Advanced mucosal neoplasia of the anorectal junction: endoscopic resection technique and outcomes (with videos)

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Background: EMR at the anorectal junction (ARJ) is technically challenging. Issues of safety and procedural efficacy dictate that surgery is still performed as the primary management for noninvasive lesions in most centers. Modifications to the standard EMR technique may help to address the unique features and achieve safe and curative resection of most lesions.

Objective: To describe an effective and safe, modified EMR technique to remove advanced mucosal neoplasia (AMN) of the ARJ.

Design: Prospective, observational cohort study.

Setting: Academic, tertiary care referral center.

Patients: Patients undergoing EMR for AMN at the ARJ over 4.5 years, from June 2008 to December 2012.

Interventions: Use of long-acting local anesthetic in the submucosal injectate, endoscopic resection over the dentate line and hemorrhoidal columns, prophylactic antibiotics for resection of lesions at high risk for bacteremia, and cap and gastroscope-assisted resection.

Main Outcome Measurements: Procedural success and safety.

Results: Twenty-six patients with lesions involving the ARJ were referred for EMR (males 53.8%, median age 63, median lesion size 40 mm). Two patients went directly to surgery because of an endoscopic diagnosis of adenocarcinoma. EMR was performed in 24 lesions with complete adenoma clearance achieved in 100%. Four patients were admitted to the hospital. Focal adenoma recurrence was seen in 4 of 18 patients (22%) at first surveillance colonoscopy and was managed by snare diathermy resection. No recurrences were found at the second follow-up colonoscopy. Procedural success, adenoma recurrence, and admission rates were similar between EMRs performed at the ARJ and proximal rectum on univariate analysis (all $P > .05$).

Limitations: Single tertiary center, nonrandomized study.

Conclusions: Simple modifications to the EMR technique allow safe and effective treatment of AMN at the ARJ on an outpatient basis and should be the first-line management when the risk of invasive disease is low. (Gastrointest Endosc 2014;79:119-26.)

Abbreviations: AMN, advanced mucosal neoplasia; ARJ, anorectal junction.

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Large prospective multicenter studies have proven the safety and efficacy of endoscopic resection of large sessile polyps and laterally spreading tumors ≥ 20 mm (or advanced mucosal neoplasia [AMN]) in the colorectum.[1] These may uncommonly involve the very distal rectum and anorectal junction (ARJ).

Endoscopic resection at the ARJ is technically challenging because of the regions distinctive anatomic and physiologic characteristics. Endoscopic access is often restricted, and visualization may be poor. The unique innervation and lymphovascular supply require specific measures to limit pain and bleeding from resecting over the dentate line and hemorrhoidal vessels. There is also the theoretical risk of systemic bacteremia because of direct drainage into the systemic circulation.[2] Thus, the threshold to defer to inpatient care, surgical management, and general anesthesia may be decreased because of clinician concern about safety, procedural complexity, and efficacy.

A preferred or ideal EMR strategy for these lesions has not been defined. Safe and effective endoscopic management could offer substantial clinical gains and cost savings.[3] We describe our EMR technique at the ARJ and report prospective patient outcomes in an effort to standardize and improve the endoscopic management of this important subgroup of lesions. We hypothesize that a simple modification to the EMR technique, including the method of injection and resection over hemorrhoidal columns, addition of a long-acting local anesthetic in the submucosal injectate, prophylactic antibiotics for high-risk lesions, and use of a gastroscope or transparent cap to improve lesion access, allows safe and effective treatment of AMN at the ARJ on an outpatient basis, with comparable outcomes with those achieved with EMR in the proximal rectum.

Take-home Message

- Modification of the EMR technique, including long-acting local anesthetics in the submucosal injectate, intravenous antibiotics for lesions at high risk of bacterial translocation, and methods to optimize tissue capture and lesion positioning, may improve outcomes.
- Success rates of EMR for advanced mucosal neoplasia (AMN) involving the anorectal junction (ARJ) are similar to more proximal rectal lesions, allowing for resection on an outpatient basis with minimal patient morbidity.

