

*Review***Argon plasma coagulation: Clinical applications in Gastroenterology**

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SUMMARY

Argon plasma coagulation (APC) is a method of non-contact endoscopic thermal coagulation. According to recent data, it can safely be used in clinical practice and there are indications that APC is undoubtedly preferable to laser treatment in some cases. So, hemostasis of diffuse superficial vascular lesions, such as angiodysplasia, gastric antral vascular ectasias, radiation proctitis, bleeding ulcers and obstructed stents are some of these clinical indications. There is a lack of published experience of APC and ablation therapy, such as large villous adenomas, rectal and stomach cancer thus further studies are necessary to define the results and technical details of the procedure.

Key words: Argon plasma coagulation, clinical indications, hemostasis, tumour ablation

INTRODUCTION

Interventional endoscopy is a well-established breakthrough in the endoscopy of the digestive tract and Argon Plasma Coagulation (APC) is a new technique recently included in the endoscopic armamentarium. This device is intended for thermal coagulation of tissues and originally APC developed as a thermal method, alternative to laser in open and laparoscopic surgery.¹ APC was adapted for use in flexible endoscopy in the early '90s.² Through a device, argon gas is delivered via a flexible catheter through the endoscopic biopsy channel to tis-

sue and most importantly in a non-conduct mode. APC has revealed a remarkable spectrum of clinical applications, raising questions as to whether it should replace laser in clinical practice. The more gastroenterologists familiarize themselves with this technique, the more they appreciate its usefulness. Among its many advantages, the following should be borne in mind: effective and safe coagulation, non-contact mode of action, marked desiccation, no destruction of metal stents, little smoke or vapor, easily handled device, lower cost compared to laser, and finally, no extended safety precautions. However, to date, no formal cost-effectiveness study has been published. In this review we summarize the main indications of APC in gastrointestinal diseases. We also describe basic physical principles, equipment and technique.

Physical principles – Equipment

Basically, APC applies high frequency (HF) current to a prelocated tissue in a non-contact mode, despite other thermal coagulation methods. According to this method, argon gas is substituted for the usual electrical current. The whole device includes an argon source, an HF current source and the appropriate applying catheter. The APC catheter contains an electrode. A second neutral electrode patch is placed at the hip of the patient. As soon as sufficient HF voltage is generated between the first electrode and the tissue, argon gas flows out of the catheter and becomes ionised in the high voltage electric field that has been created. Thus, argon gas is transformed to plasma beams and HF current completes the electrical circuit via the second neutral electrode patch. The heat which is generated devitalises, coagulates, desiccates and ultimately shrinks the tissue. A desiccated tissue loses electric conductivity because of its higher electrical resistance.^{3,4} Therefore the APC beam moves to the next viable area. In this way, the whole area is uniformly desiccated and, most importantly, at the same depth. The depth is limited to 3 mm at most, depending

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upon the application time.¹ The automatically limited depth, as well as the absence of tissue vaporisation, are safety guards against thin wall perforations. Consequently, APC can hardly remove bulky tumour masses.

There are two APC systems available on the market, the ERBE Elektromedizin, Tübingen, Germany; and Conmed, Utica, N.Y. The ERBE type includes an electrosurgical unit that generates a high frequency electrical current, an argon gas cylinder and a gas flow meter. The whole APC apparatus is accompanied by a foot switch to activate both HF current source and gas. There are two types of probe catheters to deliver the argon plasma beam parallel or perpendicular to the catheter axis. These catheters are covered with teflon material and are disposable. There are two sizes available; 2.3 mm in diameter –2.2m length and 3.2 mm-2.2 m. According to the manufacturer's manual the ERBE argon flow varies from 0.1 L/min to 9 L/min.

Procedure

The appropriate device settings vary between manufacturers, indications and protocols. There is a step-up concept of power and flow settings so that superficial vascular lesions are treated with settings of 40 to 50 W and 0.8 L/min. Tissue ablation is achieved with settings of up to 70-90 W and 1 L/min.⁵ Higher settings result in intraluminal gaseous distension and patient discomfort.

