Turk J Gastroenterol *2014; 25 (Suppl.-1): 38-42*

Role of argon plasma coagulation in management of bleeding GI tumors: evaluating outcomes and survival

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Original Article

ABSTRACT

Background/Aims: Tumor related gastrointestinal (GI) bleeding is a challenging clinical problem in cancer patients. Argon plasma coagulation (APC) is preferred for the management of bleeding arterio-venous malformations. Our objective was to assess the role of APC in the management of bleeding GI tumors.

Materials and Methods: This is a retrospective review of endoscopies performed at the UT MD Anderson Cancer Center over 3 consecutive years (2009-2011). This study involved patients with primary or metastatic gastrointestinal cancer with suspected GI bleeding and interventions included were endoscopies with APC. Our main outcome measurements were immediate hemostasis rate, change in transfusion requirements, re-bleeding rate, and 30-day mortality.

Results: Immediate hemostasis was achieved in all 10 (100%) patients, with either APC performed alone (8 patients) or with adjuvant epinephrine (2 patients). There were no procedure related complications. The pooled transfusion requirements for all 10 patients 48 hours prior to the procedure were 26 packed red blood cells units, 11 platelet units and 6 fresh frozen plasma units, while the overall requirements in the 48 hours after the procedure were 5 packed red blood cells units, 6 platelet units and no fresh frozen plasma units. Re-bleeding occurred in 3 (30%) patients during follow up. Thirty day mortality rate was 0%. Total of 7 (70%) of patients were able to continue cancer specific therapy of either chemotherapy, radiation or both.

Conclusion: APC is feasible and safe in routine practice to manage bleeding GI tumors. It is very effective in achieving initial hemostasis (100%) and allows majority of the patients (70%) to undergo cancer specific therapy.

Keywords: GI bleeding, cancer, APC

INTRODUCTION

Gastrointestinal bleeding (GIB) continues to be a challenging clinical problem, especially in patients with cancer. Though tumor related bleeding is rarely massive and seldom causes hemodynamic instability (1,2) it is difficult to control and is associated with 30-day re-bleeding rates as high as 80% (2). Although endoscopic hemostasis is the first line treatment of choice in cases of non-tumor related causes of GIB, its efficacy and beneficial impact on survival in patients with bleeding gastrointestinal tumors are debated (1-4).

Argon plasma coagulation (APC) is one of the endoscopic hemostatic methods, shown to be effective for the management of non-neoplastic causes of GIB including gastric antral vascular ectasia, arterio-venous malformation and radiation proctitis (5-8). APC is also used for ablation of gastrointestinal tumors (7-13). However; limited information is currently available on its role in the management of actively bleeding primary and metastatic tumors in the gastrointestinal tract. The aim of this study was to assess the safety and efficacy of APC in the management of bleeding GI tumors.

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Received: January 18, 2013 **Accepted:** March 07, 2013
 • Available online at www.turkjgastroenterol.org • DOI: 10.5152/tjg.2014.4867

PATIENTS AND METHODS

Patients

We performed a retrospective review of all endoscopies performed at UT MD Anderson Cancer Center over 3 consecutive years (2009-2011) and identified cases of bleeding gastrointestinal tumors treated by APC. Patients with benign causes of GIB and bleeding tumors treated with modalities other than APC were excluded from the analysis. Medical records and the clinical course of each patient, including follow-up till June 2012 were analyzed. Data related to demographic details, clinical presentation, type of underlying malignancy, laboratory parameters, transfusion requirements, endoscopic findings and clinical course including survival were abstracted for computer-assisted analysis.

Endoscopic APC Therapy

The APC therapy was carried out using the APC probe (ERBE USA, Marietta, GA). An APC is a noncontact electrocoagulation device that uses high-frequency monopolar alternating current conducted to target tissues through ionized argon gas (argon plasma)(14). This causes tissue desiccation at the contact interface of target tissue (14). Tissue desiccation leads to loss of electrical conductivity at the tissue surface and the plasma stream shifts to adjacent nondesiccated (conductive) tissue, which limits the depth of tissue injury (14). APC therapy for all tumor bleed was carried out at power output of 35 watts (W) and argon gas flow rate of 1 L/min.