METHODS

Data were collected and analyzed for all patients with lesions involving the ARJ and rectum as part of a prospective, observational study of consecutive patients referred to a single tertiary care referral center for EMR of AMN ≥ 20 mm from June 2008 to December 2012. Hospital research ethics committee approval was obtained (HREC2008/9/6.1 [2858] QA). ARJ location was defined as involving the dentate line or lying within 2 cm of the dentate line. All procedures were performed or directly supervised by 2 senior endoscopists (M.J.B. and S.J.W.). The EMR technique was previously described in detail.[4,5]

Resections were performed using a microprocessor-controlled electrosurgical generator (VIO 300D; Erbe, Tübingen, Germany). Normal saline solution was used as the injection fluid until January 2010, and succinylated gelatin (Gelofusine; B. Braun, Crissier, Switzerland) was used thereafter when its technical superiority was proven.[6] The injectate additionally contained indigo carmine blue (80 mg per 500 mL solution) and 1:100,000 adrenaline. Procedures were performed with air insufflation only from June 2008 to March 2010 and with CO_2 insufflation only from August 2010 to December 2012.[7] Procedures were performed on an outpatient basis.

Intravenous sedation was performed using a combination of midazolam, fentanyl, and propofol. Patients were observed for 4 hours after EMR and, if well, were discharged with instructions to maintain a clear fluid diet overnight, resuming a normal diet the following day. First and second surveillance colonoscopy were scheduled at 4- and 12-month intervals (ie, 4 and 16 months after EMR). Primary outcome measures were procedural success and adverse event frequency. Procedural success was defined as complete adenoma resection at the time of EMR. Adverse events were defined as the need for postprocedural hospital admission.

Technical aspects specific to ARJ lesions

The following describes specific aspects of the procedures used for AJR lesions (see Video 1, available online at www.giejournal.org):

1. Endoscopic resection over hemorrhoidal columns
   - Tangential submucosal injection in the forward view (with the colonoscope or gastroscope at the dentate line) elevates the mucosa away from the hemorrhoidal columns beneath, reducing the risk of vessel entrapment within the snare during snare closure (Fig. 1).
2. Long-acting local anesthetic in the submucosal injectate
   - Ropivacaine or bupivacaine .5% was used in the submucosal injectate, to a maximum dose of 40 mg. Patients require cardiac monitoring.[8] Painless resection over the dentate line ensues. Anesthesia is provided for 4 hours and analgesia for at least 12 hours.
3. Prophylactic antibiotics
   - Antibiotics should be considered for lesions with an increased risk for direct systemic bacterial translocation, particularly lesions > 40 mm with a rich vascular network within the EMR defect or multiple exposed hemorrhoidal vessels.
4. Optimization of access and lesion positioning
   - A transparent cap deflects mucosal folds and improves access, particularly within the confines of the anal canal and distal rectum.
   - Gastroscopes have a shorter bending section with a narrower radius of 180-degree angulation. This

