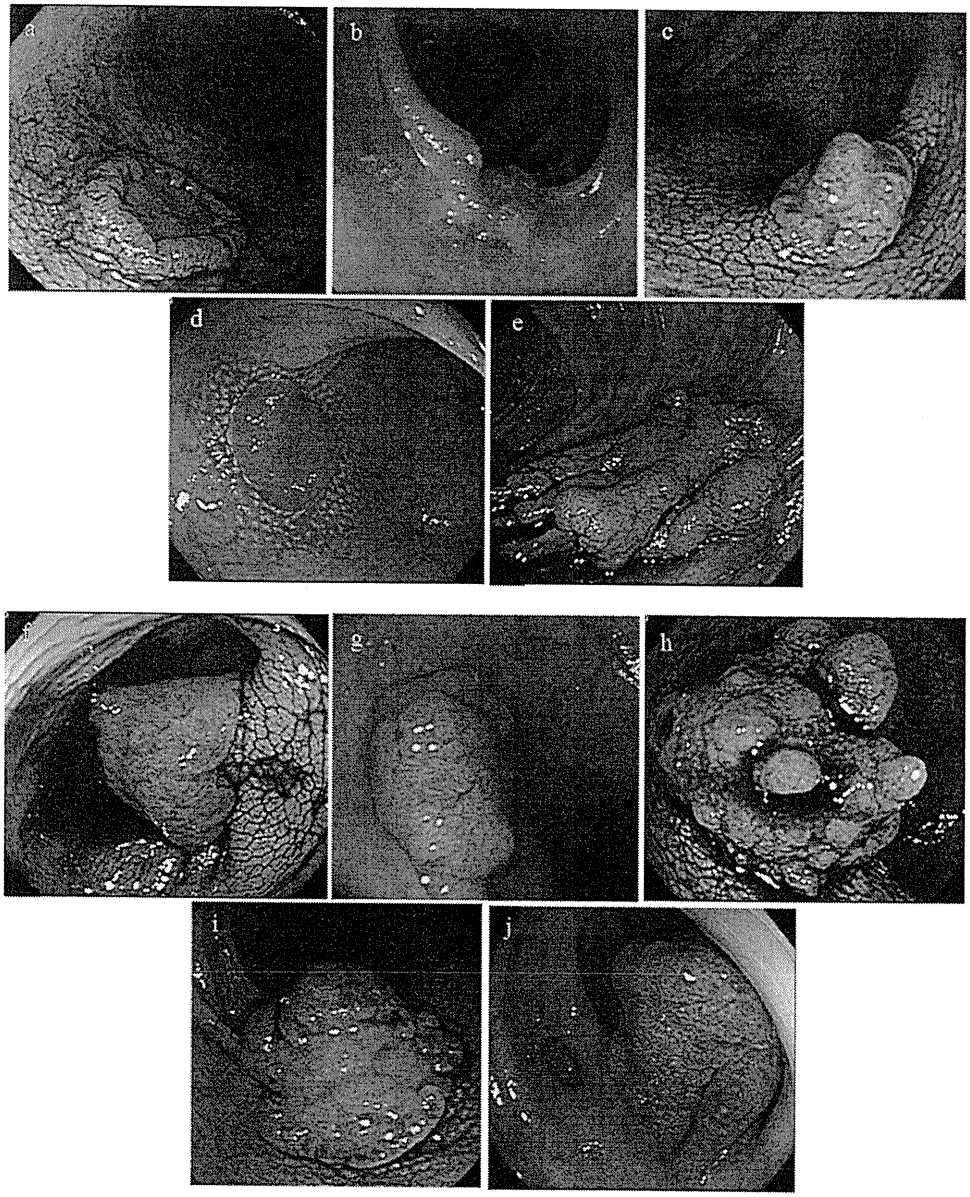

Figure 1 Typical findings of submucosal invasive cancer. (a) Deep depression, (b) fold convergency, (c) irregular bottom of depression surface, (d) white spots (chicken skin appearance), (e) redness, (f) expansion, (g) firm consistency, (h) irregular surface, (i) loss of lobulation, and (j) thick stalk. (Color figure is available online at www.techgiendoscopy.com.)

tumor" was considered an independent risk factor for submucosal deep invasion in the superficial type (odds ratio = 9.25). There were no independent risk factors for submucosal deep invasion in the pedunculated type.

Typical findings of submucosal invasive cancer

To clarify the clinically important characteristic colonoscopic findings, the authors reviewed all conventional colonoscopic images of submucosal invasive colorectal cancers treated endoscopically or surgically. In this current retrospective review, the following 10 characteristic colonoscopic findings were recognized as indicating an increased risk of submucosal invasion: deep depression, fold convergence, irregular bottom of depression surface, white spots (chicken skin appearance), redness, expansion, firm consistency, irregular surface, loss of lobulation, and thick stalk (Figure 1).