Statistical Analysis

The demographic and clinical features of the study population were described in median and interquartile ranges where data was continuous, while the dichotomous data was reported as percentages. Transfusion requirements prior to and after APC were compared using non-parametric Wilcoxon sign rank test. Our primary outcome measures included re-bleeding rate and mortality. Mortality was analyzed using Kaplan-Meier product limit method and reported as median time to mortality. All the data was censored till the last follow-up in June 2012. All statistical analysis was performed using Stata Statistical Software: STATA Release 12 (Statacorp LP, College Station, TX).

RESULTS

A total of 533 patients with various cancer diagnoses underwent endoscopic evaluation at our institute between 01/2009 to 12/2011 for suspected gastrointestinal bleeding from various indications including anemia, melena, hematemesis or hematochezia. Of the total, 200 patients had upper endoscopy, 286 patients had colonoscopy and 47 patients had both. APC was performed on 10 patients (8 male and 2 female) with bleeding GI tumors. The median age was 58 (20-67) years. Majority of the patients were Caucasians (90%). The diagnoses included 3 (30%) cases of esophageal cancer, 2 (20%) cases of colorectal cancer, and 1 (10%) case each of gastric adenocarcinoma, gastrointestinal stromal tumor, metastatic renal cell cancer, multiple myeloma and large B cell lymphoma. Four patients presented with hematemesis (40%), four had melena (40%) and two presented with hematochezia (20%). Metastatic disease was present in all (100%) patients, with intraabdominal metastasis in 90% and intrathoracic metastasis in 60% of patients. The clinical characteristics, endoscopic findings, treatment, and outcomes for each patient are shown in detail in Table 1.

Eight patients underwent upper endoscopy (80%), while one patient each underwent flexible sigmoidoscopy (10%) and colonoscopy (10%). APC was performed either alone (8 patients) or with adjuvant epinephrine at 1:10000 concentration (2 patients). Immediate hemostasis was achieved in all 10 (100%) patients. Figure 1 A-D shows the endoscopic appearance of bleeding GI tumors before and after the APC treatment. None of the patients developed any procedure related complications. The pooled transfusion requirements for all 10 patients 48 hours prior to the procedure were 26 packed red blood cells units, 11 platelet units and 6 fresh frozen plasma units, while the overall requirements in the 48 hours after the procedure were 5 packed red blood cells units, 6 platelet units and no fresh frozen plasma units. Re-bleeding occurred in 3 (30%) patients during follow up at 48 hours, with first patient at 48 hours, second one at 72 hours and last one at 1 year. One patient was managed by conservative treatment with blood transfusion only; while 2 patients underwent intervention radiology guided embolization therapies. Median time between procedure to discharge was 5 (Range: 1-106) days. Thirty day mortality rate was 0%. Mortality occurred in 7 (70%) patients over a mean follow-up of 230 (range: 59-660) days. The median time to mortality was 144 days. A total of 7 (70%) patients were able to continue cancer specific therapy including chemotherapy, radiation or both. A Kaplan-Meier estimate of overall survival is shown in Figure 2. Evaluation of outcomes and survival are shown in detail in Tables 1, 2.

DISCUSSION

Bleeding from gastrointestinal tumors is an increasingly identified condition among cancer patients and its management is clinically challenging. Prospective studies by Lightdale et al and Shivshanker et al have shown that bleeding from gastrointestinal tumors accounts for 12% (15) and 26% (16) of the episodes of acute gastrointestinal hemorrhage respectively. Subgroup analysis of these studies for patients with neoplastic involvement of the gastrointestinal tract showed that tumor related bleeding accounted for 17% (15) and 65% (16) of episodes of acute gastrointestinal hemorrhage. Thus patients with primary and metastatic tumors to the gastrointestinal tract have a high risk of tumor related bleeding.