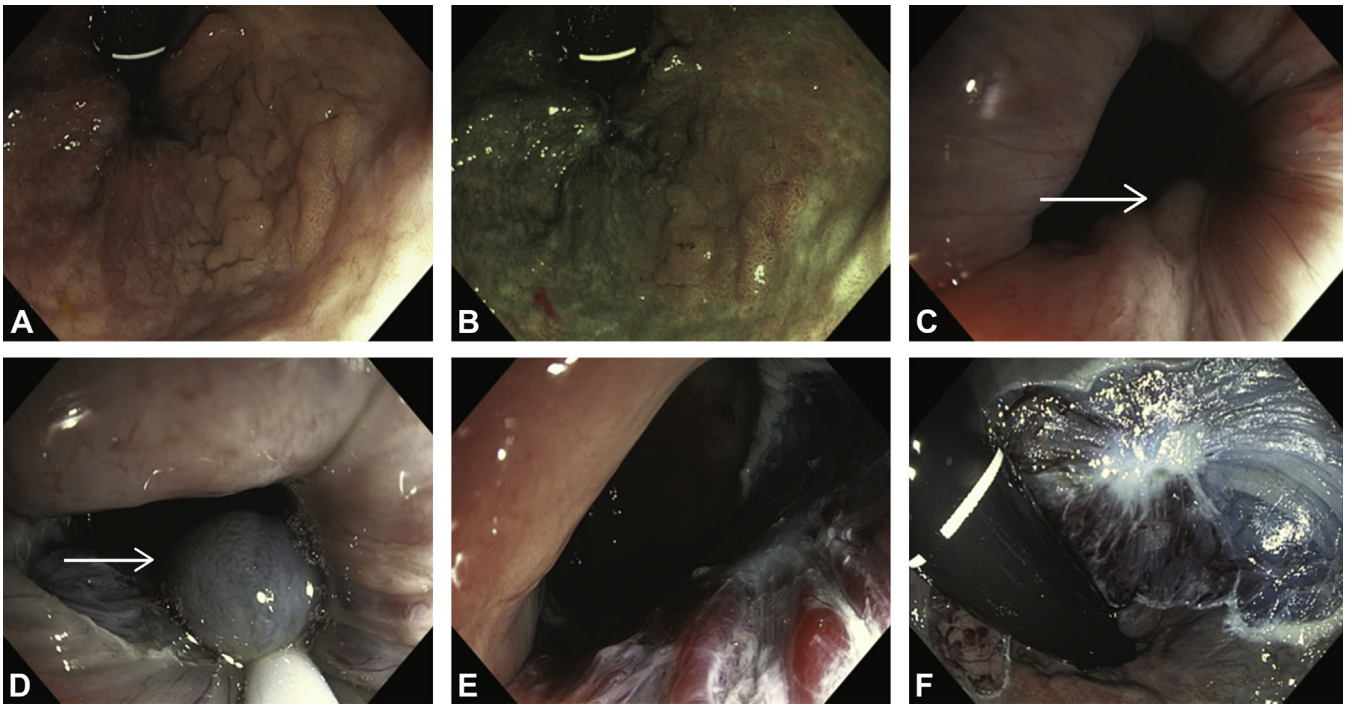

Figure 1. A and **B**, A 60-mm Paris 0-IIa/b granular advanced mucosal neoplasia (AMN) located in the distal rectum, involving the anorectal junction (ARJ). The full extent of the lesion is best seen with narrow-band imaging. **C** and **D,** Complete adenoma removal involves resection across the dentate line *(adenoma indicated by the white arrow)*. **E,** Multiple large hemorrhoidal columns are located in the submucosa. **F,** The 60% circumferential defect contains a central area of submucosal fibrosis, exposed rings of circular muscle fibers, and multiple submucosal vessels.

Figure 2. A, A gastroscope is used for resection of a 50-mm 0-IIa+Is granular lesion involving the anorectal junction (ARJ), viewed in retroflexion after submucosal injection. The 0-Is component is removed first. **B,** The uninjured circular muscle layer is clearly visible. The muscle layer typically stains poorly with indigo carmine. **C,** The final mucosal defect.

enhances access to the lesion and snare placement, particularly when retroflexed (Fig. 2).
- Lesion exposure can be improved by changing the patient's position to use the effect of gravity on the rectal mucosa and fluid pools, thus orienting the lesion in line with the colonoscope working channel in the 5 o'clock to 6 o'clock positions.

5. Discharge management
   - Advise to maintain soft stools for 1 to 2 weeks.
   - Analgesia: oral paracetamol 1 g every 4 to 6 hours for 3 days if required.

Statistical analysis

Statistical analysis was performed using SPSS 19.0 (SPSS Inc., Chicago, IL, USA). Comparison was made between the ARJ and the proximal rectal AMN. The main outcomes were number of attempted EMRs, success of EMR, recurrence at initial follow-up colonoscopy, and hospital admissions. The Pearson χ^2 test or Fisher exact test as appropriate was used to test for association between categorical variables and outcome. The Mann-Whitney *U* test was applied for comparison of continuous variables. A 2-tailed probability (*P*) value $< .05$ was considered to be significant.

