

Treatment of chronic radiation proctopathy with radiofrequency ablation (with video)

Tarun Rustagi, MD,¹ F. Scott Corbett, MD,² Hiroshi Mashimo, MD, PhD³

New Haven, Connecticut; Sarasota, Florida; Boston, Massachusetts, USA

Background: Chronic radiation proctopathy (CRP) is a common sequela occurring even many years after pelvic radiation. Current ablative therapies for bleeding ectatic vessels have the potential for deep tissue injury leading to ulcerations, perforation, and fistulas. Radiofrequency ablation (RFA) therapy avoids deep tissue injury and is a promising treatment for CRP.

Objective: To assess the long-term safety and efficacy of RFA for the treatment of CRP.

Design: Multicenter, retrospective analysis of a prospectively collected database.

Setting: Veterans Affairs Boston Healthcare System, Massachusetts; Sarasota Memorial Hospital and Suncoast Endoscopy of Sarasota, Florida.

Patients: A total of 39 consecutive patients with CRP.

Interventions: Endoscopic RFA of CRP.

Main Outcome Measurements: The primary endpoint of the study was complete resolution of rectal bleeding. Secondary endpoints included visually scored improvement of CRP on endoscopic follow-up by using a rectal telangiectasia density (RTD) grading score, improvement in hemoglobin level, and adverse events related to the procedure.

Results: A total of 39 male patients (mean [\pm standard deviation {SD}] age 72.9 ± 6.6 years) were included in the study. The mean number of RFA sessions was 1.49 (median 1, interquartile range [IQR] 1-2, range 1-4), with a mean interval of 18 weeks between sessions. Rectal bleeding stopped completely in all patients during the mean follow-up of 28 months (range 7-53 months). A significant improvement occurred in the mean (\pm SD) hemoglobin level from 11.8 ± 2 to 13.5 ± 1.6 g % ($P < .0001$). Endoscopic severity also improved significantly with an improvement in the median RTD score from 3 (IQR 2-3) to 0 (IQR 0-1) ($P < .0001$). Treatment with RFA led to discontinuation of blood transfusion and iron therapy in 92% and 82% patients, respectively.

Limitations: Retrospective analysis, lack of control group.

Conclusion: RFA therapy led to complete resolution of rectal bleeding in all treated CRP patients, with improvement in clinical and endoscopic indices without any major adverse events. Further controlled studies are needed to establish RFA as the endoscopic therapy of choice for treatment of CRP. (Gastrointest Endosc 2015;81:428-36.)

(footnotes appear on last page of article)

Chronic radiation proctopathy (CRP) occurs in 5% to 20% of patients after pelvic radiotherapy for prostate or



This video can be viewed directly from the GIE website or by using the QR code and your mobile device. Download a free QR code scanner by searching "QR Scanner" in your mobile device's app store.

gynecologic malignancy¹⁻⁷ and is marked by endothelial dysfunction, microvascular injury with intimal fibrosis, and fibrin thrombi of small arteries and arterioles leading to ischemia, fibrosis, and development of neovascular lesions.^{1,2,7} Rectal bleeding can start many years after the radiation treatments and may become annoying or embarrassing to the individual or clinically significant with possible iron deficiency anemia requiring blood transfusion.^{4,7} Other symptoms of CRP include diarrhea, mucoid discharge, urgency, tenesmus, rectal pain, and fecal

incontinence. CRP can resolve spontaneously in many cases but in some can lead to persistent rectal bleeding and fecal seepage.

Treatments for CRP generally remain unsatisfactory. Medical measures, including formalin application,^{5,8-11} topical sucralfate,^{6,12,13} 5-amino salicylic acid enemas,^{14,15} short-chain fatty acids,^{16,17} and antioxidants such as vitamin E¹⁸ and pentoxifylline¹⁹ have been used with limited success. Endoscopic therapies such as argon plasma coagulation (APC) appear to achieve faster responses and have been suggested as a first-line therapy of CRP for most patients.^{7,20,21} Although APC and various electrocautery techniques are used to treat acute bleeding, the general depths of tissue damage with these modalities are 2 to 3 mm from the luminal surface on single application and can be deeper with multiple applications, leading to non-healing ulcerations, stricturing, and even rectovaginal or colovesicular fistulas.²²⁻²⁷ Moreover, controlled data to suggest safety and efficacy are lacking. Radiofrequency ablation (RFA) was approved by the U.S. Food and Drug Administration in 2001 for the treatment of Barrett's esophagus and for hemostatic applications in the stomach.²⁸⁻³⁰ It achieves superficial and broad fields of ablation in the esophagus, with minimal stricturing or ulcerations,^{31,32} suggesting that similar benefits could be achieved in the colon and rectum. RFA with the Halo90 system (BARRx/Covidien, Sunnyvale, Calif, USA) for treatment of CRP has been described in 3 case reports (total 5 patients),³³⁻³⁵ but its efficacy, safety, and long-term follow-up have not been reported. The aim of this study is to assess the safety and efficacy of RFA for the treatment of CRP and to define a consensus for optimal methodology in RFA treatment and follow-up based on experiences from high-volume endoscopic centers.