Deep depression (Figure 2). The definition of this finding is "deep depression with demarcated area." Chromoendoscopy (using indigo carmine) is helpful in recognizing this finding. Nonpolypoid growth type IIa + IIc lesions are usually submucosal or deeper cancers. The size of these lesions is relatively small compared with polypoid growth type submucosal cancers.

Fold convergence (Figure 3). The definition of this finding is the "existence of 3 or more folds convergence toward the tumor." Sometimes a laterally spreading tumor, nongranular

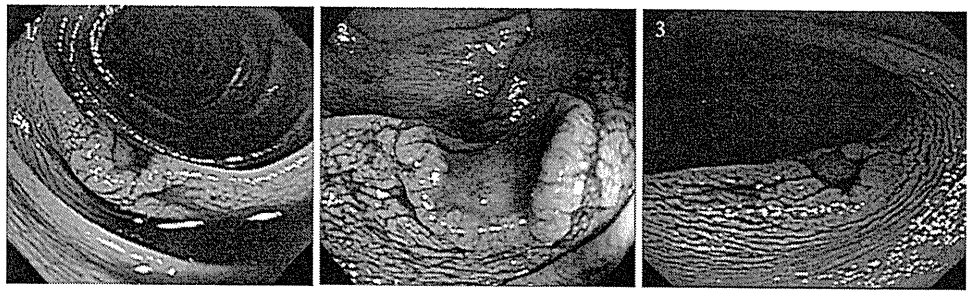

Figure 2 Deep depression. (1 and 2) IIc, SM deep cancer; and (3) IIc, SM superficial cancer. (Color figure is available online at www.techgiendoscopy.com.)

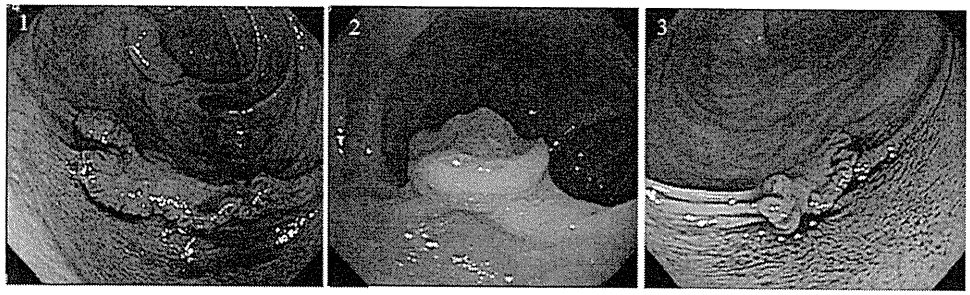

Figure 3 Fold convergence. (1) IIa + IIc (LST-NG), SM deep cancer; (2) Is + IIc, SM deep cancer; and (3) IIa + IIc (LST-NG), SM superficial cancer. (Color figure is available online at www.techgiendoscopy.com.)

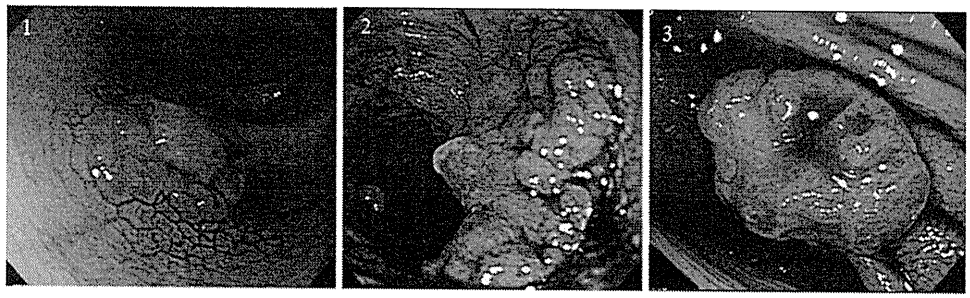

Figure 4 Irregular bottom of depression surface. (1) Is + IIc, SM deep cancer; (2) IIa + IIc, SM deep cancer; and (3) Is + IIc, SM deep cancer. (Color figure is available online at www.techgiendoscopy.com.)