TABLE 1. Patient and lesion characteristics of ARJ AMNs

Characteristic	Value (%)
Gender	
Male	14 (53.8)
Female	12 (46.2)
Median age, years (range)	63 (26-87)
ASA grade	
1	16 (61.5)
2	8 (30.8)
3	2 (7.7)
4	0
Median polyp size, mm (range)	40 (25-180)
Paris classification	
0-Is and 0-IIa/b + Is	18 (69.2)
0-IIa/b	7 (26.9)
0-IIa/b +c or 0-IIc	1 (3.8)
Morphology	
Granular	24 (92.3)
Nongranular	1 (3.8)
Mixed	1 (3.8)
Endoscopic features of invasion	
Yes	2 (7.7)
No	24 (92.3)
Histology	
TVA	17 (70.8)
TA	1 (4.2)
TSA	4 (16.7)
SSA	1 (4.2)
TVA + SSA	1 (4.2)
Dysplasia	
LGD	19 (73.1)
HGD	5 (19.2)
Cancer	2 (7.7)

ARJ, Anorectal junction; *AMN,* advanced mucosal neoplasia; *ASA,* American Society of Anesthesiologists; *TVA,* tubulovillous adenoma; *TA,* tubular adenoma; *TSA,* traditional serrated adenoma; *SSA,* sessile serrated adenoma; *LGD,* low-grade dysplasia; *HGD,* high-grade dysplasia.

RESULTS

One hundred sixty-three patients with rectal AMNs were referred for EMR. Twenty-six AMNs (16%) involved the ARJ. Patient and lesion characteristics are described in Table 1.

Features suspicious for submucosal invasion were seen on endoscopic inspection of 2 lesions. A biopsy sample was taken from the lesions, and EMR not attempted. Both were proven to have invasive cancer and were referred for surgical treatment. One patient had an abdominoperineal resection, and no further treatment is planned because of comorbidities. The second patient had a total proctocolectomy in a setting of familial adenomatous polyposis and subsequent adjuvant chemotherapy for node-positive disease.

Twenty-four ARJ AMNs were suitable for EMR, and complete endoscopic adenoma clearance was achieved in 100%. Median resection time was 26 minutes (range, 5-80 minutes). Intraprocedural bleeding requiring intervention occurred during 6 resections (25%), and endoscopic hemostasis was achieved with snare-tip soft coagulation in all cases[9] (Fig. 3). No hemorrhoidal bleeding occurred, and there were no perforations.

Two patients were referred for surgery of proximal colonic lesions after successful ARJ lesion resection. One was a 59-year-old woman with an appendiceal adenoma who had an uncomplicated laparoscopic ileocecal resection after successful EMR of a 40-mm Paris 0-IIa granular tubulovillous adenoma with low-grade dysplasia at the ARJ. The second patient was a 26-year-old woman with attenuated familial adenomatous polyposis who had an EMR of a 25-mm Paris 0-IIb nongranular traditional serrated adenoma with low-grade dysplasia at the ARJ. She underwent colectomy and ileorectal anastomosis after a scheduled surveillance colonoscopy after 4-months confirmed absence of adenoma recurrence.

The submucosal injectate of all ARJ resections included a long-acting local anesthetic (ropivacaine or bupivacaine), and no immediate adverse events were seen. Prophylactic intravenous antibiotics were given in 8 patients thought to be at risk for direct systemic bacterial translocation because of resection defect size and the rich vascular network within. Five patients were discharged on oral antibiotics.

