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Editorial Board Member of *World Journal of Gastrointestinal Endoscopy*, Marcela Kopacova, MD, PhD, Professor, 2nd Department of Internal Medicine - Gastroenterology, Charles University Teaching Hospital, Hradec Kralove 500 05, Czech Republic

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EDITORIAL OFFICE

Xiu-Xia Song, Director
World Journal of Gastrointestinal Endoscopy
Baishideng Publishing Group Inc
7901 Stonenidge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
Help Desk: <http://www.wjgnet.com/helpdesk>
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PUBLISHER

Baishideng Publishing Group Inc
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Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.wjgnet.com/helpdesk>
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Retrospective Study

Case series on multimodal endoscopic therapy for gastric antral vascular ectasia, a tertiary center experience

Tasnia Matin, Mohammed Naseemuddin, Mohamed Shoreibah, Peng Li, Kondal Kyanam Kabir Baig, Charles Mel Wilcox, Shajan Peter

Tasnia Matin, Internal Medicine, UAB Hospital, Birmingham, AL 35233, United States

Tasnia Matin, Division of Gastroenterology, University of Alabama School of Medicine, Birmingham, AL 35294, United States

Mohammed Naseemuddin, Department of Gastroenterology, Emory, Atlanta, GA 30322, United States

Mohamed Shoreibah, Kondal Kyanam Kabir Baig, Charles Mel Wilcox, Shajan Peter, Division of Gastroenterology, University of Alabama at Birmingham, Birmingham, AL 35233, United States

Peng Li, School of Public Health, University of Alabama at Birmingham, Birmingham, AL 25294, United States

ORCID number: Tasnia Matin (0000-0001-6255-0946); Mohammed Naseemuddin (0000-0002-0648-2747); Mohamed Shoreibah (0000-0002-8461-3976); Peng Li (0000-0002-9026-9999); Kondal Kyanam Kabir Baig (0000-0003-1550-4853); Charles Mel Wilcox (0000-0001-5246-3419); Shajan Peter (0000-0003-3214-2989).

Author contributions: Matin T was responsible for design, data collection/analysis/interpretation and drafting article; Naseemuddin M was responsible for additional design, data collection and drafting article; Shoreibah M was responsible for critical revision of the article; Li P was responsible for statistical analysis of data; Kyanam Kabir Baig K was responsible for critical revision of the article for important intellectual content; Wilcox CM was responsible for critical revision of the article for important intellectual content; Peter S was responsible for conception and design, critical revision and final approval of article.

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Correspondence to: Tasnia Matin, MD, Division of Gastroenterology, University of Alabama School of Medicine, 1720 2nd Avenue South, BDB 380, Birmingham, AL 35294, United States. tasniamatin@uabmc.edu
Telephone: +1-205-9962459
Fax: +1-205-9756201

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Abstract**AIM**

To study and describe patients who underwent treatment for gastric antral vascular ectasia (GAVE) with different endoscopic treatment modalities.

METHODS

We reviewed patients with GAVE who underwent treat-

ment at University of Alabama at Birmingham between March 1, 2012 and December 31, 2016. Included patients had an endoscopic diagnosis of GAVE with associated upper gastrointestinal bleeding or iron deficiency anemia.

RESULTS

Seven out of 15 patients had classic watermelon description for GAVE, 1/15 with diffuse/honeycomb pattern and 6/15 with nodular GAVE per EGD description. Seven out of 15 patients required multimodal treatment. Four out of six of patients with endoscopically nodular GAVE required multimodal therapy. Overall, mean pre- and post-treatment hemoglobin (Hb) values were 8.2 ± 0.8 g/dL and 9.7 ± 1.6 g/dL, respectively ($P \leq 0.05$). Mean number of packed red blood cells transfusions before and after treatment was 3.8 ± 4.3 and 1.2 ± 1.7 ($P \leq 0.05$), respectively.

CONCLUSION

Patients with nodular variant GAVE required multimodal approach more frequently than non-nodular variants. Patients responded well to multimodal therapy and saw decrease in transfusion rates and increase in Hb concentrations. Our findings suggest a multimodal approach may be beneficial in nodular variant GAVE.

