

Endoscopic Treatment Outcomes in Watermelon Stomach Patients with and without Portal Hypertension

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Background and Study Aims: Watermelon stomach is a source of recurrent gastrointestinal hemorrhage and anemia. The aims of this study were to describe the endoscopic appearance and treatment outcomes in watermelon stomach patients with and without portal hypertension.

Patients and Methods: All patients with watermelon stomach enrolled in a hemostasis research group's prospective studies from 1991 to 1999 were identified. Investigators collected data using standardized forms. Comparisons were made using the chi-squared test, Wilcoxon rank-sum test, and Wilcoxon signed-rank test.

Results: Twenty-six of 744 (4%) consecutively enrolled patients with nonvariceal upper gastrointestinal hemorrhage had watermelon stomach as the cause. Eight of these 26 patients (31%) also

had portal hypertension. These patients had diffuse antral angiomata, as opposed to the classic linear arrays seen in those without portal hypertension. The demographic data and clinical presentations of the two groups were otherwise similar. Palliative endoscopic treatment was associated with a significant rise in hematocrit and a decrease in the need for blood transfusion or hospitalization in watermelon stomach patients with and without portal hypertension.

Conclusions: Watermelon stomach patients with and without portal hypertension had similar clinical presentations. The endoscopic findings differed in that those with portal hypertension had more diffuse gastric angiomata. Bleeding was effectively palliated by endoscopic treatment, regardless of the presence of portal hypertension.

Introduction

Watermelon stomach, or gastric vascular ectasia, is an unusual but clinically significant source of recurrent upper gastrointestinal hemorrhage and iron-deficiency anemia [1,2]. The diagnosis of watermelon stomach is most commonly based on the characteristic endoscopic appearance of red antral stripes radiating in linear arrays to the pylorus in the appropriate clinical setting [3]. A variant with more diffuse red lesions has also been described [4–7]. The etiology of watermelon stomach remains unknown, and specific medical therapy has not been developed. Previous investigators have established the efficacy of endo-

scopic thermocoagulation techniques, including Nd:YAG laser [6,8–13], heater probe treatment [7,14], bipolar probe [15,16], and argon plasma coagulation [17,18] in the palliative treatment of patients with classic watermelon stomach.

Some patients with watermelon stomach also have portal hypertension [7,19–25]. Evidence suggests that watermelon stomach in patients with portal hypertension and the entity known as portal hypertensive gastropathy are distinct lesions, with the latter having a prominent mosaic or “snakeskin” appearance at endoscopy. Neither the characteristic endoscopic appearance of watermelon stomach in patients with portal hypertension nor

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the outcomes of endoscopic treatment in this subgroup of patients have previously been described. The aims of this study were to describe the endoscopic appearance and to compare the outcomes of endoscopic treatment in watermelon stomach patients with and without portal hypertension.

Patients and Methods

Case Identification

This was a cohort study with an uncontrolled pre-test–post-test design. Cases were identified among 744 consecutive patients with nonvariceal upper gastrointestinal hemorrhage who were enrolled in prospective studies being conducted by the Hemostasis Research Group at the University of California at Los Angeles Center for Ulcer Research and Education (UCLA/CURE) from January 1991 to November 1999. The study was approved by the UCLA Office for the Protection of Research Subjects. Informed consent was obtained from patients before each clinically indicated procedure. In total, 26 of 744 consecutive, prospectively enrolled patients were diagnosed with watermelon stomach as the cause of their upper gastrointestinal hemorrhage and anemia. Nearly one-third of these patients with watermelon stomach (eight of 26) had documented evidence of portal hypertension.

