RECTAL BAND LIGATION AS A TREATMENT FOR CHRONIC RADIATION PROCTITIS: A FEASIBILITY STUDY

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Conflict of Interest: The authors declare that they have no conflict of interest.

Abstract:
Background and study aims: Chronic radiation proctitis (CRP) occurs in 5-20% of patients undergoing pelvic radiation therapy and frequently manifests with rectal bleeding. Endoscopic management of more severe and refractory cases can be challenging. Rectal band ligation (RBL) has been shown to be a feasible alternative to current available techniques, especially in extensive CRP. Our aim is to evaluate clinical and technical success of RBL.

Patients and methods: We enrolled all consecutive patients treated with RBL for severe or recurrent hemorrhagic CRP. Success was defined as endoscopic evidence of complete rectal healing and/or cessation of bleeding not requiring further treatment or blood transfusion.

Results: We enrolled 10 patients (7 males, mean age 75.6 years). Median length of the CRP from the anal verge was 4.5 cm and mean surface area involved was 89%. Eight patients (80%) were naïve of endoscopic treatment, while 2 underwent APC. Median follow-up was of 136.5 days. Success was achieved in 100% of patients after a mean number of 1.8 RBL sessions. A mean number of 4.7 bands were released in the first session while a mean of 3.1 and 2 bands were respectively placed in the second and third session. As for adverse events, only 1 patient reported mild tenesmus and pelvic pain after the procedure.

Conclusions: RBL is a safe and effective therapeutic modality for the treatment of hemorrhagic CRP. It could be considered a valid first-line option in case of extensive rectal involvement as well as a viable rescue treatment after failed APC.

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**Fig.1** Extensive hemorragic CRP with telangiectasias on about 75% of the rectal circumference.

**Fig.2** Rectal band ligation technique on extensive CRP with placement of 5 bands until complete obliteration of visible teleangectasia (a) with complete restoration of rectal mucosa at 3-month revaluation (b).

**Tab.1** Summary of results
Table 1. Summary of results.

<table>
<thead>
<tr>
<th>Summary of results</th>
<th>Patient number = 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>70%</td>
</tr>
<tr>
<td>Mean age</td>
<td>75.6 y</td>
</tr>
<tr>
<td>Median follow up</td>
<td>136.5 d</td>
</tr>
<tr>
<td>RBL characteristics</td>
<td></td>
</tr>
<tr>
<td>Previous endoscopic treatment</td>
<td>20%</td>
</tr>
<tr>
<td>Median CRP length</td>
<td>4.5 cm</td>
</tr>
<tr>
<td>Mean surface area involved</td>
<td>89%</td>
</tr>
<tr>
<td>Mean RBL sessions</td>
<td>1.8</td>
</tr>
<tr>
<td>Technical success</td>
<td>100%</td>
</tr>
<tr>
<td>Clinical success</td>
<td>100%</td>
</tr>
<tr>
<td>Adverse events</td>
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</table>
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Running head: RBL and radiation proctitis

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ABSTRACT

Background and study aims: Chronic radiation proctitis (CRP) occurs in 5-20% of patients undergoing pelvic radiation therapy and frequently manifests with rectal bleeding. Endoscopic management of more severe and refractory cases can be challenging. Rectal band ligation (RBL) has been shown to be a feasible alternative to current available techniques, especially in extensive CRP. Our aim is to evaluate clinical and technical success of RBL.

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Conclusions: RBL is a safe and effective therapeutic modality for the treatment of hemorrhagic CRP. It could be considered a valid first-line option in case of extensive rectal involvement as well as a viable rescue treatment after failed APC.