Key words: Gastric antral vascular ectasia; Upper GI bleed; Radiofrequency ablation; Endoscopic band ligation; Argon plasma coagulation

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Core tip: Over the past several years, treatment for gastric antral vascular ectasia (GAVE) has continued to evolve and the number of available treatments has continued to increase. However, the optimal treatment of GAVE is currently unknown and there currently aren't any studies comparing every modality. However, it is becoming apparent that patients with severe, diffuse or refractory disease require multimodal therapy. Our case series not only shows that but also that patients specifically with nodular variant GAVE require and respond well to multimodal therapy.

Matin T, Naseemuddin M, Shoreibah M, Li P, Kyanam Kabir Baig K, Wilcox CM, Peter S. Case series on multimodal endoscopic therapy for gastric antral vascular ectasia, a tertiary center experience. *World J Gastrointest Endosc* 2018; 10(1): 30-36 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v10/i1/30.htm> DOI: <http://dx.doi.org/10.4253/wjge.v10.i1.30>

INTRODUCTION

First described in 1953 by Rider *et al*^[1], gastric antral vascular ectasia (GAVE) is now a well-recognized cause of chronic upper gastrointestinal bleeding (UGIB) accounting for 4% of non-variceal UGIB^[2] and an important cause of chronic iron deficiency anemia.

Endoscopically, GAVE can appear as organized red spots emanating radially from the pylorus (watermelon stomach), arranged in a diffuse manner (honeycomb stomach), or as nodules^[3]. Histologically, GAVE appears as ectatic mucosal capillaries with fibrin thrombi, spindle cell formation and fibrohyalanosis^[4]. Immunohistochemical staining for CD61, a platelet marker, further confirms a diagnosis of GAVE^[5]. GAVE has been associated with cirrhosis, chronic kidney disease, diabetes mellitus, autoimmune diseases, hypothyroidism, bone marrow transplant and left ventricular assist devices^[6-8]. Over the past two decades, many therapeutic options have been implemented for treatment of GAVE including surgical, medical and endoscopic therapies. Data is emerging on the resolution of GAVE following liver transplant in cirrhotics^[9]. Endoscopic therapies have rapidly become the mainstays of first line therapy namely with argon plasma coagulation (APC) as the most common modality and more recently with radiofrequency ablation (RFA) using Halo⁹⁰ catheter^[9] and endoscopic band ligation (EBL) both of which have been shown to be safe and effective for GAVE treatment^[10,11]. The latter two have been utilized in treatment of severe, diffuse, APC refractory GAVE^[10,21]. Furthermore, there has been the advent of BARR χ Through The Scope technique (Covidien, TTS-1100) for RFA, which posits some advantages over the traditional Halo⁹⁰ system. Despite these advances, the best therapeutic approach has yet to be defined. This case series describes patients who underwent treatment for GAVE with TTS-RFA alone or part of a multimodal approach incorporating other methods such as APC and EBL (Figure 1). We believe that the multimodal approach may be appropriate for certain subsets of patients, namely patients with severe nodular GAVE.

MATERIALS AND METHODS

We reviewed patients with GAVE who underwent treatment at University of Alabama at Birmingham (UAB) between March 1, 2012 and December 31, 2016. Included patients had an endoscopic diagnosis of GAVE with associated UGIB or iron deficiency anemia. Medical history including demographic data and chronic medical conditions associated with GAVE were collected. Patients receiving transfusions for other issues outside of GAVE (*i.e.*, for surgeries) were excluded.

Outcomes

The primary outcomes measured included number of packed red blood cells (pRBC) transfusions required and hemoglobin (Hb) concentrations 6 mo prior to and after initiation of treatment, either with TTS-RFA alone or multimodal therapy. In case of patients in the multimodal group, the same variables were collected 6 mo before and after initiation of an alternative modality (APC, EBL or TTS-RFA). Secondary outcome measures included adverse events, post-treatment adverse events, and number of hospitalizations at University of