Although tumor related bleeding is commonly submassive and manifests as melenic stool or the gradual development of anemia, in some cases the bleeding may be brisk and causes hemodynamic compromise, warranting frequent transfusions and hospitalization (1). As GIB is often in the form of diffuse oo-

Table 1. Demographics details, clinical presentation, endoscopic findings, relevant outcomes, and follow-up of patients

Pt. No	Age	Sex	Primary Diagnosis	Indication	Procedure	Site of lesion	Appearance of lesion	Enodscopic management	Rebleed	Rebleed Time	Dead	F-U (Days)
1	37	M	Multiple myeloma	Hemetemesis	EGD	Fundus	Multiple umbilicated lesions with central ulcerations	APC alone	no	n/a	Yes	106
2	59	M	Adenocarcinoma of stomach	Hemetemesis	EGD	Distal body and antrum	Large fungoid mass with friable mucosa	APC with epinephrine	no	n/a	Yes	46
3	67	M	Gastro-esophageal carcinoma	Hemetemesis	EGD	Distal esophagus	Severe ulceration	APC with epinephrine	yes	2 days	Yes	144
4	20	F	Gastrointestinal stromal tumor	Hemetemesis	EGD	Cardia	Large bulky tumor with large area of ulceration	APC alone	yes	1 year	No	538
5	47	M	Supra glottic carcinoma & Colorectal carcinoma	Hematochezia	Colonoscopy	Ascending colon	Ulcerated mass	APC alone	no	n/a	No	660
6	63	M	Colorectal carcinoma	Hematochezia	Flexible Sigmoidoscopy	Rectum	Friable mass	APC alone	yes	3 days	Yes	297
7	57	M	Renal Cell carcinoma	Melena	EGD	Entire stomach	Multiple broad based nodules with central ulceration	APC alone	no	n/a	Yes	118
8	63	M	Esophageal carcinoma	Melena	EGD	GE junction	Circumferential, nodular, exophytic mass with ulceration	APC alone	no	n/a	Yes	47
9	52	M	Gastro-esophageal carcinoma	Melena	EGD	GE junction	Mass with Stricture	APC alone	no	n/a	No	339
10	59	M	Large B cell lymphoma	Melena	EGD	Fundus and body	Multiple ulcers	APC alone	no		No	9

M: male; F: female; EGD: esophagogastroduodenoscopy; GE: gastroesophageal; APC: argon plasma coagulation; F-U: follow-up

Table 2. Evaluation of outcomes and survival after endoscopic management with APC

Initial hemostasis	10 (100%)		
Need for adjuvant therapy	2 (20%)		
Transfusion requirement (pooled)	48 hours before the procedure	48 hours after the procedure	p value
1. Packed red blood cells (Units)	26	5	0.01
2. Platelets (Units)	11	6	0.3
3. Fresh frozen plasma (Units)	6	0	0.3
Procedure related complications	0 (0%)		
Re-bleeding	3 (30%)		
Time between procedure to discharge	5 (Range: 1-106) days		
30 day mortality rate	0 (0%)		
The median time to mortality	144 days		
Continued cancer therapy	7 (70%)		

APC: argon plasma coagulation; 95% CI: 95% confidence interval for survival

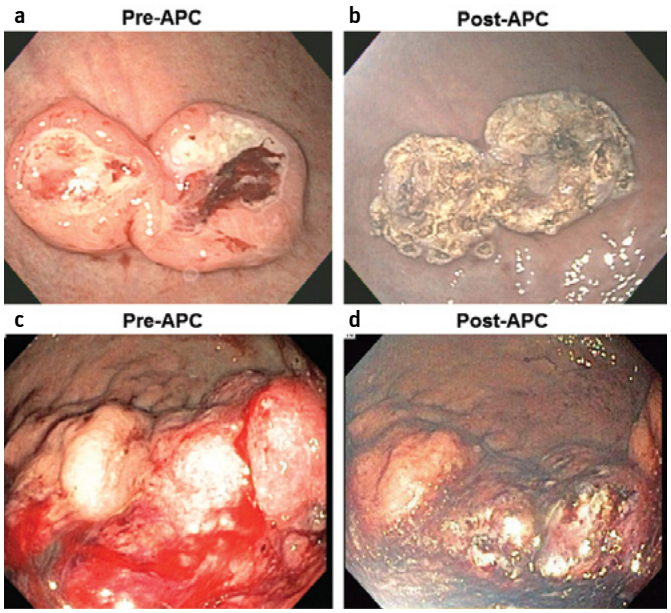

Figure 1. a-d. Active bleeding from the ulcerated tumor implants in gastric body from metastatic breast cancer **(a)**, S/P control of bleeding with argon plasma coagulation treatment **(b)**, Active bleeding from gastric cancer in cardia **(c)**, and S/P control of bleeding with argon plasma coagulation treatment **(d)**.