Comparison between resections performed at the ARJ and proximal rectum showed no difference in proportion of EMRs attempted, procedural success, or hospital admissions (Table 2). Four patients required hospital admission after ARJ resection (15%). Two were admitted from recovery (1 with morbid obesity because of concern about care at home and 1 with rigors who was treated with intravenous antibiotics; both were discharged the following day). Two presented to the hospital after discharge: 1 had right-sided lower back pain and 1 had delayed bleeding. Both were managed conservatively and were discharged on days 2 and 3, respectively. Two patients developed mildly symptomatic anal strictures after circumferential EMR at the ARJ, which were successfully managed with digital dilation at surveillance colonoscopy.

Initial follow-up colonoscopy at 4 months has been performed in 18 patients with ARJ lesions (75%). Six patients

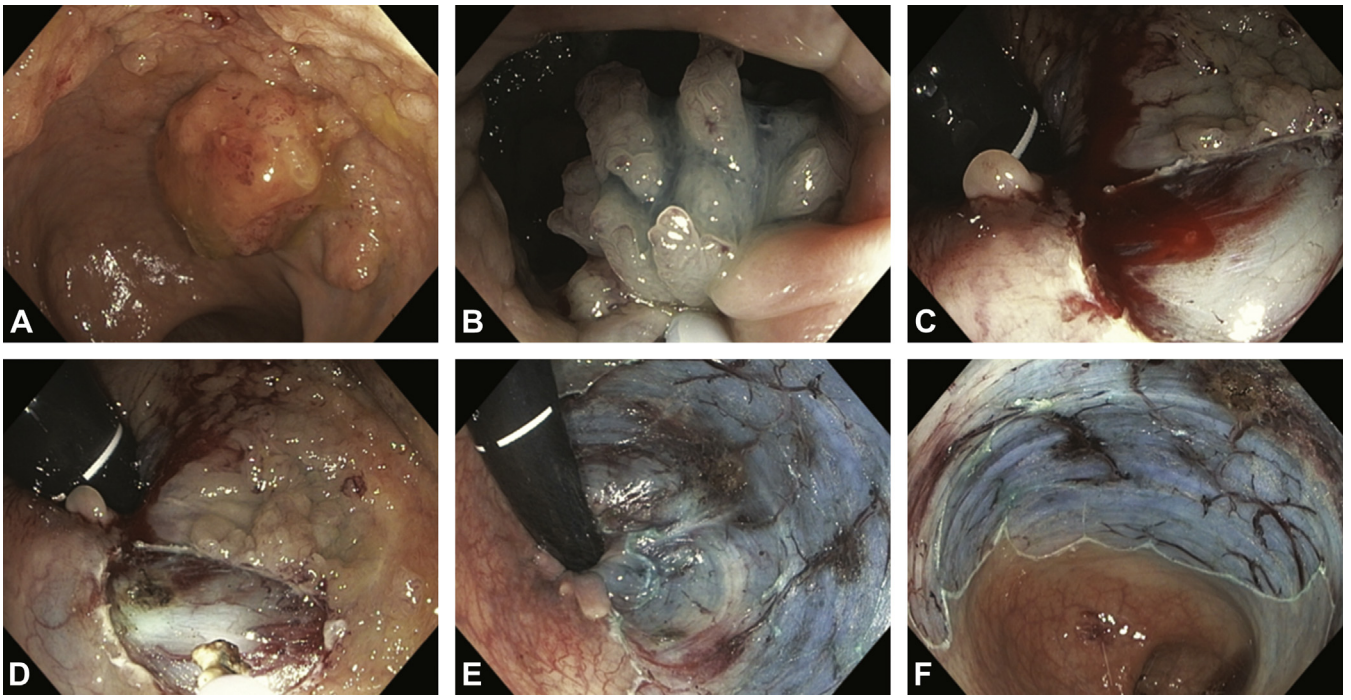

Figure 3. A, An extensive, hemicircumferential 70-mm Paris 0-IIa+Is mixed granular and nongranular AMN involves the anorectal junction (ARJ). **B,** Resection commences in the forward view, with the pediatric colonoscope positioned within the anal canal. Injection containing ropivacaine .5% and 1:100,000 adrenaline lifts the lesion into the rectal lumen, and resection commences with a thin wire snare. **C** and **D,** Pulsatile bleeding is effectively controlled with snare-tip soft coagulation. **E** and **F,** The final result is a 60% circumferential defect, extending from the ARJ to mid-rectum.