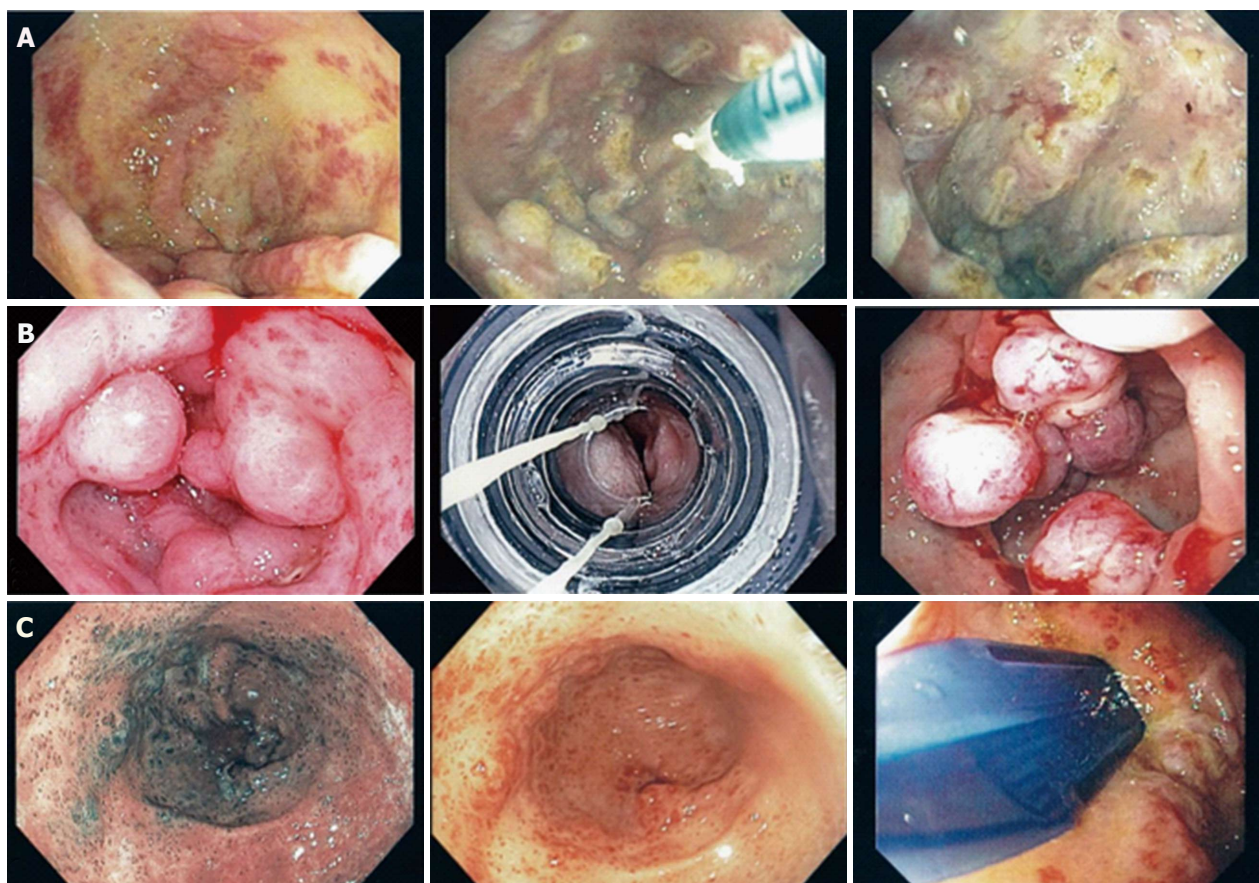


Figure 1 Argon plasma coagulation (A), endoscopic band ligation (B) and TTS- radiofrequency ablation (C).



Figure 2 White light endoscopy.

Alabama (UAB).

Technique

Informed consent was obtained from all patients prior to the procedure. All antiplatelet/anticoagulant therapy was discontinued prior to the procedure. High-resolution endoscopy was performed using white light endoscopy (Figure 2) as well as narrow band imaging. Focal ablation was performed using TTS-RFA catheter. The catheter, consisting of 15.7 mm × 7.5 mm transparent electrode array, was passed through the 2.8 mm working channel of the endoscope. The electrode was

the placed in opposition of the GAVE lesions and two consecutive pulses of energy at settings 12-15 J/cm², 40 W/cm² were delivered. Circumferential ablation of antral lesions was achieved using the external rotatory function of the catheter (Video 1). Repeat endoscopies and RFA was performed at intervals of 6-8 wk until all lesions appeared healed.

Statistical analysis

Frequencies (%) were used for categorical variables. For continuous variables, mean ± SD was used. Non-parametric, matched pairs, two-tailed Wilcoxon signed rank tests were used to assess differences in pRBC transfusions before and after treatment. Paired T test was used to compare pre and post treatment Hb concentrations. All the analysis were conducted with SAS 9.4 (Cary, NC, United States) and *P* < 0.05 was considered statistically significant.