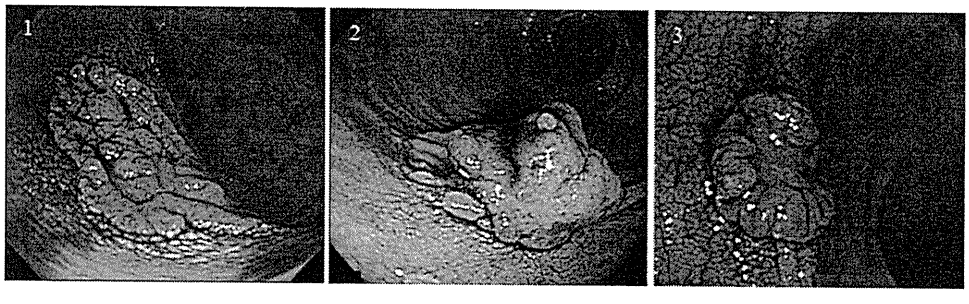

Figure 5 White spots (chicken skin appearance). (1) IIa + IIc (LST-NG), SM deep cancer; (2) Is, SM deep cancer; and (3) IIa + IIc, SM deep cancer. (Color figure is available online at www.techgiendoscopy.com.)

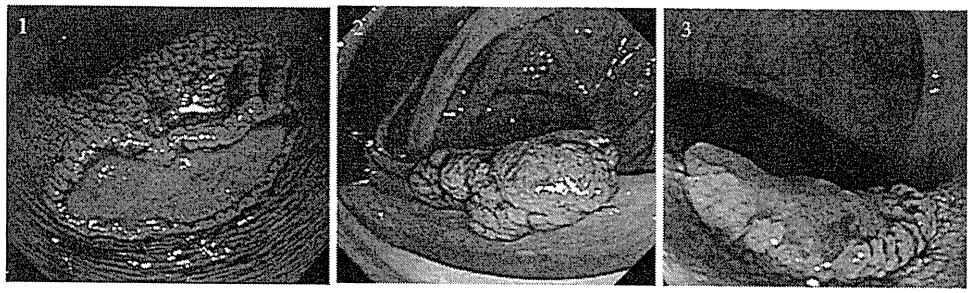

Figure 6 Redness (reddened area). (1) IIc (LST-NG), SM superficial cancer; (2) Is, SM deep cancer; and (3) IIa + IIc, SM deep cancer. (Color figure is available online at www.techgiendoscopy.com.)

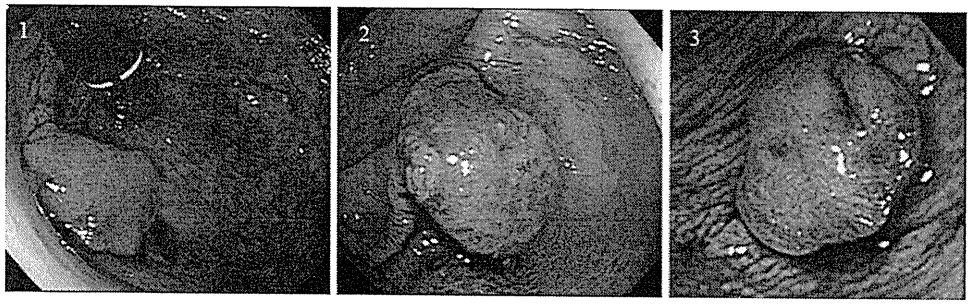

Figure 7 Expansion. (1) Is, SM deep cancer; and (2 and 3) Is + IIc, SM deep cancer. (Color figure is available online at www.techgiendoscopy.com.)

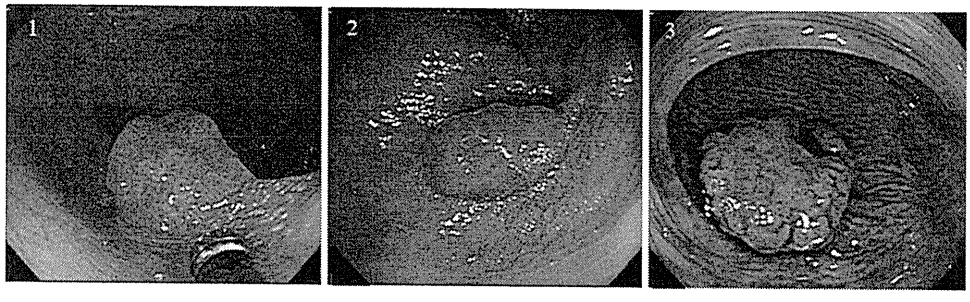

Figure 8 Firm consistency. (1 and 2) Is, SM deep cancer; and (3) IIa + IIc, SM deep cancer. (Color figure is available online at www.techgiendoscopy.com.)