INTRODUCTION

Radiation therapy (RT) is indicated in the treatment of various pelvic tumors and the most frequent indications are for prostate neoplasia, bladder cancer, gynecological malignancies and ano-rectal
Due to the rapid gut epithelial turnover and to the fixed position of the rectum, pelvic RT is burdened by toxicity on the gastrointestinal tract, among which chronic radiation proctitis (CRP), also referred as radiation associated vascular ectasia (RAVE), affected around 30% of patients up until few years ago [2]–[4]. Thanks to advances in conformal radiation, the delivery of more targeted external beam radiation and, to a lesser extent, also to prophylactic measures, the incidence of CRP has declined to 5-20%, although it keeps being a cumbersome RT complication [5]. Rectal bleeding is the most frequent symptom of CRP [4]. Its management includes medical treatment, with topical drug administration, and interventional treatment. Endoscopic therapy is a cornerstone for CRP-related bleeding and relies on various techniques such as argon plasma coagulation (APC), radiofrequency ablation (RFA), cryotherapy, laser therapy and Heater probe and BiCAP - contact therapy [6]. Mangiavillano et al. reported, in two case reports, a new treatment option to control rectal bleeding from CRP based on the rectal band ligation (RBL) technique, but no other study or casuistry is actually published [7], [8]. Endoscopic band ligation has already been used to treat lower gastrointestinal bleeding from sources different from CRP, with good results [9]–[11].

Our believe is that RBL can be a valid further treatment modality for bleeding CRP, above all in those scenarios of extensive disease with recurrent hemorrhage.

The primary aim of this study was to evaluate clinical and technical success of this new treatment for bleeding from CRP. The second aim was to evaluate the possible adverse events (AEs) related to the procedure.

**MATERIALS AND METHODS**

*Study population and Data record*

All included patients were treated in Humanitas - Mater Domini (Casellanza - VA - Italy) and Humanitas Research Hospital (Rozzano - MI - Italy) for persistent bleeding from CRP. After pre-operative endoscopic assessment, we considered RBL in those cases with telangiectasias on more
than 50% of the rectal circumference during luminal insufflation. Demographic and anamnestic data were retrospectively analyzed, as well as endoscopic aspects before and after RBL.

Rectal band ligation technique

All procedures were performed under conscious or deep sedation after bowel preparation with enemas. After endoscopic evaluation, a multi-band ligator (6 Shooter Multi-Band Ligator, Cook Medical) was mounted on a standard gastroscope and the bands were released until complete obliteration of visible rectal telangiectasias, up to and including the entire circumference. Attention must be paid after releasing the band since excessive insufflation may cause early slippage of the band. Standard protocol after RBL included daily mesalamine enemas for 1 month. Endoscopic control was planned between 2 and 3 months after the procedure, although earlier evaluation was performed in case of relevant recurrent bleeding. Success was defined as endoscopic evidence of complete rectal healing and/or cessation or significant reduction in bleeding not requiring further treatment or blood transfusion. Technical success was determined by the capability to place at least one band on the rectal area of interest.

RESULTS

We enrolled and retrospectively evaluated a total of 10 patients, treated between February 2016 and February 2020. There were 7 males (70%) and mean age was 75.6 years. Median follow-up was of 136.5 days (range 21-979 days). All male patients had received local RT for prostate cancer. Of the remaining 3 women, one had been treated for endometrial cancer and the other two for a rectal adenocarcinoma.

Eight patients (80%) were naïve of endoscopic treatment, while in 2 (20%) APC had already been performed without any beneficial.
Median length of affected rectum from the anal verge was 4.5 ± 3.12 cm (range 3-12 cm) and mean surface area covered by telangiectasias was 89% (range 50-100%) (Fig.1).

At least one band was released in every patient, with a technical success of 100%. Clinical success was achieved in 100% of patients after a mean number of 1.8 ± 0.8 RBL sessions (range 1-3) (Fig.2) (Video 1). A mean number of 4.7 ± 2.0 bands were released in the first session while a mean of 3.1 and 2 bands were placed in the second and third session respectively. Only 1 patient experienced an early AE: mild tenesmus and pelvic pain the day after the procedure, with spontaneous resolution after 30 days of topical therapy with mesalamine enema. Results are summarized in Tab.1.