APC is a non-contact technique providing an operative distance from probe to tissue from 2 to 8 mm.⁶ If the endoscopist holds the probe too far from the tissue there will be no argon plasma beam at low power settings. On the other hand, tissue contact with the probe results in the untoward effect of tissue-probe sticking and thermal injury. Deep thermal injury allows argon gas to flow into the submucosa, producing pneumatosis and even extraintestinal gas. So tissue contact with the probe should be avoided. There must be no intermediate liquid, (included blood) between the argon probe and the tissue surface, otherwise a coagulation film develops and the underlying tissue surface remains inadequately treated. This has an immediate impact on active bleeding. Thus, surface fluids should be rinsed or sucked out as indicated.⁷

APC is performed by applications of 0.5 to 2 seconds duration.² The probe tip is directed in a paintbrush-like manner on extended confluent or linear areas. Direct vision of the probe tip is essential, throughout the application. Misdirection of the plasma beam to the endoscope tip may result in video chip damage.⁷ Frequent suctions are needed to decompress the intraluminal

argon gas and clear the smoke from the visual field. When treating tissue in contact with metal implants such as stents, settings should be reduced. Although there is heterogeneity in study designs, indications and definition of complications that limit the interpretation of safety data, complication rates vary from 0% to 24%.⁷

When combustible gas, such as methane, remains in the organ where APC is to be applied there is a danger of explosion within the organ. The colon must therefore be carefully cleansed before the session. Stenotic areas in the colon should first be dilated with bougienage or ballooning so that possible explosive gases entrapped may be evacuated.⁸ In summary, complications that have been reported are gaseous distension, pneumatosis intestinalis, pneumomediastinum and pneumoperitoneum, subcutaneous emphysema, pain, chronic ulceration, stricture, bleeding, transmural burn syndrome, perforation and death. It is therefore highly recommended that APC applications should follow the "10 rules of APC use" (Table 1). Another interesting recommendation is the power limit and single-shot duration of APC, according to various indications (Table 2).

Table 1. Practical points of APC use.

1. Do not confuse APC with argon laser. They are completely different in physics, application, and effect.
2. Always check argon gas flow as well as plasma beam outside the endoscope before inserting the probe into the working channel.
3. Advance the APC probe far enough, so that the first black ring is clearly visible in the endoscopic field.
4. Always perform APC under continuous visual control.
5. Be sure that the APC probe neither touches the target tissue nor is too far away during performance.
6. Never press the activated probe against the organ wall or into tissue for this may result in emphysema or wall damage or perforation.
7. Do not touch metal stents directly with the APC probe; keep the appropriate distance.
8. Avoid overinflation by checking for abdominal distention; deflate repeatedly as indicated.
9. Set the power limit of the electrosurgical unit and the duration of the APC supply as indicated by the affected organ (e.g. upper limit of max. 50 Watt in the right colon or cecum, but higher for tumor ablation).
10. Many short duration applications are more effective than a few long-duration ones. Control the penetration depth by altering the duration rather than lowering the settings.

Adapted from⁸

Table 2. Power limit and single shot duration in APC application.

	Power limit (Watts)	Single shot duration (seconds)
Normal settings for esophagus, stomach, small intestine and rectum	60-80	1-3
Stomach	70-99	1-3
Stent in-over growth conditioning of fistula	60	1-3
Large tumours (over 1.5 cm)	99	3-10
Medium size (from 0.5-1.5)	80	3-5
Small tumours	60	0.5-5
Right colon	40-50	0.1-0.5-1
Remaining colon	40-60	1-2

Adapted from⁸

Indications and efficacy

Basically, there are two main axes of APC use in clinical practice; hemostasis and ablation. The best results are expected to be found in hemorrhagic lesions. However, ablation still remains a fascinating practice for the endoscopist and quite helpful to patients, at least as a palliative therapy.

Hemostasis

APC has been involved in the treatment of vascular ectasias, bleeding ulcers, and bleeding varices.

1. Vascular Ectasias. This is a general term involving lesions located in the upper or lower gastrointestinal track. More specifically, APC has been used in the treatment of gastric antral vascular ectasias (GAVE) formerly known as watermelon, sporadic or inherited angiodysplasias, hemorrhagic telangiectasias and post-radiation enteropathy or proctopathy.^{4,9-13}

GAVE can successfully be eliminated by APC¹⁴. In one study, 17 patients were treated with this technique in 1 to 4 sessions. After 30.4 months follow-up GAVE recurred and needed further treatment in only 5 of them.¹⁵ In another study, disappearance of bleeding and endoscopic improvement was observed even in the first session.¹⁶ In the case of angiodysplasias, the number of patients treated and the follow-up are enough to conclude that APC is a safe method of treatment compared to laser.^{4,9,14-18} Although perforation is rare, about 0.31 %, ¹⁹ it is still possible. Other side-effects that have been reported are submucosal emphysema usually mild,¹⁹ inflammatory polyps²⁰ and gas explosion.²¹