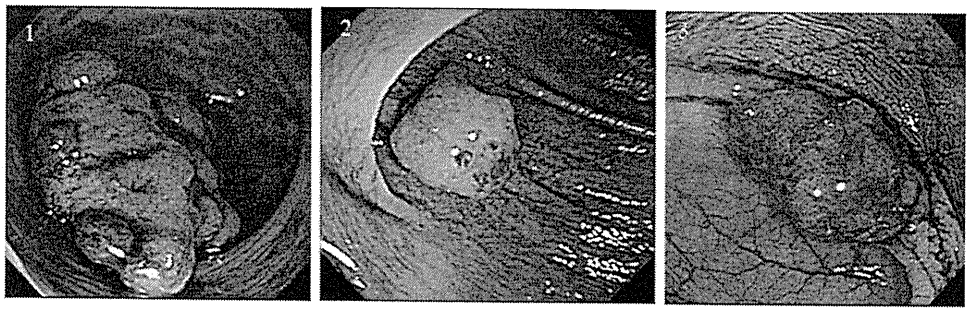

Figure 9 Irregular surface. (1-3) Is, SM deep cancer. (Color figure is available online at www.techgiendoscopy.com.)

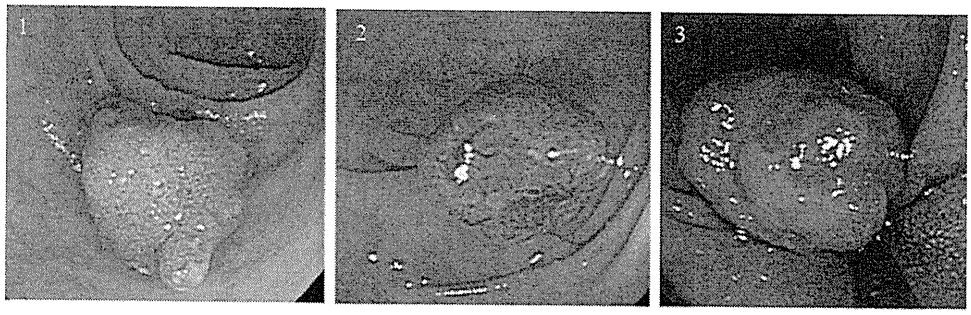

Figure 10 Loss of lobulation. (1-3) Is, SM deep cancer. (Color figure is available online at www.techgiendoscopy.com.)

(LST-NG) type, which has no submucosal invasion resembles this finding because of submucosal fibrosis.

Irregular bottom of depression surface (Figure 4). Most of these lesions have cancer cells already invading deeply into the submucosal layer. Morphologically, such lesions are usually named Is + IIc type.

White spots (chicken skin appearance; Figure 5). Sometimes intramucosal lesions (adenoma or intramucosal cancer) indicate this finding.

Redness (reddened area; Figure 6). Chromoendoscopy (with indigo carmine) is helpful in recognizing this finding. Intramucosal lesions (adenoma or intramucosal cancer) sometimes resemble this finding. A combination of this finding and the other findings (eg, deep depression, irregular surface, expansion) are significant indicators of submucosal deep cancer.

Expansion (Figure 7). Most of these lesions have cancer cells already invading deeply into the submucosal layer. Morphologically, such lesions are usually named Is type. There is a strong relationship between this finding and loss of lobulation.

Firm consistency (Figure 8). It is crucial to confirm this finding under air volume control during observation. Lesions should be judged not only under deflated conditions but also under full inflation.

Irregular surface (Figure 9). Most of these lesions have cancer cells already invading deeply into the submucosal layer. There is a strong relationship between this finding and loss of lobulation.

Loss of lobulation (Figure 10). Most of these lesions have cancer cells already invading deeply into the submucosal layer. Morphologically, such lesions are usually named Is type. There is a strong relationship between this finding and expansion/irregular surface.

Thick stalk (Figure 11). The definition of this finding is "a thickened and expanded stalk." There is a strong relationship between this finding and submucosal deep invasion (ie, stalk invasion) in pedunculated lesions.

Magnifying colonoscopy (magnifying chromoendoscopy, NBI with magnification)

Magnifying chromoendoscopy is a validated method that facilitates detailed analysis of the morphologic architecture of colonic mucosal crypt orifices (pit pattern) in a simple and efficient manner. However, magnifying colonoscopes are still rarely used in endoscopy units. An unrecognized need and lack of randomized studies validating the effectiveness of magnifying chromoendoscopy are possible reasons for this. We believe that magnifying chromoendoscopy is an essential tool in gastrointestinal endoscopy units, with its main clinical significance being the in vivo diagnosis of the nature of colorectal lesions to determine the appropriate treatment modality. Recently, NBI, a modified technique that provides a unique image emphasizing the CP, as well as the surface pattern, has become widely available. Its