RESULTS

Fifteen patients were included in this case series Table 1 describes the demographics. The mean patient age was 62.9 ± 8.7 (range 46-79). Seven out of 15 were women (47%). Included patients underwent a mean of 2.7 ± 1.8 TTS-RFA sessions. TTS-RFA was performed in all patients without adverse events. In addition to TTS-RFA, 7/15 (47%) patients required multimodal

Table 1 Patient demographics, medical history and gastric antral vascular ectasia characteristics

Patient	Age	Sex	Race	GAVE associated conditions	Description	Biopsy confirmed?	ASA	On anticoagulation?	Sedation used	MELD-Na
1	65	F	W	Cirrhosis	Watermelon	N	3	No	MAC	15
2	58	M	W	Cirrhosis	Watermelon	N	3	Yes	MAC	17
3	75	F	B	LVAD	Watermelon	Y	4	No	MAC	n/a
4	55	M	W	Cirrhosis, DM	Nodular	N	3	No	MAC	15
5	79	F	W	Hypothyroidism	Watermelon	Y	3	No	MAC	n/a
6	65	F	W	Cirrhosis	Nodular	Y	3	No	MAC	11
7	70	F	B	Hypothyroidism	Watermelon	Y	2	No	MAC	n/a
8	53	M	W	Cirrhosis	Watermelon	N	3	No	MAC	26
9	70	M	W	DM	Diffuse	N	4	Yes	MAC	n/a
10	46	F	W	CKD	Nodular	Y	3	No	MAC	n/a
11	60	M	W	DM	Watermelon	N	4	No	MAC	n/a
12	68	F	W	Cirrhosis, DM	Watermelon	N	3	No	MAC	18
13	59	M	W	Cirrhosis, DM	Nodular	N	2	No	MAC	14
14	62	M	W	Cirrhosis, DM, LVAD	Nodular	N	4	Yes	MAC	25
15	58	M	W	Cirrhosis, DM	Nodular	Y	3	No	MAC	23

GAVE: Gastric antral vascular ectasia; F: Female; M: Male; LVAD: Left ventricular assist device; DM: Diabetes mellitus; CKD: Chronic kidney disease; Y: Yes; N: No; ASA: American Society of Anesthesiologists score; MAC: Monitored Anesthesia Care; MELD-Na: Model for end-stage liver disease-with sodium.

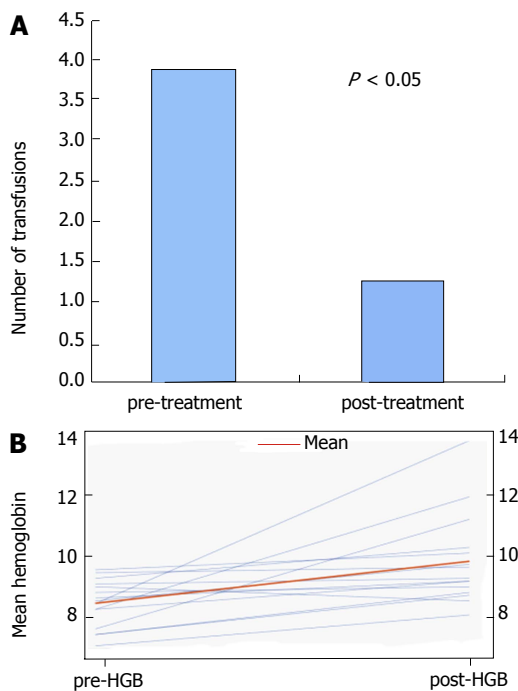


Figure 3 Number of transfusions (A) and mean hemoglobin (B) in 6-mo period pre- and post-treatment for gastric antral vascular ectasia. HGB: Hemoglobin.

approach with APC and/or EBL as well. Average amount of hospitalizations prior to first intervention was 1.4 ± 1.3 and average after initial intervention was 1.1 ± 1.4 ($P > 0.05$). Average time between initial intervention and second intervention was 2.35 ± 2.27 mo. Overall, mean pre- and post-treatment Hb values were 8.2 ± 0.8 g/dL and 9.7 ± 1.6 g/dL, respectively ($P \leq 0.05$) (Figure 3A). Mean number of pRBC transfusions before and after treatment was 3.8 ± 4.3 and 1.2 ± 1.7 ($P \leq 0.05$), respectively (Figure 3B).