METHODS

This was a multicenter, retrospective analysis of a prospectively collected database of all CRP patients treated with RFA at Veterans Affairs Boston Healthcare System in Massachusetts and Sarasota Memorial Hospital and Suncoast Endoscopy of Sarasota (Florida Digestive Health Specialists) in Florida. The study protocol was approved by the respective institutional review boards. Written informed consent was obtained from each patient before the procedure, explaining the risks, benefits, and novelty of this therapeutic approach and allowing use of pathology and endoscopic photographs and videos for research and publication.

Patient population

Thirty-nine consecutive patients seen through inpatient and outpatient referrals for hemorrhagic CRP at the centers of interest who underwent RFA treatment were included in this study for data analysis. Inclusion criteria for RFA treatment were a history of pelvic radiation, with the last

radiation treatment >6 months before study enrollment, recurrent hematochezia for >3 months, age >18 years, and endoscopic evidence of radiation proctitis. Exclusion criteria for RFA treatment were evidence of active infection; concomitant treatment with other forms of medical or endoscopic therapy; endoscopic evidence of other sources of hematochezia including ulcers, colon cancer, inflammatory bowel disease, and hemorrhoids; age <18 years; anorectal fistula; anal fissure; anorectal abscess; anorectal stenosis or stricture that may preclude retroflexion or passage of the gastroscope; severe thrombocytopenia (platelet count <30,000/mm³; range 150,000-400,000/mm³); hemodynamic instability; and previous rectal surgery.

Endoscopic scoring

Endoscopic assessment of severity of CRP was measured by using the well-validated rectal telangiectasia density (RTD) grading scale.^{36,37} RTD is a scale of 0 to 3, with grade 0 denoting normal mucosa, grade 1 denoting fewer than 10 discrete telangiectasias, grade 2 denoting a single coalescing patch and/or 10 or >10 discrete telangiectasias, and grade 3 denoting ≥ 2 coalescing patches.³⁶ Two senior gastroenterologists (S.C., H.M.) independently reviewed the archived endoscopic images to retrospectively assign RTD scores, and images were compared between the 2 endoscopists. Discrepancies were reviewed for consensus scores. RTD scores were assigned to endoscopic images obtained before RFA therapy (before-treatment score) and to the images obtained at the last follow-up endoscopy (after-treatment score).

All patients underwent digital examination and proctoscopy by using a flexible gastroscope as detailed in guidelines (following), and CRP was confirmed. A gastroscope was used instead of a colonoscope because it is thinner and more flexible, enabling easier retroflexion and with a sharper angle to allow best apposition to the mucosal surface near the dentate line. Retroflexion in a less-compliant rectum is easier with the gastroscope, especially with the RFA catheter attached. Second, the HALO spot treatment devices (90 and 60) were designed to be used with a gastroscope, not a colonoscope. Thus, attachment to the gastroscope is easier. All patients then underwent RFA treatment as described in the following. Participants underwent repeat proctoscopy with RFA if needed for persistent bleeding at 12- to 16-week intervals. All patients had follow-up clinic appointments or telephone calls at 4 and 16 weeks after RFA to ensure that there were no untoward side effects or potential adverse events. The primary endpoint of the study was complete resolution of the rectal bleeding. Secondary endpoints included endoscopic improvement of CRP based on a change in the RTD score at the follow-up, improvement in hemoglobin level, and adverse events related to the procedure.

Radiofrequency protocol

The Halo90 procedure. Before ablation, the standard bowel preparation (polyethylene glycol based, eg, CoLyte

[Meda Pharmaceuticals, Somerset, NJ, USA] or Halflytely [Braintree Laboratories, Braintree, Mass, USA] and bisacodyl) was recommended to all patients to minimize the unlikely chances of ignition. A digital rectal examination was performed before the endoscopy to exclude fluctuance, mass, or tenderness that may be suggestive of abscess or fissures and to exclude tight strictures. A gastroscope without the HALO device was first inserted to assess whether a retroflexed position could be attained, to photographically document the rectal area, and to evaluate the left side of the colon to rule out other sources of bleeding (Video 1, available online at www.giejournal.org).