TABLE 2. Comparison of ARJ and proximal rectal EMRs: a univariate analysis

		ARJ (%)	Proximal rectal (%)	Odds ratio	95% confidence interval	*P*
EMR attempted	Yes	24 (92.3)	132 (96.4)	2.2	0.4–12.0	.310
	No	2 (7.7)	5 (3.6)			
EMR success	Yes	24 (100)	123 (93.2)	0	0–NA	.356
	No	0 (0%)	9 (6.8)			
Admission	Yes	4 (15.4)	12 (8.9)	.6	0.2–2.0	.295
	No	24 (84.6)	123 (91.1)			

ARJ, Anorectal junction; *NA,* not available.

have not had initial follow-up colonoscopies (1 postsurgical recovery, 1 significant comorbidities, and 4 not yet due). Adenoma recurrence was seen in 4 of 18 patients at initial follow-up colonoscopy (22%). All recurrences were unifocal, small, and successfully treated by snare diathermy with coagulating current; these patients have not yet had the second scheduled surveillance. Seven patients have had a second per protocol surveillance procedure, and no recurrence was found (Fig. 4).

DISCUSSION

The unique lymphovascular supply, innervation, and anatomy of the distal rectum and anus necessitates modification to the standard EMR technique to optimize efficacy and safety. The sensory nerve supply around the dentate line is somatic, and anesthesia for resection is required. Ideally, a long-acting local anesthetic is administered at the time of resection to decrease the depth of procedural sedation necessary and provide analgesia postprocedurally. Local anesthetic perianal block is commonly used in the surgical setting, with minimal adverse events and significant cost benefits compared with spinal or general anaesthesia.[10,11] Our practice is to combine long-acting local anesthetics such as ropivacaine or bupivacaine in the submucosal injection fluid, because they have favorable safety profiles in comparison with other amide local anesthetics. Intravascular injection is the main risk, manifesting as lightheadedness with visual and auditory disturbances in the conscious patient or muscular twitching or fitting in the sedated patient.[8] These serious reactions

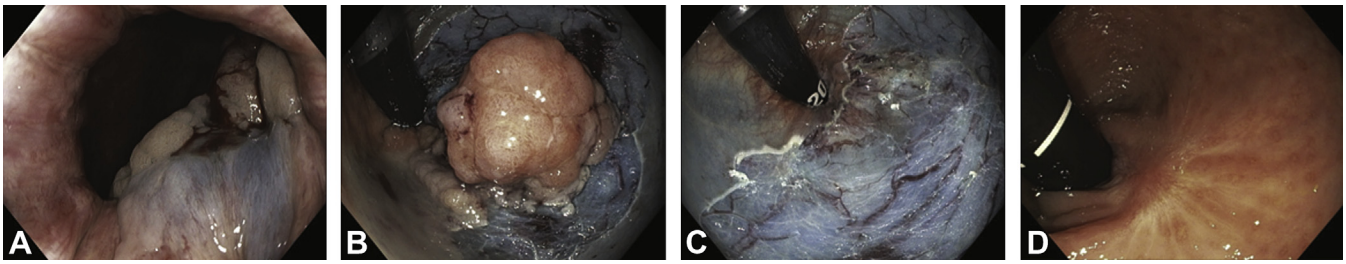

Figure 4. A, Resection of this 60-mm Paris 0-IIa+Is nongranular advanced mucosal neoplasia (AMN) commenced with injection at the dentate line to elevate the lesion above the underlying hemorrhoidal columns. **B** and **C,** The 0-IIa component is resected from around the central 0-Is component with a thin wire snare. The 0-Is component is then removed en bloc with a serrated snare and sent separately to pathology. **D,** A well-healed scar with no adenoma recurrence is seen at the 4-month follow-up colonoscopy.