In patients who were primarily treated with TTS-RFA (patients 1-8, $n = 8$), mean number of sessions was 2.8 ± 1.5 . Mean number of transfusions was reduced from 3.0 ± 2.7 to 1.2 ± 1.9 ($P > 0.05$). Mean Hb increased from 8.3 ± 1.0 g/dL to 9.9 ± 1.2 g/dL ($P > 0.05$). In patients who required multimodal therapy (patients 9-15, $n = 7$), mean number of TTS-RFA, APC and EBL sessions was 2.9 ± 2.0 , 2.9 ± 3.1 and 1.6 ± 2.2 , respectively. The mean number of transfusions decreased from 4.9 ± 5.7 to 1.3 ± 1.7 ($P > 0.05$) and the mean Hb increased from 8.1 ± 0.7 g/dL to 9.5 ± 2.1 g/dL ($P > 0.05$). Overall, 8 out of 15 patients were weaned off transfusions (53%) entirely at 6-mo follow-up (Figure 4) and 13/15 saw a decrease in requirements (87%). Only one out of the 15 saw an increase in requirements, while 2 had no change in requirements.

Seven out of 15 patients had classic watermelon description for GAVE, 1/15 with diffuse/honeycomb pattern and 6/15 with nodular GAVE per EGD description. Four out of six of patients with endoscopically nodular GAVE required multimodal therapy. Of the 7 patients requiring multimodal therapy, 4 (57%) had nodular GAVE. Three of these four patients were completely weaned off transfusions in the post-treatment period.

DISCUSSION

GAVE is an important cause of chronic anemia^[7]. Though, often asymptomatic and an incidental finding, it can lead to chronic transfusion dependence. Over the past several years, treatment for GAVE has continued to evolve as the number of available effective therapeutic interventions has increased. These included: YAG laser, APC, EBL, cryotherapy and surgical antrectomy (Figure 5)^[10,13-15]. APC is most commonly used but has been associated with sepsis, post-APC bleeding, gastric outlet

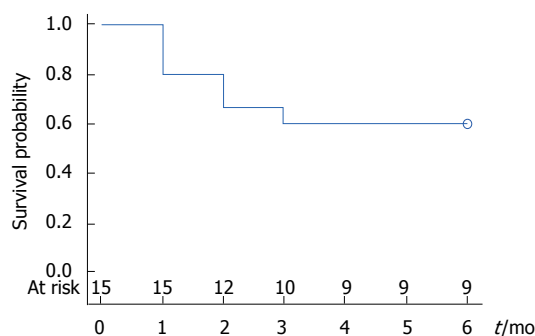


Figure 4 Transfusion free survival curve.

obstruction and increased incidence of hyperplastic polyps^[16-18]. Recently, the BARR x Halo⁹⁰ system (Covidien, Sunnyvale, CA, United States), which mounts on to the tip of the standard endoscope, has been successfully used for treatment of GAVE^[19,20]. Given the fixed positioning of the electrode, the Halo⁹⁰ catheter requires removal of the endoscope for rotation of the electrode for exact apposition to the mucosa. Repeated intubations are cumbersome and can increase the risk of adverse events, including gastroesophageal junction laceration^[21].

The newly introduced TTS-RFA is an improvement over the Halo⁹⁰ system as it enables the endoscopist to reach all areas of the antrum by internally rotating the catheter without having to remove the endoscope. While it does have a reduced ablative area (1.2 cm²)^[22], it delivers up to 120 pulses per session compared to 80 pulses delivered by the Halo⁹⁰ systems. While TTS-RFA is an effective treatment for GAVE, it may not be sufficient to some subgroups of patients.

EBL has lately been demonstrated as a good alternative to APC especially in refractory cases of GAVE and has been found to have a similar safety profile and per Zepeda's randomized controlled time performed better than APC^[11,24].

The optimal treatment for GAVE is still unknown and currently there are no studies comparing every modality. However, it is becoming more apparent that patients with more severe, diffuse or refractory GAVE would benefit from multimodal therapy^[11,18].

From our review, our numbers indicate that patients undergoing single modality treatment with TTS-RFA and multimodality treatment had overall increase in mean Hb concentrations and decreased transfusion requirements in the 6 mo following treatment.