**DISCUSSION**

Pelvic radiotherapy represents a fundamental step for the treatment of pelvic tumors. Unfortunately, the gut wall is particularly radiosensitive due to its high epithelial turnover, and the fixed position of the rectum in the pelvis makes it prone to damage, with symptoms of CRP occurring approximately from 3 to 6 months after radiation exposure [12]. Persistent bleeding is the typical symptom, with concomitant complaint about tenesmus, urgency and fecal incontinence. To date, medical therapies and endoscopic interventions are the best treatment modalities for CRP [2], [6]. As regard to endoscopic treatments, APC is usually the first-choice treatment modality for CRP, despite no consensus regarding the best APC settings has been reached. Reported success for APC is between 70% and 90%, with at least 2 sessions in most of the treated patients [6], [13]–[15]. However, more extensive disease could require even more than two sessions, and the presence of telangiectasias on more than 50% of the surface area has been demonstrated to be related to APC failure [14]. Promising results have been reported with radiofrequency ablation (RFA), with clinical and endoscopic success rates of 99% and 100% respectively, and a mean number of 1.71 RFA sessions needed to achieve response [16]. To date, the use of band ligator to treat acute lower gastrointestinal...
bleeding (ALGIB) has been commonly reported in the setting of colonic diverticular bleeding and is indicated as one of the first endoscopic treatment options [17]. However, the band ligation technique has been applied also in other settings of ALGIB, like post-polypectomy bleeding and Dieulafoy’s lesion, with a rate of success around 93%. Cases of RBL applied to rectal bleeding sources exist and refer to the management of acute hemorrhagic rectal ulcer, rectal varices, post-prostate biopsy bleeding and rectal Dieulafoy’s lesion [9], [10]. De Robles et al. reported their experience with rubber band ligation as often a necessary complement in the management of hemorrhagic radiation proctitis with concomitant symptomatic hemorrhoids, even though they released bands on hemorrhoids rather than on proctitis [11]. Mangiavillano et al. reported for the first time in literature, in two different case reports, the possibility to apply band ligation on CRP with severe bleeding, with excellent results although the wide disease extension [7], [8]. The supposed mechanism of action of RBL should be comparable to band ligation in esophageal varices, with induced ischemic necrosis and superficial ulceration as the main modifications in the trapped tissue, with extension of histological changes limited to the mucosa and submucosa, with intent to create a scarring tissue avoiding relapsing angiogenesis [18]. Our data show a 100% of technical and clinical success using RBL for the treatment of the CRP with less endoscopic sessions (mean of 1.8) if compared to APC. At the same time, RBL appears also as effective as RFA, with similar rate of success and number of endoscopic sessions required. However, it deserves attention that the HALO catheter for RFA is not largely available and more expensive, if compared to an endoscopic band ligation system. Although being increasingly used for a variety of gastrointestinal conditions, RFA is primarily used in third level centers for Barrett’s esophagus ablation [19]. On the contrary, every interventional endoscopy unit owns a band ligator, thus making RBL also easily viable. Apart from being effective, RBL is also safe since no serious adverse events were recorded, apart from tenesmus and pelvic pain in one patient, with spontaneous improvement. However, a severe complication has been reported from Pita et al. describing the development of a rectourethral fistula after a rectal ulcer following haemorroid elastic band ligation in a patient with grade 1 CRP.
Although ulcers and fistula are counted as rare complications in CRP, this experience must
aware consciousness on possible adverse events in a frail irradiated mucosa. It distinguishes from
APC, which is associated with 3-40% of adverse events that include ulcerations, perforations,
strictures, and fistulae [14], [15]. The most common procedure-related complication with APC is
rectal or anal pain, with or without tenesmus, probably related to treatment too near the dentate line.
Coriat et al. proposed to use a transparent distal attachment to improve visualization on the distal
part of the rectum to ensure a proper distance for safe APC application [21]. The natural presence of
the transparent cap in the ligator set allows to overcome this problem. Moreover, RBL does not
require particular endoscopic skills or learning curve and is applicable in all endoscopic centers.

This study has some strengths; is a description of a novel, cheap, safe and widely available technique
to treat a common disease. Limitations reside in its retrospective design and the small sample
analyzed. Further studies are needed to confirm its efficacy, both for bleeding as well as for other
CRP-related symptoms, since APC has been proved also to improve tenesmus, diarrhea and
urgency in up to 75% of cases. An additional suggestion for next studies could be to apply an
endoscopic severity score to grade CRP, in order to make results comparable [22]. To our
knowledge, this is the first study reporting the use of the RBL for the treatment of CRP.

In conclusion, RBL could be a valid, cheap and easily alternative for the treatment of persistent
bleeding from CRP, in particular for cases with a wide disease extension, with a very low rate of
AEs and no need for particular operator skills.

REFERENCES

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