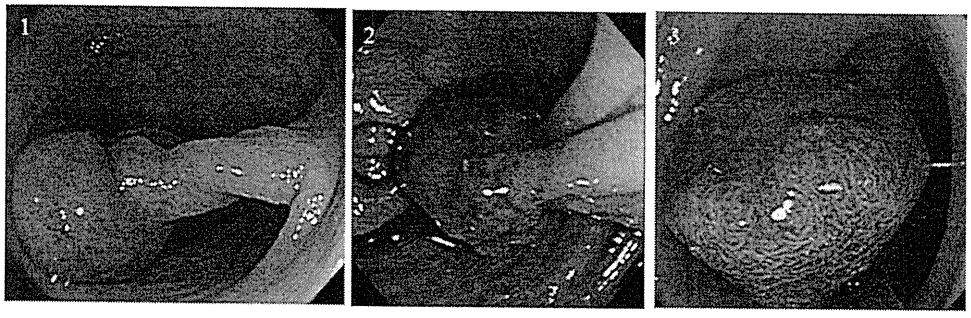

Figure 11 Thick stalk. (1) Ip, SM deep (stalk invasion) cancer; (2) Ip, SM superficial (head invasion) cancer; and (3) Ip + IIc, SM deep (stalk invasion) cancer. (Color figure is available online at www.techgiendoscopy.com.)

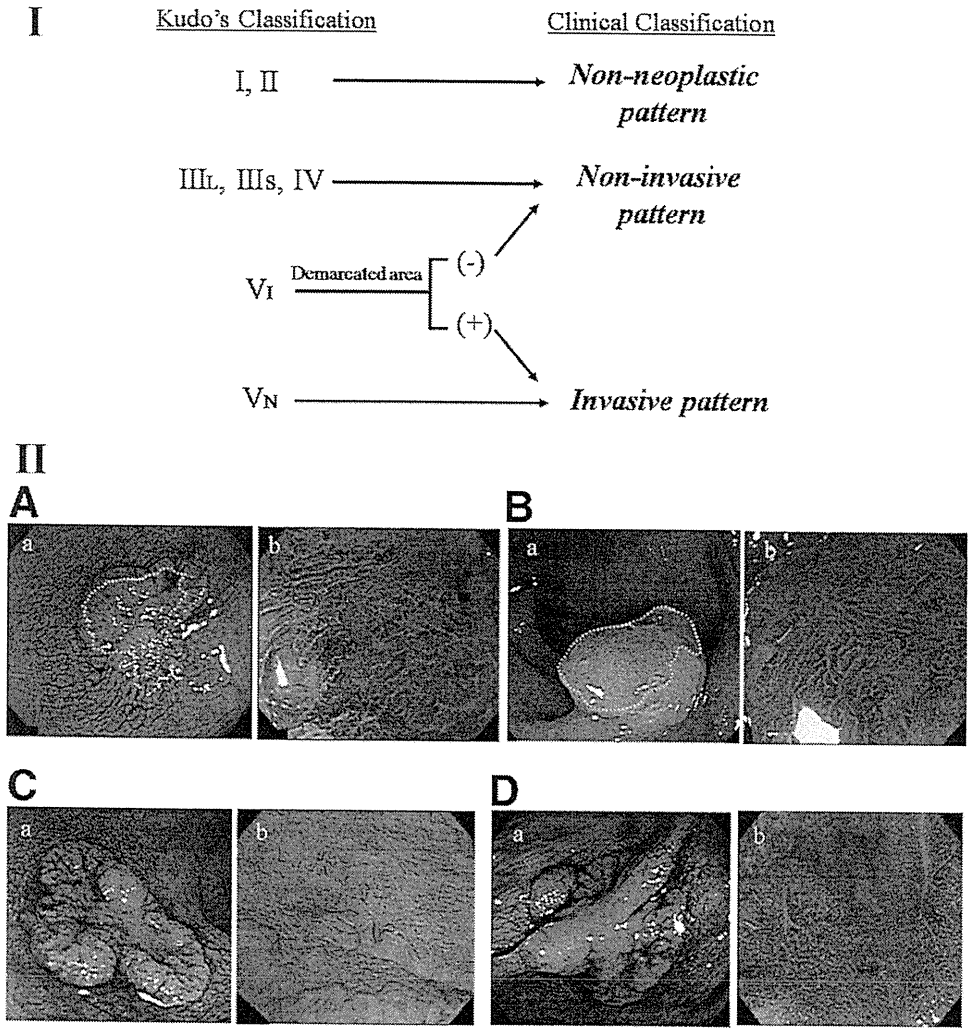

Figure 12 Definition of invasive/noninvasive pattern. (A and B) Invasive pattern: irregular or distorted pit with demarcated area. (C and D) Noninvasive pattern: regular pit with or without demarcated area or irregular pits without a demarcated area. (Color figure is available online at www.techgiendoscopy.com.)