During the ablation procedure, the HALO 90 ablation catheter was mounted on the endoscope, with the electrode array in the 6 o'clock position (as opposed to the 12 o'clock position typically used for ablation of Barrett's esophagus). We used surgical lubricant only in the anal canal and applied water on the gastroscope to avoid lubricant on the electrode array of the ablation catheter. If there was anal pain or itch before treatment, we preferred using a lubricant containing 2% lidocaine. We used an ablation energy setting of 12 J/cm² for all of our applications. We applied RFA once to assess patient discomfort and to note the area of the resulting coagulum relative to the dentate line. Generally, 2 applications of the RFA were performed per site, in the retroflexed position, to best visualize the dentate line. Ablations were placed approximately 1 mm proximal to the dentate line to avoid the sensory tissues of the anal mucosa. Removal of the ablated mucosa by scraping, as is performed in esophageal RFA ablations, was purposely avoided. We restricted treatments to relatively short length (≤ 6 cm) along the rectum in any 1 session and did not treat circumferentially during any single session (<270 degrees of circumference) to minimize the potential risk of stricture formation. When seepage of blood was seen immediately after the 2 applications, we avoided the urge to apply more applications. In general, we restricted treatments to from 8 to 20 RFA applications per session. If retroflexion could not be performed in the rectum owing to lack of distensibility, the HALO 90 was advanced a little more proximal into the rectum in the forward flexed position off to 1 side, and then a single application of RFA was delivered, leaving a footprint of the HALO 90. By judging this footprint, distance from the dentate line in the forward flexed position was assessed, and the next applications based on this first footprint were adjusted by adjusting the distance accordingly to avoid treatments below the dentate line. Retreatment was performed only if the patient experienced continued rectal bleeding and usually was done 12 to 16 weeks after the first treatment.

Statistics

Standard descriptive statistics were used to summarize demographic characteristics at baseline. Mean and standard deviation (SD) were used to describe continuous variables, whereas nonparametric data were described by

median and interquartile range (IQR). Categorical (dichotomous) variables were compared with the use of the Fisher exact test or chi-square test as appropriate. The Wilcoxon signed rank test was used for nonparametric analyses, whereas the paired *t* test was used to compare continuous variables before and after treatment. All calculated *P* values were 2-sided, and *P* values $< .05$ were considered statistically significant. The statistical analyses were performed by using SPSS Version 19.0 (Chicago, Ill) and MedCalc Version 13.1 (Ostend, Belgium).

RESULTS

A total of 39 consecutive patients who underwent RFA for treatment of CRP were included in this retrospective study. Baseline characteristics are shown in Table 1. The average age of the patients was 72.9 ± 6.6 years (range 63-83 years). All treated patients were male, and all except for one had received radiation therapy for treatment of prostate cancer. One patient (2.5%) received radiation therapy for treatment of urethral cancer.

The majority of patients (72%) received only a single endoscopic session of RFA. The remaining 11 patients (28%) underwent multiple sessions (2-4), with a mean (\pm SD) interval of 18 ± 18 weeks between sessions (SD 18.3). On average, patients received a mean of 13 ± 6.5 applications of RFA per session. The mean follow-up was 28 months after treatment (range 7-53 months) (Table 2).

Effect of RFA on rectal bleeding and hemoglobin levels

Complete cessation of visible bleeding was achieved in all 39 patients (100%) enrolled in the study. After-RFA hemoglobin levels were available in 37 of 39 patients (95%). There was an overall significant (14%) improvement in mean hemoglobin level from 11.8 ± 2 at baseline to 13.5 ± 1.6 gm % after treatment ($P < .0001$), with an absolute mean increase of 1.7 ± 1.4 gm % (95% confidence interval [CI], 1.2-2.2) (Fig. 1A). This was accompanied by discontinuation of blood transfusion in 11 of 12 patients (92%) and discontinuation of iron therapy in 14 of 17 patients (82%).