Endoscopic Diagnosis and Treatment

All upper gastrointestinal endoscopies were performed by experienced endoscopists (D.M.J., T.O.G.K., R.J.). Careful examination of the esophagus, stomach (including retroflexed view), and duodenum was undertaken in each case. The number of gastric red spots or stripes, presence of active gastric bleeding, and any other endoscopic lesions were recorded at the time of each endoscopy. When counting angiomas, endoscopists did not count beyond 100, so that subjects with over 100 or confluent gastric angiomas were recorded as having 100 angiomas. Investigators reviewed video images printed out using Mavigraph devices (Sony, Inc.) and agreed on the presence and pattern (i.e., diffuse vs. discrete linear) of the angiomas, as well as on the presence and size of any varices after procedures were performed. The modalities of endoscopic hemostasis used included bipolar electrocoagulation (Gold probe, Boston Scientific, Inc., Natick, Massachusetts, USA), heater probe (Olympus, Inc., Lake Success, New York, USA), and argon plasma coagulation (Erbe, Inc., Marietta, Georgia, USA). The treatment used was based on the availability of hemostasis devices and the investigator's choice.

Gold probe treatment was conducted using a 10-Fr probe at a generator setting of 15 W and with a pulse duration of 1–2 s. Heater probes were set to 15 J. Argon plasma coagulation was conducted with a gas flow rate of 0.5–1.6 l/min and a generator setting of 50–60 W, with a preference for the lowest settings necessary to achieve satisfactory coagulation while minimizing gastric distension. The end points of each treatment session were control of active bleeding and coagulation of as many angiomas as possible, while avoiding circumferential coagulation or repeated treatment of the same lesion. The first three treatment sessions were generally at intervals of 4–6 weeks, and thereafter follow-up was at the discretion of the treating endoscopist. All patients were placed on acid suppression (histamine

type-2 receptor antagonists or proton-pump inhibitors) and instructed to avoid aspirin and nonsteroidal anti-inflammatory drugs. The ultimate goals of treatment were control of gastrointestinal bleeding and anemia, as well as the obliteration of all gastric angiomas.

Data Collection

Using standardized data abstraction forms, one physician (G.S.D.) and two skilled research nurses collected retrospective (before initial therapeutic endoscopy) and prospective data on all patients. Medical records of all patients were reviewed and abstracted for the year before the first treatment session. Medical record data were supplemented and confirmed by telephone calls to blood banks, clinics, physician offices, and hospitals. In addition, all patients underwent routine clinical, laboratory, and endoscopic evaluation before each session of endoscopic treatment as well as at each follow-up visit. Key paired outcome measurements included the number of packed red blood cell transfusions over the year before the first treatment session and over the course of follow-up, the number of hospitalizations for gastrointestinal hemorrhage over the year before first treatment and over the course of follow-up, the hematocrit at time of initial the UCLA treatment session and at the most recent UCLA follow-up visit. The total follow-up time was equal to the number of days from the first endoscopic treatment session to the most recent UCLA follow-up visit.

Data Management and Analysis

The SAS program (SAS Institute, Carey, North Carolina, USA) was used for data management and analysis. Missing or inconsistent data were addressed by a series of checks and corrections. Firstly, manual checks of completed data collection forms were carried out by the principal investigator (G.D.). Secondly, manual checks were conducted by the data manager during data entry. Thirdly, an automated check was carried out after data entry had been completed for each subject file. Missing or inconsistent data were brought to the attention of the principal investigator and resolved by a joint review of the medical record. Comparisons were made using Wilcoxon rank-sum tests for between-group comparison and signed-rank tests for within-group comparisons of ordered variables. Chi-squared tests were used for nonordered categorical variables. A two-sided *P* value less than 0.05 was considered statistically significant.

Results

The study group consisted of 26 patients with watermelon stomach, eight of whom had portal hypertension, and 18 of whom were without portal hypertension. Baseline demographic and endoscopic data are presented in Table 1. The majority of patients in both groups were women in their eighth decade of life, who presented with anemia and gastrointestinal hemorrhage manifested by melena. Evidence of overt bleeding in those without melena included hematemesis or active gastric bleeding, or both, at the time of initial endoscopy. Only one patient with portal hypertension and one patient without portal hypertension gave a history of using aspirin or nonsteroidal anti-inflammatory drugs before the onset of bleeding. The endoscopic findings differed between groups in that watermelon stomach patients with

Table 1 Baseline clinical and endoscopic data for patients with watermelon stomach, by group