visual effect is similar to that of chromoendoscopy. Because of the layered nature of the gastrointestinal mucosa, assessment of the CP is critical for the diagnosis of superficial lesions. Otherwise, this system can be installed by changing the optical filters from the conventional broadband type to a narrow-band type and is available for existing endoscopes, including the magnifying endoscope.[11,22-24]

How to differentiate between mucosal/submucosal superficial and submucosal deep cancers?

Magnifying chromoendoscopy (pit pattern diagnosis). Clinical classification of the colonic pit pattern (invasive and noninvasive) using magnifying chromoendoscopy was originally described by Fujii in 1998 with the aim of discriminating between intramucosal–submucosal superficial invasion and submucosal deep invasion.[7] Contrary to the anatomic classification of Kudo et al,[5] the rationale for the clinical classification is based on the identification of irregular or distorted crypts in a demarcated area, which highly suggests that the cancerous lesion is already invading deeply into the submucosal layer.

Some studies have already reported the clinical usefulness of detailed determination of the V pit pattern using magnifying chromoendoscopy for predicting the depth of invasion of submucosal cancers.[5,9,25] We recently carried out a large prospective study of 4215 lesions in 3029 consecutive patients between 1998 and 2005. All lesions were detected by conventional endoscopic observation and assessed using magnifying chromoendoscopy for evidence of invasive features according to pit pattern evaluation.

Clinical classification

1. Nonneoplastic pattern: normal mucosa and star-shape crypts as observed in Kudo's type I or II, respectively (eg, hyperplastic, hamartomatous, and inflammatory polyps).
2. Noninvasive pattern: regular crypts with or without demarcated area or irregular pits without a demarcated

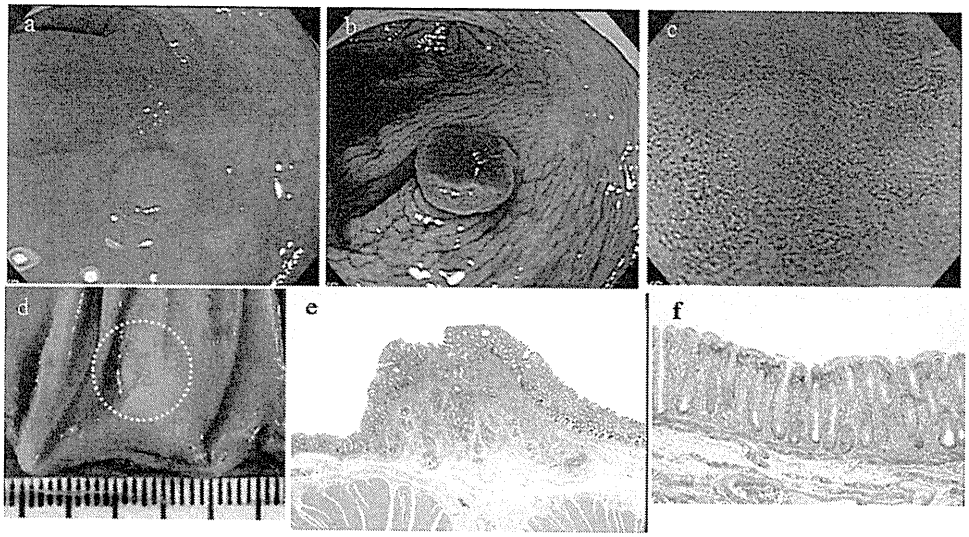

Figure 13 SM deep sigmoid colon cancer , IIa + IIc, 5 mm. Moderately differentiated adenocarcinoma with collagenous colitis. pSM (2500 μm), ly1, v0, n0. Final treatment, surgery. (Color figure is available online at www.techgiendoscopy.com.)

area. Usually observed in Kudo's type IIIs, IIIL, and IV and in selected cases of VI (eg, adenomatous polyps, intramucosal and submucosal superficial cancers), where endoscopic resection is appropriate.

3. Invasive pattern: irregular and distorted crypts in a demarcated area as observed in Kudo's type VN and selected cases of VI (eg, deep submucosal invasive cancers), where surgical resection is the appropriate treatment. Kudo's type VI is observed in both noninvasive and invasive patterns (Figures 12 and 13).