Effect of RFA on severity as assessed by endoscopic RTD score

There was a very good level of agreement of endoscopic RTD scoring among the 2 endoscopists (kappa 0.87; 95% CI, 0.70-1.00). A majority of patients (75%) had an RTD score of 3 at baseline, whereas the other 10 patients (25%) had a score of 2. Endoscopic improvement of at least 1 RTD score point was observed in 23 of 24 patients (96%) who underwent repeat endoscopy. No change was observed in only 1 of 24 patients (4%), and an increased RTD score was seen in no patients (0%) after RFA therapy. There was a significant improvement in median RTD score from 3 (IQR 2-3) at baseline to 0 (IQR 0-1) after therapy

TABLE 1. Baseline characteristics of study patients

Variable	Result
Total patients, no.	39
Age, mean (\pm SD), y	72.9 (\pm 6.6)
Male sex, no. (%)	39 (100)
Reason for radiation exposure, no. (%)	
Prostate cancer	38 (97.5)
Urethral cancer	1 (2.5)
Type of radiation exposure, no. (%)	
External beam	33 (84.6)
Brachytherapy	18 (46.1)
Proton beam	3 (7.7)
Prior medical therapy, no. (%)	23 (59)
Prior endoscopic therapy, no. (%)	14 (36)
Anticoagulation use, no. (%)	7 (18)
Antiplatelet use, no. (%)	16 (41)
Baseline hemoglobin, mean (\pm SD), g %	11.8 (\pm 2.0)
Iron therapy, no. (%)	17 (43)
Requiring blood transfusion before RFA, no. (%)	12 (31)
Baseline RTD score, median (IQR)	3 (2-3)

SD, Standard deviation; RFA, radiofrequency ablation; RTD, rectal telangiectasia density; IQR, interquartile range.

TABLE 2. Procedure characteristics

Variable	Result
Type of Halo device, no. (%)	
Halo90 in	38 (97.5)
Halo60 in	1 (2.5)
No. of RFA sessions, mean (\pm SD), median, (IQR) (range)	1.49 (\pm 0.9), 1, (1-2), (1-4)
No. of applications per session, mean (\pm SD)	13 (\pm 6.5)
Time between sessions, mean (\pm SD), wk	18.1 (\pm 18.3)
Increase in hemoglobin level, mean (\pm SD), gm %	1.7 (\pm 1.4)
Decrease in RTD score, mean (\pm SD)	2 (\pm 0.8)
Follow-up, mean (\pm SD), mo	28 (\pm 15.5)

RFA, Radiofrequency ablation; SD, standard deviation; IQR, interquartile range; RTD, rectal telangiectasia density.

($P < .0001$) (Fig. 1B). By using analysis similar to that of Hou et al,³⁷ there was an overall significant (75%) improvement in mean RTD score from 2.68 ± 0.48 at baseline to 0.68 ± 0.95 after therapy ($P < .0001$), with an absolute mean decrease of 2 ± 0.8 (95% CI, 1.64-2.36).

Fifteen patients (38%) did not undergo a repeat endoscopic examination, given that the rectal bleeding had completely stopped in all of these patients and that there was a significant improvement in hemoglobin levels (mean hemoglobin level increase in these 15 patients was 2.04 g %; 11.3 ± 2 vs 13.4 ± 1.6 gm %, before-RFA vs after-RFA, respectively; $P = .0001$) and no further requirement of blood transfusion or iron therapy.

Fourteen of 39 patients (36%) enrolled in the study had received endoscopic therapy for CRP with minimal or no improvement in rectal bleeding before receiving RFA therapy. Thirteen of these 14 patients (93%) had received APC, and one patient had received cryoablation therapy, with a mean (\pm SD) of 12 ± 11 months before application of RFA. One patient had a non-healing rectal ulcer as an adverse event of prior APC therapy. We compared these 14 patients (36%) who had received prior endotherapy

to the remaining 25 patients (64%) without prior endoscopic therapy and found no statistically significant difference between the groups in terms of mean number of RFA sessions (1.8 ± 1.1 vs 1.3 ± 0.8 ; $P = .13$), response to RFA (cessation of rectal bleeding [14/14 patients vs 25/25 patients; $P = 1$], improvement in hemoglobin level [mean increase 1.4 ± 1.4 g % vs 1.9 ± 1.4 g %; $P = .29$], improvement in endoscopic RTD scoring [mean decrease 2.2 ± 0.6 vs 1.8 ± 0.9 ; $P = .24$]), or adverse events secondary to RFA (bleeding 0/14 patients vs 1/25 patients; $P = 1$).

Additionally, in an effort to define the appropriate timing for retreatment (if needed), we attempted to define how long the healing process would take after RFA in the radiation-damaged tissue of the rectum. A highly motivated patient agreed to return nearly weekly after his initial RFA and have an endoscopic photograph taken of the treatment site to measure healing. The patient had daily hematochezia before and immediately after treatment but sustained cessation of bleeding after treatment. Complete re-epithelialization appeared to occur between 12 and 16 weeks (Fig. 2). There has been no further bleeding in 2 years of follow-up; additional photographs at 2 years after RFA are shown in Figure 3.