There are many studies suggesting efficient results among patients with post-radiation proctopathy.^{11,22-}

²⁷ In the above studies, various definitions of response to treatment were applied. Thus, clinical success varies from 90% to 94%, while complete disappearance of bleeding from 81% to 86%. Despite angiectasias, side-effects are more common during treatment for post-radiation proctopathy, rising to 14%.²⁵ This higher side-effect rate seems to be associated with the power setting of the device. So a power of less than 45 W should be used to avoid injuries to a fragile, thinned rectal wall, previously irradiated. Among the side-effects there are symptom-free stenosis as well as pain which can be treated with the usual analgesics. Only one perforation and one extensive necrosis have been reported.²⁵

2. Bleeding ulcers. There are studies suggesting a favourable result of APC in stopping a bleeding peptic ulcer.^{2,28,29} The operative distance between the APC probe and the tissue was 2 to 8 mm and the power setting 40 and 70W.²⁹ When APC was compared to the heater probe as a hemostatic device the results were similar. Argon plasma coagulation provided faster hemostasis.²⁹ However, this was a small randomised trial with limited statistical power. We should always keep in mind the pros and cons previously reported in the procedure section. There has been concern that it may have an inadequate effect if blood interferes between APC beam and the tissue, especially in spurting bleeding. Additionally, care must be taken to avoid submucosal accumulation of the gas, which may lead to delayed perforation. No major complication has been observed during APC procedure except for transient pain and tachycardia due to gut overinflation.²⁹ APC has also been used in diffuse bleeding from a large area, coagulation disorders and tumour bleeding.¹⁷ Finally, APC has success-

fully been involved in the treatment of active bleeding due to Dieulafoy's lesion.⁸

- 3. Bleeding varices.** To date, there are two reported randomised controlled studies of 30 patients each, indicating that APC appliance of the distal oesophageal mucosa after banding ligation of oesophageal varices, is safe and effective for reducing the rate of variceal recurrence.^{6,30} According to the above studies, the mean power output was 60W, while the sessions of each patient ranged from 1-3. During the procedure, circumferential coagulation of the entire oesophageal mucosa was performed, starting from the Z line to 5 cm proximally. Immediate complications were transient fever, dysphagia, and retrosternal pain/discomfort. All of them resolved spontaneously within 24 hours. At a mean follow-up of 16 months (range 9-28 months) variceal recurrence was significantly less frequent in the APC group. Table 3 compares APC vs. laser treatment in various hemostatic indications.

Ablation

APC has always been used for the treatment of benign and malignant tumours of the digestive tract. Results of each indication except oesophageal cancer are presented in table 3.

- 1. Barrett oesophagus.** A number of case series report the use of APC in treating Barrett oesophagus, including patients with low-grade dysplasia or adenocarcinoma in situ.³¹⁻³⁹ Best results were obtained in short segment non-circumferential Barrett.³³ Most patients were under concurrent high dose proton pump inhibitor therapy. Additionally, some others had undergone anti-reflux surgery. Although the data in the above studies present a great variability, successful ablation of Barrett oesophagus was achieved in 68%

of patients, after a mean 2.5 sessions per patient. The follow up was 6 to 36 months.^{31,33,35,36}

There have been post-ablation complications, which can be mild or serious: chest pain and odynophagia within 3 to 10 days, high fever and pleural effusions.³⁶ In addition, mild complications include severe oesophagitis requiring transfusion, oesophageal strictures, pneumomediastinum and subcutaneous emphysema.^{33,36,40} A true perforation with consequent death reported in one patient is an example of a complication.³⁸ Finally, we should not forget that Barrett island relapsing under a normal-appearing mucosa, as well as a true adenocarcinoma, have been reported.^{33,41} This is an alarm message that should always keep endoscopists alert. To date, Barrett's oesophagus ablation by APC remains investigational, and could not be suggested as a routine therapeutic option.