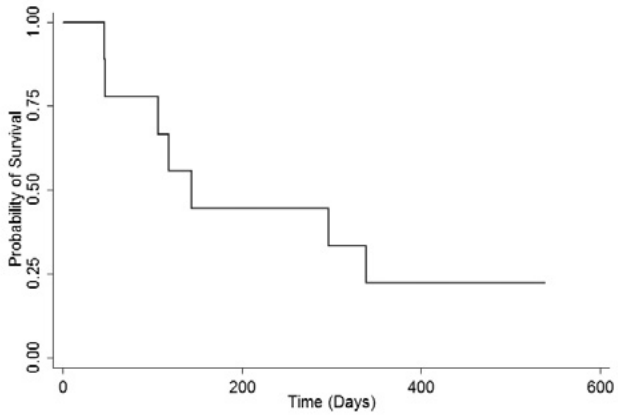

Figure 2. Kaplan-Meier estimate of overall survival in patients with gastrointestinal bleeding related to metastatic cancer.

zing from the tumor with extensive necrosis and unidentifiable anatomy (1,17,18) the conventional endoscopic hemostatic methods like heater probe coagulation, banding or hemoclip application, are not believed to be very effective (1,3,18). Two retrospective evaluations of different modes of thermal and injection therapy such as heater probe, bipolar electrocautery, argon plasma coagulation, laser photocoagulation, and epinephrine injection for the control of tumor related bleeding showed initial hemostasis rates of 67 to 100%, 30 day rebleeding rates as high as 80%, and no reduction in transfusion requirements or mortality rates with endoscopic management (2,4). However it is believed that the temporary control of bleeding by endoscopy enables the patient to continue cancer specific therapy and averts the need for emergent surgery (1,3).

APC is a noncontact ablative technique and is the modality of choice for the control of upper and lower GIB related to GAVE and AVM (5-7), owing to its superior efficacy, easy application, and low complication rate (5,6,19,20). In patients with gastrointestinal tumors, the use of APC for the curative ablation of early stage lesions, decreasing tumor bulk and preserving luminal patency has been known (21,22). Akhtar et al. (13) evaluated the role of APC in the management of 48 patients with esophagogastric tumors. Bleeding from the tumor was the indication for treatment in 5 of these patients and complete control of bleeding was achieved with APC in 3 (60%) of them. Chang et al. (18) evaluated of the role of APC in endoscopic hemostasis for non-ulcer non-variceal gastrointestinal bleeding and hemostasis was successfully achieved in 62.5% (5/8) of the patients with tumor related bleeding. Since APC also provided contact free ablation and could be easily used with brush like strokes over the diffusely oozing tissue, the study concluded that APC is the therapy of choice for tumor with diffuse bleeding (18).

In our study, among the 10 patients with bleeding gastrointestinal tumors, immediate hemostasis was achieved with APC alone in 8 patients and with adjuvant epinephrine in the other 2 patients. There were no procedure related complications. A decrease in the transfusion requirement was also noted after the procedure, further supporting the hemostatic efficacy of APC in this group of patients. Re-bleeding occurred in 3 patients, 2 of those failed conservative and repeated endoscopic managements and underwent intervention radiology guided embolization therapies. Following endoscopic hemostasis, 7 (70%) patients were able to continue cancer-specific therapy including chemotherapy, radiation or both and the 30 day mortality rate was 0%, further supporting the efficacy of APC treatment. In summary, endoscopic hemostasis with APC in our study successfully achieved 100% immediate hemostasis, reduced bleeding-related transfusion requirements, and allowed the patients to resume cancer specific therapy. Major short comings for this study are the retrospective nature and a small number of patients.

Thus to conclude, in our experience, APC is feasible and safe in routine practice to manage bleeding gastrointestinal tumors. APC therapy is a promising technique in tumor-related GIB to achieve initial hemostasis; however larger clinical trials are warranted to compare APC either singly or in combination with other hemostatic modalities before adopting it universally in clinical practice.

Conflict of Interest: No conflict of interest was declared by the authors.

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