Adverse events

Patients generally tolerated the procedure well. Mild-to-moderate anorectal pain was reported after 7 of a total of 58 treatment sessions (12%). This was transient (lasting a median of 7 days; range 3 days-3 weeks), mostly described as rectal discomfort and a burning sensation, which was managed conservatively with oral analgesics

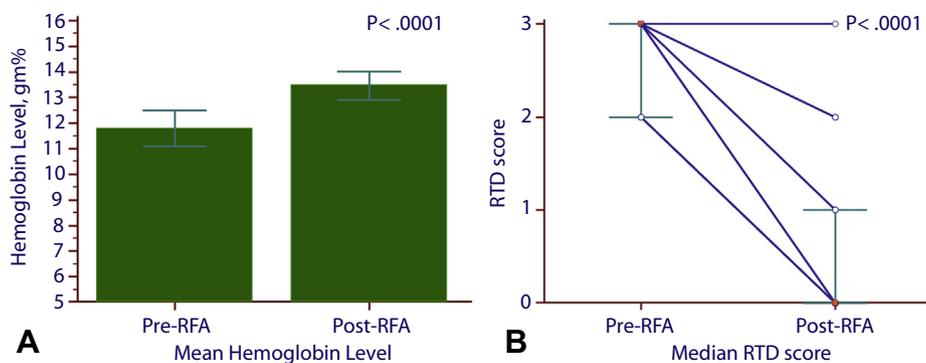


Figure 1. **A**, Changes in hemoglobin level after RFA. **B**, Changes in endoscopic RTD score after RFA. *RFA*, radiofrequency ablation; *RTD*, rectal telangiectasia density.

(acetaminophen alone or combination with hydrocodone) and/or topical (lidocaine/hydrocortisone suppository) therapy. One patient was successfully managed for less-severe discomfort with liquid sucralfate slurry instilled rectally via a bulb syringe. Transient fecal incontinence was reported in 2 patients. Rectal ulcers, fistulas, or stricture formation were not seen in any patient. One patient with a bleeding, non-healing ulcer from prior APC therapy was treated with RFA with complete resolution of bleeding and was noticed to have slow healing on 2 subsequent follow-up endoscopies. In addition, 1 significant hemorrhagic adverse event occurred in a single patient when we deviated from our suggested protocol of limiting treatment in a single session to 2 ablations of 12 J/cm² per treatment site in an effort to control oozing of heme after the initial 2 ablations at that site. Three days subsequently, the patient presented to the emergency department with significant but hemodynamically stable anorectal hemorrhage. Prompt endoscopic examination showed arterial-like bleeding from a vessel in a shallow erosion at the site of excessive ablation. This responded to a single hemostatic clip (Resolution clip, Boston Scientific, Natick, Mass), and bleeding stopped without a need for transfusion. Intermittent, small-volume hematochezia continued, although it stopped abruptly at 10 weeks, without need for further treatment.

Besides those needed for rebleeding, all patients had follow-up clinic visits or telephone calls to endure that there were no other untoward side effects including fevers, chills, or new or worsened defecatory disorders.

DISCUSSION

Our study describes 39 patients with CRP treated with RFA by using consensus treatment methods as described. To the best of our knowledge, this is the first study to report the efficacy, safety, and long-term follow-up in patients with CRP treated with RFA. Endoscopic severity improved as measured by RTD scores. All enrolled patients

achieved complete resolution of symptoms, and the overall mean hemoglobin level increased significantly.