- 2. Polyps and remnant adenomatous tissue after polypectomy.** The usefulness of APC device as a complimentary step following piecemeal snare polypectomy has been reported in two studies.^{42,43} According to one study, 15 out of 30 patients had complete eradication of the residual adenomatous tissue after one session of APC and all of them after two sessions.⁴³ Additionally, APC has been applied as a first step therapy for the ablation of intestinal polyps or papillomatosis in case series.^{4,8,9} For example, multiple small polyps, as in familial adenomatous polyposis syndrome have easily been fulgurated by APC.⁴⁴ However, long-term results are not available.
- 3. Debulking malignant tumours.** Tumour debulking is an APC indication. In a large study APC was applied as palliative therapy in 83 patients with oesophageal and gastric cardia tumours. Recanalization was managed in 58% allowing normal food passage and

Table 3. Comparison of results of APC and laser treatment in hemorrhagic lesions.

Indications	Angiodysplasia		Gave		Radiation Proctitis		Bleeding Ulcer
	APC	Laser	APC	Laser	APC	Laser	APC
No of patients	65	205	16	45	129	47	27
Success	68-100%	78-82%	75%	86%	91%	87%	93%
Recurrence	ND	15-47%	ND	ND	0	ND	15%
Complications	2.5%	2-5%	4%	ND	7%	ND	0
No of sessions	1-3	1-3	1-8	ND	1-4	1-3	ND
MNS	1.3-2	1	2	2-5	2.24	2	ND
Follow up (months)	1.5-14	11.5-19.5	1-14	3	1-48	14	ND

ND: no data, MNS: mean number of sessions

Adapted from¹⁶

dysphagia relief even after one session. Twenty-six percent needed two sessions, while the rest reported dysphagia score improvement by at least one grade. Perforation occurred in 8.3% of patients and was treated conservatively in all but one.⁴⁵ Other reports have also strengthened the previous findings for a successful treatment of dysphagia, in a total of over 152 patients.⁴⁵⁻⁴⁸ Additionally, APC has been used in association with other treatments, like dilatation, radiotherapy, and chemotherapy^{45,46} or just before stenting.^{4,45} The APC has been used in small series to treat tumours of the ampula of Vater and nonsuperficial colonic tumours.^{4,9} In another study, patients with oesophageal, stomach and rectal cancer, staged by EUS and histology as T 1 were treated by APC. The treatment achieved local response in 9 out of 10 patients over a 9.5 months follow-up.⁴⁹ Table 4 summarises the results of APC and laser treatment in benign and malignant tumours and preneoplastic lesions.

4. Miscellaneous. Dysplastic heterotopic mucosal ablation, tumour ingrowth or overgrowth in metal stents

or cut off displaced metal stents are some other interesting applications of APC.^{2,37,50-53} Post-interventional hemostasis required, for example, after polypectomy, mucosectomy, or bougienage can be achieved by APC. A special indication of APC is septotomy in Zenker's diverticulum.^{9,54} According to the above studies, APC seems to be an effective and safe tool, in order to offer patients a therapy other than open surgery. Finally, the condition of fistulas prior to the use of fibrin glue is an extra indication for APC. This situation requires a superficial destruction of the epithelium around the opening and within the fistula. This process enhances adhesion of the glue for closing the fistula.

To summarise, the use of APC has recently been expanded and will continue. Although such a development is welcome, there is still a necessity for further studies to refine assessment of results and technical details of the procedure. However, it seems that APC is best accepted for hemostasis while there is limited data with regard to ablation therapy.

Table 4. Comparison of results of APC and laser treatment in benign and malignant tumours and in preneoplastic lesions

Indication	Rectal Ca		Dysplasia Superficial Ca	Residues post polypectomy multiple polyps		Large villous adenoma		Gastric Ca	Barret		
	APC	Laser	APC	APC	Laser	APC	Laser	APC	APC	Laser	
No of pts	6	63	16	72	21	28	244	10	57	19	
Success	6/6	75-82%	94%	100%	100%	100%	84-92%	80%	38/57	59%	
Recurrence	0	85%	0	ND	0	ND	26-29%	ND	ND	ND	
	at 12 mo										
Complication	0	16%	0	17%	ND	0	5.6%	0	5/57	0	
No of sessions	1-5	ND	1-2	1-9	ND	1-5	ND	1-21	1-7	1-6	
MNS	2.7	3/2	ND	1-3	5	1.5-3	3.6-6.7	4.9	2.2	ND	
Follow up (mo)	ND	ND	5-14	1-12	60	3-18	17-57	ND	6	ND	

ND: no data, MNS: mean number of sessions

Adapted from¹⁶

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