Interesting, of the 6 patients described as having nodular GAVE, 4 required multimodal therapy suggesting perhaps the multimodal approach should be applied to this newly described variant. Outcomes were favorable with multimodal approach in this group showing increased Hb and decreased transfusion requirements. Increased Hb concentrations and subsequent decreased transfusion requirements together decrease patient costs with fewer hospitalizations related to anemia and

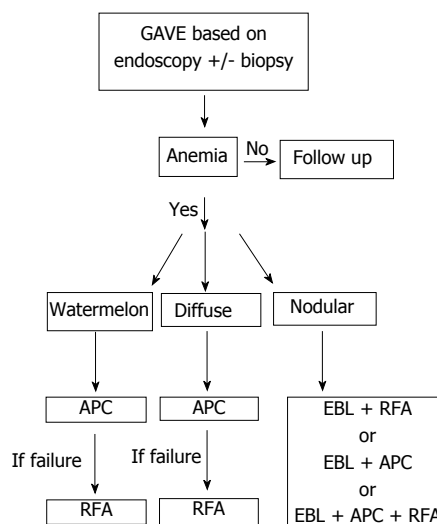


Figure 5 Suggested flow chart for treatment algorithm. GAVE: Gastric antral vascular ectasia; APC: Argon plasma coagulation; RFA: Radiofrequency ablation; EBL: Endoscopic band ligation. Can consider radiofrequency ablation as first line therapy as well for watermelon and diffuse type.

outpatient costs. We did not see a statistically significant decrease in hospitalizations in our case series and this may be due to a myriad of factors including the fact that hospitalizations may be due to another of patients' comorbidities. Also, it is difficult to attain data on number of hospitalizations outside of our facility.

There are several limitations to the conclusions that can be drawn from this study that need to be addressed. First, this is a small, single center, single operator, retrospective study. Second, GAVE was not confirmed on biopsy on all patients. Third, this study is observational and cannot ascertain if any one therapy is superior over other modalities as study design was not to compare modalities. Lastly, patients were followed for a period of 6 mo after the initiation of treatment. While the data is promising, it is not clear if GAVE lesions recur or if patients have worsening anemia after our follow-up period of 6 mo.

In conclusion, patients with nodular variant GAVE required multimodal approach more frequently than non-nodular variants. Patients responded well to multimodal therapy and saw decrease in transfusion rates and increase in Hb concentrations. Our findings suggest a multimodal approach may be beneficial in nodular variant GAVE.

ARTICLE HIGHLIGHTS

Research background

At present, optimal treatment of gastric antral vascular ectasia (GAVE) is unknown but it is apparent that severe cases require multimodal therapy. The newly discovered nodular variant, from our study, appears to more often require multimodal therapy.

Research motivation

GAVE is an important cause of chronic anemia and can lead to chronic blood transfusion dependence. Having effective treatment is an important for patient

quality of life.

Research objectives

Main objectives were to study patients presenting with GAVE and chronic anemia and following outcomes based on type of GAVE as well as type of intervention.

Research methods

We reviewed patients with GAVE who underwent treatment at University of Alabama at Birmingham. Included patients had an endoscopic diagnosis of GAVE with associated upper gastrointestinal bleeding or iron deficiency anemia. Medical history including demographic data and chronic medical conditions associated with GAVE were collected. Patients receiving transfusions for other issues outside of GAVE (*i.e.*, for surgeries) were excluded.

Research results

Seven out of 15 patients had classic watermelon description for GAVE, 1/15 with diffuse/honeycomb pattern and 6/15 with nodular GAVE per EGD description. Seven out of 15 patients required multimodal treatment. Four out of six of patients with endoscopically nodular GAVE required multimodal therapy. Overall, mean pre- and post-treatment hemoglobin (Hb) values were 8.2 ± 0.8 g/dL and 9.7 ± 1.6 g/dL, respectively ($P \leq 0.05$). Mean number of pRBC transfusions before and after treatment was 3.8 ± 4.3 and 1.2 ± 1.7 ($P \leq 0.05$), respectively.

Research conclusions

Patients who received TTS-radiofrequency ablation and patient with multimodal therapy, both had decrease in transfusion requirements and improvement in mean Hb. Our study found that patients with nodular variant GAVE tended to require multimodal therapy more frequently. We believe patients with nodular variant GAVE would benefit from a multimodal approach.

Research perspectives

Lessons learned from this study include importance of larger study population. Future directions include involving larger patient pool and possibly attempting a prospective approach based on suggested algorithm.

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