The rectal mucosa after radiation can be vascularly compromised and may not heal as efficiently as normal tissue. Thus, biopsies have been discouraged because of the possibility of creating non-healing ulcers or fistulas. Several treatment modalities for CRP have been proposed. However, the optimal method of safe and effective therapy remains unclear. Studies to evaluate safety and effectiveness have been limited by the lack of standardized assessments of clinical symptoms or endoscopic severity. Topical therapy with mesalamine, pentoxifylline, metronidazole, butyrate, and sucralfate has shown conflicting results in small trials.^{7,16,17,38} Topical application of formalin may be effective in as many as 48% of patients with CRP; however, there is a concern about a high rate of adverse events such as rectal pain, incontinence, diarrhea, formalin-induced colitis, anal and rectal strictures, rectal ulcerations, rectal perforation, and fistulas.^{8,11,39,40} APC has reported response rates as high as 80% in uncontrolled series but is associated with adverse events such as rectal stenosis, rectovaginal fistulas, recto-vesicular fistulas, tenesmus, rectal pain, gas explosion, and perforation.²²⁻²⁷ The adverse event of recto-vesicular fistula typically necessitates the diversion of both the urinary and fecal streams to prevent recurrent urinary sepsis and may still result in the ultimate demise of the patient. The rates of adverse events are difficult to assess without controlled studies. Hyperbaric oxygen is the only modality with randomized, controlled data to suggest benefit in CRP; however, unfortunately, hyperbaric oxygen is not readily available, has considerable expense involved, and has a unique set of adverse events.^{7,41,42} Another endoscopic therapy that has been recently described is cryoablation, which has shown benefit in small series. However, the reported efficacy was lower, and there is a lack of long-term data.^{37,43} Adequate venting of the expanding nitrogen gas to avoid overdistention and possible perforation remains a concern. In addition, current commercially available cryotherapy apparatuses are less mobile and somewhat more

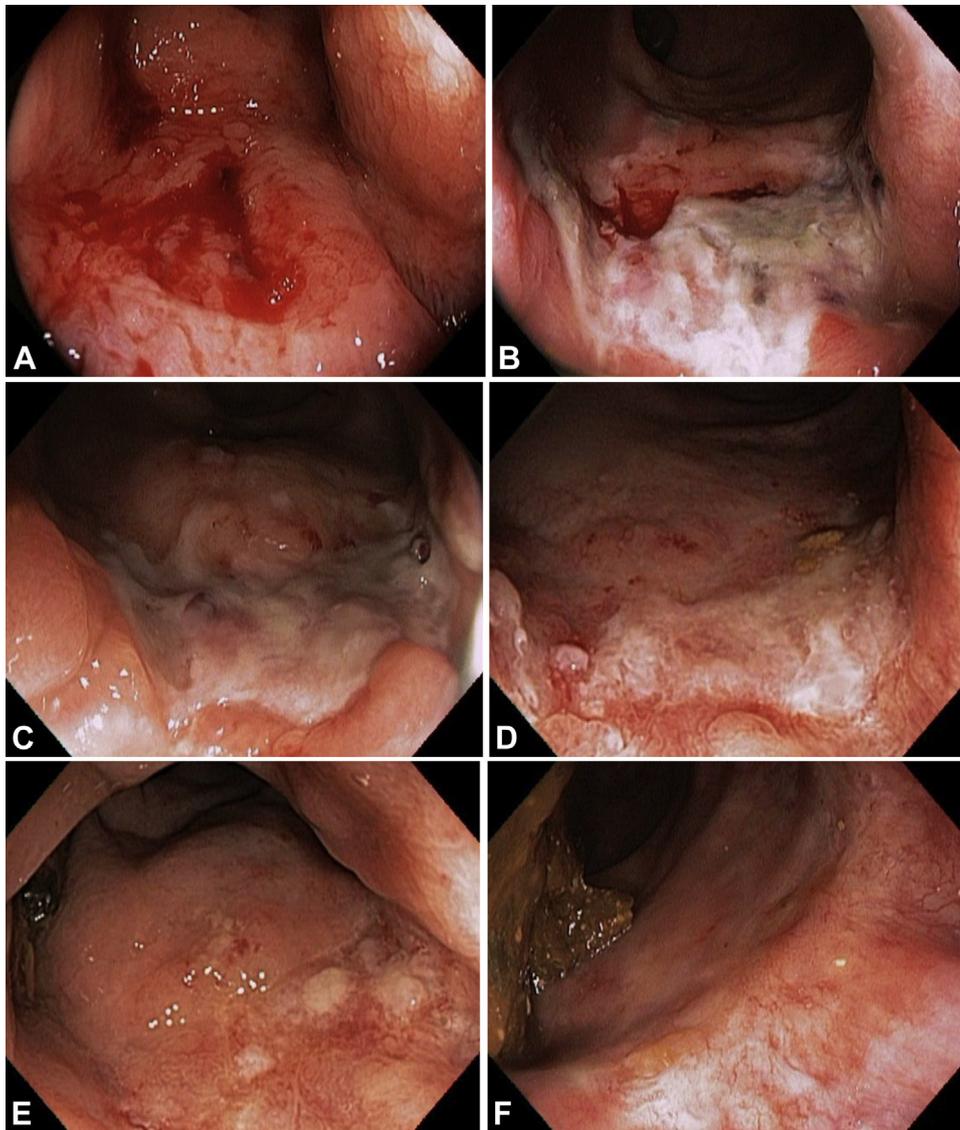


Figure 2. Follow-up endoscopic images showing gradual healing and complete re-epithelialization after RFA: **A**, Hemorrhagic CRP with active bleeding before RFA. **B**, Two weeks after RFA. **C**, Four weeks after RFA. **D**, Eight weeks after RFA. **E**, Twelve weeks after RFA. **F**, Sixteen weeks after RFA. RFA, radiofrequency ablation.