reflect acute systemic toxicity and are uncommon. Cardiac arrhythmias may also arise. Patients always require cardiac monitoring during this procedure, with careful avoidance of injection into deep submucosal vessels. Because the total dose is capped and analgesia is not required in the more proximal rectum, we restrict the use of the local anesthetic containing submucosal injectate to around the anorectal region. The injection is commenced as the mucosa is stabbed; this technique swiftly confirms correct needle-tip placement.[4,5]

Routine antibiotic prophylaxis is not currently recommended for colonic EMR.[12] However, extensive, particularly distal, rectal EMR necessitating multiple submucosal injections into an area relatively unprotected by the reticuloenthelial function of the portal lymphovenous drainage system may increase the risk of symptomatic systemic bacteremia (Fig. 5). Prophylactic antibiotics should be considered for cases at significant risk of bacteremia, such as AMNs $>$ 40 mm in diameter located within 5 cm of the dentate line. Before initiating this approach, we have seen rigors at the completion of an otherwise uncomplicated distal rectal EMR for large lesions (Video 2, available online at www.giejournal.org). This is rarely seen with colonic EMR[13] in which we do not routinely use antibiotics even in very extensive resections.

AMN overlying hemorrhoidal columns can be safely resected by EMR. The submucosal injection creates a fluid cushion between the hemorrhoidal vessels in the deep submucosa and the resection plane in the superficial submucosa. Bleeding risk is minimized by directing the submucosal injection to avoid visible hemorrhoidal columns. Anecdotally, in our experience, after submucosal injection the thick-walled hemorrhoidal columns seem resistant to entrapment by the snare, appearing to slide out beneath as the snare is closed.

Complete adenoma resection can be affected by inadequate lesion exposure and positioning and can be improved by using a transparent cap to deflect mucosal folds. Changing to a gastroscope for increased mobility and ease of retroflexion may also assist, as may patient position change to enhance the influence of gravity on lesion elevation and access. The 8 o'clock orientation of the gastroscope working channel may make lesion capture more difficult, and this needs to be borne in mind.

Extensive rectal EMR may cause a degree of rectal luminal narrowing and occasionally loss of rectal capacitance, leading to tenesmus and incontinence. This is uncommon but should be considered during patient selection and consent. Acute urinary retention after rectal EMR can also occur and may be precipitated by acute pain or opioid analgesics or local autonomic disruption from local anesthetic, cautery, or fluid injection. It is usually self-limited but requires short-term urinary catheterization. Wide-field EMR at the ARJ can be considered as minor anorectal surgery, with a similar spectrum of potential postprocedural adverse events.[14-16] These specific adverse events were not prospectively recorded as part of this observational study.

Adenoma recurrence rate at the ARJ is similar to more proximal rectal lesions. Recurrences are typically small, unifocal, and easily amenable to endoscopic clearance at the first surveillance colonoscopy. A limitation of this study is that complete colonoscopic follow-up has not yet been performed; however, a large multicenter colorectal EMR series showed that 98% of patients after a successful initial procedure were free of recurrence at long-term endoscopic follow-up.[17]

Alternative management strategies for noninvasive ARJ adenomas include endoscopic submucosal dissection and surgical resection. Rectal lesions $>$ 25 mm can be resected en bloc with endoscopic submucosal dissection, allowing complete histologic evaluation of the lateral and deep margins. However, its application is currently limited by the significant time and specialized skills required. In a busy, poorly time-resourced endoscopy service, there is also a very significant opportunity cost related to endoscopic submucosal dissection as a primary therapy without any proven benefit over EMR for noninvasive AMN. Transanal endoscopic microsurgery has been advocated for distal rectal lesions, because of advantages of intact specimen retrieval and possible lower recurrence rates. However, it is much more expensive, requires hospital admission and general anesthesia, and is associated with significant adverse events such as incontinence. Adenoma recurrence occurs in 2.9% to 10.2%[15,18-20] of cases and usually requires