Our data showed that 99.4% of lesions diagnosed as noninvasive pattern were adenoma, intramucosal cancer, or submucosal invasion less than 1000 μm. Among lesions diagnosed with invasive pattern, 87% were cancers with submucosal deep invasion. Based on the macroscopic appearance, the diagnostic sensitivity of the clinical pit pattern to determine the depth of invasion of polypoid, flat, and depressed lesions was 75.8%, 85.7%, and 98.6%, respectively.[10]

NBI with magnification. Based on the surface characteristics of the meshed capillaries, CP type III were defined as demonstrating an irregular and unarranged pattern in the mesh-like microvascular architecture and exhibiting at least one of the following: irregular size, complicated branching,

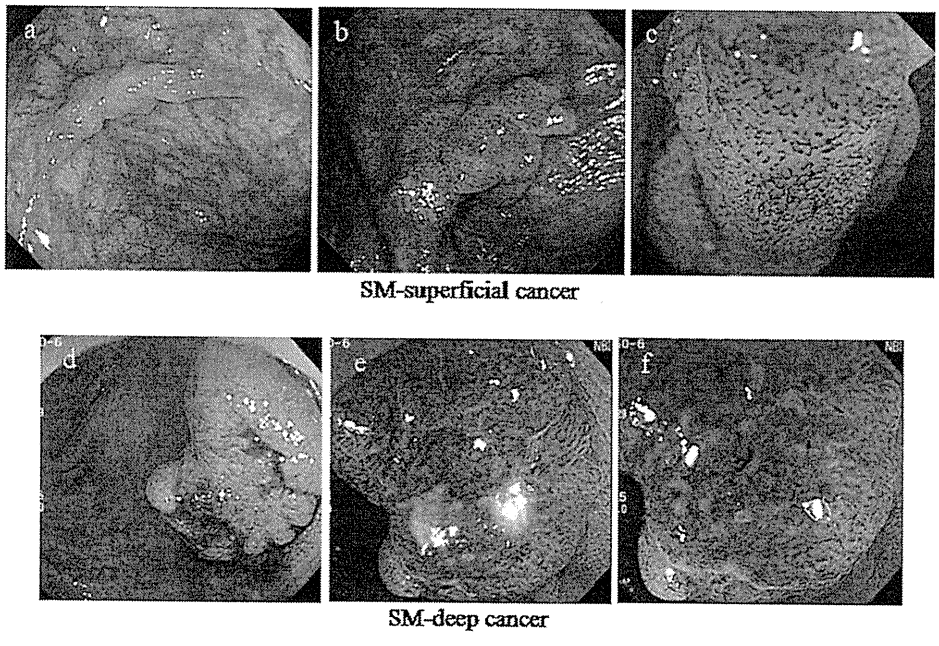

Figure 14 (a-c) CP type IIIA, SM superficial cancer; and (d-f) CP type IIIB, SM deep cancer. (Color figure is available online at www.techgiendoscopy.com.)

and disrupted irregular winding when compared with the regular small-caliber capillaries observed in adenomatous polyps (CP type II). Moreover, CP type III lesions were further classified into 2 groups: type IIIA or IIIB.

CP Type IIIA

CP type III lesions clearly show visible microvascular architecture and high microvessel density with lack of uniformity, blind ending, branching, and curtailed irregularity.

CP Type IIIB

CP type III lesions show a clear distinction between normal/cancerous mucosa on the surface (demarcated area) and the presence of a nearly avascular or loose microvascular area (Figure 14).

The diagnostic sensitivity, specificity, and diagnostic accuracy of the CP type IIIA/IIIB for differentiating intramucosal cancer or submucosal invasion less than 1000 μm from submucosal deep invasion ($\geq$1000 μm) were 84.8%, 88.7%, and 87.7%, respectively. The accuracy of CP type IIIA (negative predictive value) was 94.5% (86/91) and that for lesions of CP type IIIB (positive predictive value) was 71.8% (29/39).[11] The identification of CP type IIIA/IIIB by magnifying NBI is useful for estimating the depth of invasion of early colorectal cancers; however, there is a greater interobserver variability compared with the pit pattern diagnosis.

Conclusions

The detection and diagnosis of early colorectal cancer presents both a challenge and an opportunity. Above all, characteristic colonoscopic findings obtained by a combination of conventional colonoscopy and magnifying chromoendoscopy are useful for determining the depth of invasion of these lesions, an essential factor in selecting a treatment modality.