cumbersome than most APC equipment and the BARRX units, and they require maintaining a supply of liquid nitrogen, which lasts approximately 2 weeks in the current holding tank. Thus, treatments for incidental findings, particularly in a lower volume endoscopy unit, may be more difficult.⁷

Unlike focal “point and shoot” modalities such as APC and Gold probe electrocautery (Boston Scientific, Natick, Mass, USA) that entail variable energy settings and ablative treatments, RFA involves a device-controlled method with less user variability. The closely spaced bipolar array of electrodes and defined radiofrequency parameters provide a clear depth-restricted treatment that can theoretically minimize perforations, ulcerations, and strictures even compared with other bipolar electrocoagulation methods. Therefore, RFA has several benefits compared

with other treatment modalities for CRP. For example, APC can result in after-treatment non-healing ulceration from deeper injury in relatively ischemic mucosa.²⁵ By comparison, the RFA catheter limits the radiofrequency energy penetration, restricting the RFA treatment to the superficial mucosa, thereby avoiding deep tissue injury. This observation is consistent with previous studies that used RFA for the treatment of Barrett’s esophagus,^{32,44-46} in which superficial therapy also has avoided strictures compared with deeper treatments such as photodynamic therapy (PDT) and EMR and/or endoscopic submucosal dissection.

We observed that it took 12 to 16 weeks for healing of the RFA sites in the radiation-damaged rectal mucosa, that is, approximately twice as long as healing of the esophagus after Barrett’s esophagus ablation, in which twice the

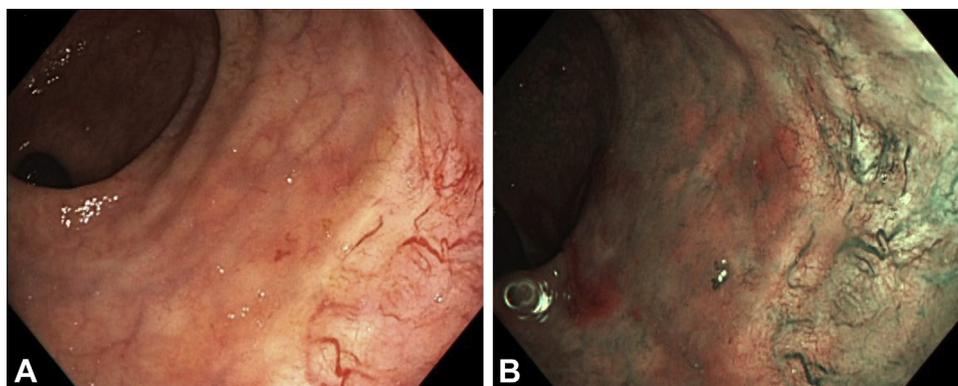


Figure 3. A, Follow-up endoscopic image after 2 years of RFA showing squamous epithelium with underlying ectatic vessels under white light. **B,** Same under narrow-band imaging.

number of RFA applications are delivered at each site. This fact suggests that retreatment of the same area may not be completely safe or necessary within 16 weeks after a treatment session. There were several treated patients with intermittent hematochezia whose bleeding stopped spontaneously by 12 to 16 weeks after RFA without the need for retreatment. The need for retreatment was uncommon.

Interestingly, the tissue that often appears over the site of RFA near the dentate line is not typical of the native rectal mucosa but is neosquamous epithelium as shown previously by optical coherence tomography imaging.³³ Epithelial cell migration (restitution) from neighboring squamous epithelium at the dentate line (analogous to squamous epithelium adjacent to Barrett's esophagus) over the area of superficial ablation may be enhancing the formation of squamous epithelium, without creating deep ulcers as found after heater or bipolar probes^{47,48} or APC,^{49,50} that has deeper energy penetration. Direct ablation of ectatic vessels may not be the only reason for success with RFA. The squamous re-epithelialization after RFA may play a significant role in the prevention of rebleeding not only by creating a potentially protective surface layer even when underlying vessels remain seemingly ectatic (Fig. 3, 2 years after RFA) but also possibly by repressing tissue factors that lead to abnormal vascular dilatation. Thus, the protracted healing process after the controlled inflammatory response initiated by the RFA may be an important mechanism in achieving long-term hemostasis. As such, overzealous treatment during therapy and premature retreatment after initial therapy may expose the patient to unnecessary risks of adverse events.