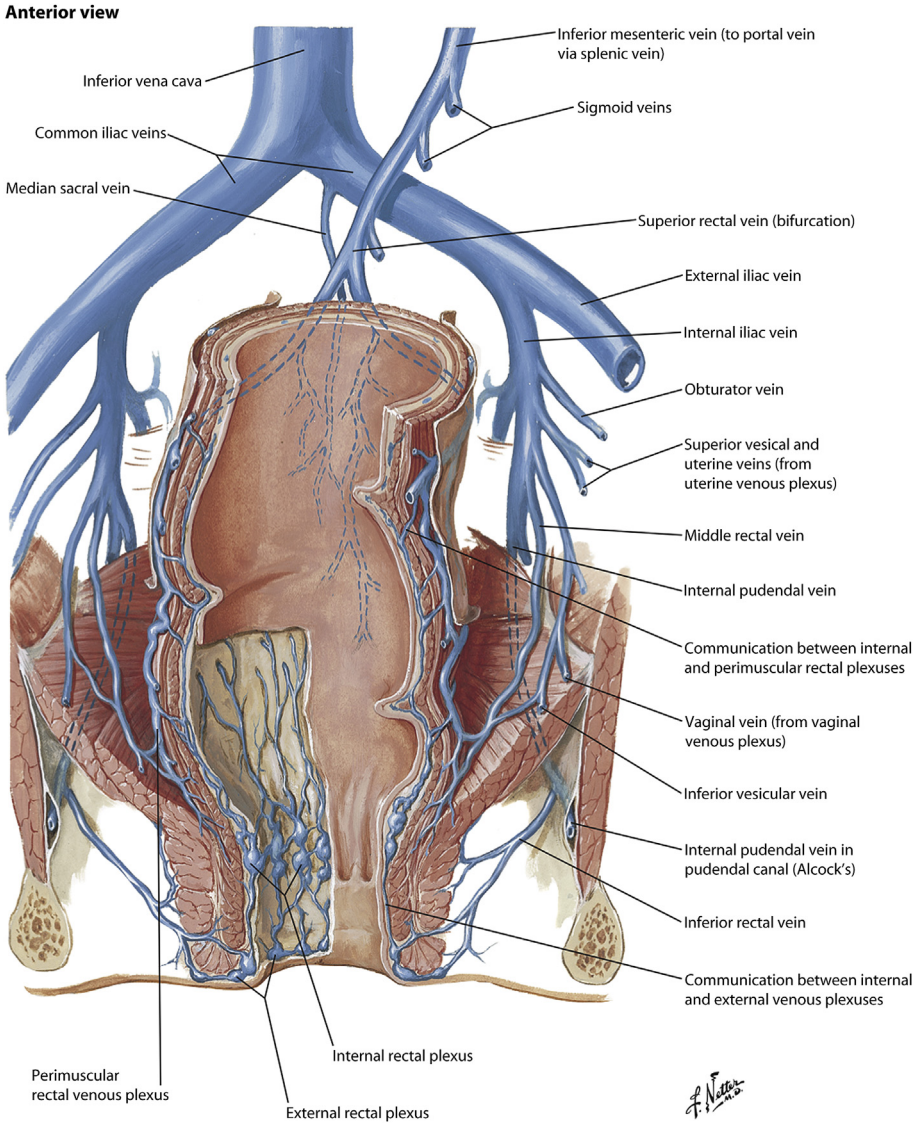

Figure 5. In contrast to the mid-to-proximal rectum that has portovenous drainage via the superior rectal vein, the distal rectum and anorectal junction (ARJ) drain directly to the systemic circulation through the middle and inferior rectal and then internal iliac veins. This theoretically increases the risk of bacteremia during distal rectal and ARJ EMR compared with more proximal colorectal resections (Netter medical illustration used with permission of Elsevier. All rights reserved).

repeat surgery. A randomized comparison is currently underway.[21]

Simple modification of the EMR technique allows safe and effective treatment of AMN at the ARJ on an outpatient basis, even when disease is extensive or the dentate line is involved. EMR should be considered as a first-line therapy in the absence of invasive disease.

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