References

1. Tanaka S, Haruma K, Teixeira CR, et al: Endoscopic treatment of submucosal invasive colorectal carcinoma with special reference to risk factors for lymph node metastasis. J Gastroenterol 30:710-717, 1995
2. Saito Y, Fujii T, Kondo H, et al: Endoscopic treatment for laterally spreading tumors in the colon. Endoscopy 33:682-686, 2001
3. Nascimbeni R, Burgare LJ, Nivatvongs S, et al: Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. Dis Colon Rectum 45:200-206, 2002
4. Kudo S, Hirota S, Nakajima T, et al: Colorectal tumours and pit pattern. J Clin Pathol 47:880-885, 1994
5. Kudo S, Tamura S, Nakajima T, et al: Diagnosis of colorectal tumorous lesions by magnifying endoscopy. Gastrointest Endosc 44:8-14, 1996
6. Sano Y, Ikematsu H, Fu KI, et al: Meshed capillary vessels using narrow band imaging for differential diagnosis of small colorectal polyps. Gastrointest Endosc 69:278-283, 2009
7. Fujii T, Hasegawa RT, Saitoh Y, et al: Chromoscopy during colonoscopy. Endoscopy 33:1036-1041, 2001
8. Fu KI, Sano Y, Kato S, et al: Chromoendoscopy using indigo carmine dye spraying with magnifying observation is the most reliable method for differential diagnosis between non-neoplastic and neoplastic colorectal lesions: a prospective study. Endoscopy 36:1089-1093, 2004
9. Kato S, Fu KI, Sano Y, et al: Magnifying colonoscopy as a non-biopsy technique for differential diagnosis of non-neoplastic and neoplastic lesions. World J Gastroenterol 12:1416-1420, 2006
10. Matsuda T, Fujii T, Saito Y, et al: Efficacy of the invasive/non-invasive pattern by magnifying chromoendoscopy to estimate the depth of invasion of early colorectal neoplasms. Am J Gastroenterol 103:2700-2706, 2008
11. Ikematsu H, Matsuda T, Emura F, et al: Efficacy of capillary pattern type IIIA/IIIB by magnifying narrow band imaging for estimating depth of invasion of early colorectal neoplasms. BMC Gastroenterol 10:33, 2010
12. Morson BC, Whiteway JE, Jones EA, et al. Histopathology and prognosis of malignant colorectal polyps treated by endoscopic polypectomy. Gut 25:437-444, 1984
13. Fujimori T, Kawamata H, Kashida H: Precancerous lesions of the colorectum. J Gastroenterol 36:587-594, 2001
14. Kyzer S, Begin LR, Gordon PH, et al: The care of patients with colorectal polyps that contain invasive adenocarcinoma. Cancer (Phila) 70:2044-2050, 1992
15. Minamoto T, Mai M, Ogino T, et al: Early invasive colorectal carcinomas metastatic to the lymph node with attention to their nonpolypoid development. Am J Gastroenterol 88:1035-1039, 1993
16. Cooper HS: Surgical pathology of endoscopically removed malignant polyps of the colon and rectum. Am J Surg Pathol 7:613-623, 1983
17. Nusko G, Mansmann U, Partzsch U, et al: Invasive carcinoma in colorectal adenomas: multivariate analysis of patient and adenoma characteristics. Endoscopy 29:626-631, 1997
18. Shimoda T, Ikegami M, Fujisaki J, et al: Early colorectal carcinoma with special reference to its development de novo. Cancer 64:1138-1146, 1989
19. Participants in the Paris Workshop. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon. November 30 to December 1, 2002. Gastrointest Endosc, 2003 58:S3-S43
20. Saitoh Y, Obara T, Watari J, et al: Invasion depth diagnosis of depressed type early colorectal cancers by combined use of videoendoscopy and chromoendoscopy. Gastrointest Endosc 48:362-370, 1998
21. Ikehara H, Saito Y, Matsuda T, et al. Diagnosis of depth of invasion for early colorectal cancer using magnifying colonoscopy. J Gastroenterol Hepatol 25:905-912, 2010
22. Machida H, Sano Y, Hamamoto Y, et al: Narrow-band imaging in the differential diagnosis of colorectal mucosal lesions: a pilot study. Endoscopy 36:1094-1098, 2004
23. Sano Y, Saito Y, Fu KI, et al: Efficacy of magnifying chromoendoscopy for the differential diagnosis of colorectal lesions. Dig Endosc 17:105-116, 2005
24. Sano Y, Ikematsu H, Fu KI, et al: Meshed capillary vessels by use of narrow-band imaging for differential diagnosis of small colorectal polyps. Gastrointest Endosc 69:278-283, 2009
25. Bianco MA, Rotondano G, Marmo R, et al: Predictive value of magnification chromoendoscopy for diagnosing invasive neoplasia in nonpolypoid colorectal lesions and stratifying patients for endoscopic resection or surgery. Endoscopy 38:470-476, 2006