Also as in the esophagus, there was a lack of strictures and deep or non-healing ulcers after RFA treatments in the rectum on follow-up of these patients. This may be further ensured by avoiding circumferential application, at least during the same treatment session. This lack of adverse events has been attributed to the broad, uniform, and superficial energy delivery of RFA compared with other ablative modalities. However, in the setting of

bleeding, and given the relative ischemia or poor healing of the rectum in patients after external beam irradiation, biopsy specimens were not obtained for histopathologic evidence to confirm the superficiality of injury in the rectum after RFA because this would not be in the interest of the patients. RFA of porcine and human esophagus demonstrated histologic changes 750 to 1000 μm in depth for an energy setting of 12 J/cm^2 .⁴⁵ When real-time depth-resolved endoscopic optical coherence tomography was used, tissue architectural changes were noted superficial at 230 to 260 μm in depth compared with approximately 640 μm for cryoablation.⁵¹ Whether these depths of treatment translate identically to the rectum is unknown, but the ulcers that occur after RFA when the treatment protocol is followed are superficial and temporary, although they may take longer to heal in irradiation-damaged rectum than they otherwise would in the esophagus.

The low rate of adverse events observed in this study vouches for the safety of this therapeutic modality. From our experience, several recommendations can be summarized: (1) Where possible, treat in a retroflexed gastroscope position with the HALO 90 device mounted at 6 o'clock to allow best visualization and treatment. (2) If retroflexion is not possible in the rectum, create a footprint mark in the forward view to help guide placement of the first ablation. (3) Standard bowel preparation is suggested to minimize unlikely ignition of bowel gas. (4) Avoid more than 2 ablations per site or overlapping treatments. Resist the urge to retreat oozing sites during the session. (5) Delay retreatment for 12 to 16 weeks when possible.

There are several limitations of our study. This study was a non-powered, retrospective study, and conclusions are limited by the lack of a control group and blinding. The aim of this study was to establish the efficacy and safety of RFA in treatment of CRP. The lack of standardized tools to assess endoscopic and clinical severity of CRP is a limitation. RTD is a reliable and reproducible endoscopic grading score that has been shown to have good interobserver and intraobserver agreement.³⁶ It

has been well-validated and has been used in prior studies evaluating the efficacy of endotherapy in CRP. Although we had a high level of agreement between investigators for RTD scoring, such an endoscopic scoring system is subject to potential subjective bias, particularly in an uncontrolled study. In addition, we do not have objective data on symptomatic improvement such as the radiation proctitis severity assessment scale that has been used in a few studies to assess comprehensive clinical improvement in CRP. Another limitation is the absence of any female patients. However, we doubt that this will have any impact on the efficacy or safety profile of the therapy. No proximal rectal or sigmoid lesions were treated, thus safety in those areas (of thinner wall) is less certain.

Our study has notable strengths. Our collaborative study was performed at multiple centers by using consensus methods and has a relatively good sample size. RFA is a procedure with inherent treatment consistency for energy delivery, unlike most other ablative methods. Limitations of the retrospective design were curbed with set inclusion and exclusion criteria and predefined endpoints and definitions. We evaluated efficacy both clinically (by showing mean hemoglobin level increase, change in blood transfusion requirements, and symptomatic improvement) and endoscopically in a quantitative manner. Long follow-up is another advantage of our study.

In conclusion, RFA is an effective and safe endoscopic therapy for CRP. Further controlled studies are needed to compare this to other treatment modalities for CRP.

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Abbreviations: APC, argon plasma coagulation; CRP, chronic radiation proctopathy; RFA, radiofrequency ablation; RTD, rectal telangiectasia density.

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Current affiliations: Section of Digestive Diseases, Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut (1), Florida Digestive Health Specialists, Sarasota Memorial Hospital, Sarasota, Florida (2), Veterans Affairs Boston Healthcare System, Harvard Medical School, Boston, Massachusetts, USA (3).

Reprint requests: Tarun Rustagi, MD, Section of Digestive Diseases, 333 Cedar Street, 1080 LMP, New Haven, CT 06520-8019.

If you would like to chat with an author of this article, you may contact Dr Rustagi at tarun.rustagi@yale.edu.