	<i>With portal hypertension (n = 8)</i>	<i>Without portal hypertension (n = 18)</i>
Median age (IQR) (y)	73.5 (62.5–81)	74.5 (67–79)
Female	5 (63%)	16 (89%)
Presenting with melena	6 (75%)	9 (50%)
Esophageal varices*	8 (100%)	0
Active bleeding*	7 (88%)	6 (33%)
Median no. of lesions (IQR)	≥ 100 (5.5–100+)**	6 (6–7)

IQR: interquartile range. * $P < 0.05$ for between-group comparison. **When angiomas were too numerous to count, they were recorded as ≥ 100 .

portal hypertension tended to have more angiomas ($P = 0.0971$) and were more likely to have active (i.e., oozing) gastric bleeding at endoscopy than were those without portal hypertension ($P = 0.011$). Although all patients with portal hypertension had esophageal varices, these were small and without stigmata of recent hemorrhage or red color signs in every case. Such varices are very unlikely to bleed and were thus not considered to be the source of hemorrhage in these patients. None of the patients had the prominent mosaic or “snakeskin” appearance ascribed to diffuse portal hypertensive gastropathy. Instead, all had diffuse or multiple discrete angiomas. Portal hypertension was secondary to cirrhosis in seven patients and secondary to portal vein thrombosis in one. All of the patients with cirrhosis were in Child’s class A. None had coagulopathy or thrombocytopenia. The etiology of liver disease was cryptogenic in six patients and alcoholic in one. None of the patients had clinical evidence of an autoimmune disease.

The typical appearance of watermelon stomach in a patient with portal hypertension, before and after treatment, is shown in Figure 1. This can be described as multiple, small, red angiomas that are not raised or arranged in linear arrays or stripes. They were concentrated in the antrum, but could also be found in the gastric fundus, gastric body, and/or duodenum ($n = 5$). Endoscopic treatment for those with portal hypertension was carried out with the Gold probe ($n = 4$), heater probe ($n = 2$), or argon plasma coagulator ($n = 2$). The typical appearance of watermelon stomach in a patient without portal hypertension, before and after

Table 2 Endoscopic treatment outcomes in groups of watermelon stomach patients with and without portal hypertension

	<i>With portal hypertension</i>	<i>Without portal hypertension</i>
Median (IQR) Hct		
Before first Rx	25 (21.5–29)	21.5 (18–25)
At most recent follow-up	33 (31–34.5)*	33.5 (31–38)*
Median (IQR) units PRBC transfused		
In year before first Rx	5.5 (4–18)	8.5 (3–12)
During follow-up since first Rx	0 (0–0)	0 (0–1)*
Median (IQR) number of hospitalizations for upper gastrointestinal hemorrhage		
In year before first Rx	1.5 (1–5)	4 (2–7)
During follow-up since first Rx	0 (0–3)	0 (0–2)*

Hct: hematocrit; IQR: interquartile range; PRBC: packed red blood cells; Rx: endoscopic treatment. Normal hematocrit values at the UCLA Medical Center’s clinical laboratories range from 34% to 42%. * $P < 0.05$ for within-group comparison of median values before vs. after treatment.

treatment, is shown in Figure 2. This is characterized by occasionally friable, usually raised, red antral stripes that converge on the pylorus. Endoscopic treatment in patients without portal hypertension was carried out using the Gold probe ($n = 9$), heater probe ($n = 5$), or argon plasma coagulator ($n = 4$).

The median follow-up period since the initiation of treatment was 6 months (interquartile range 3–10 months) for the group with portal hypertension and 24 months (interquartile range 12–42 months) for those without portal hypertension ($P = 0.0188$). The median number of palliative endoscopic treatment sessions was three (interquartile range 2.5–5.0) for those with portal hypertension and five (interquartile range 2–8) for those without portal hypertension, corresponding to the longer follow-up period in the latter group ($P = 0.3260$).

There were no complications of endoscopic therapy such as bleeding or nonhealing ulcers. Outcome data are presented in Table 2. The median stable hematocrit at most recent follow-up was significantly higher than the median hematocrit before endoscopic treatment for watermelon stomach patients with ($P = 0.0078$) and without ($P = 0.001$) portal hypertension. The number of units of packed red blood cells transfused for anemia due to upper gastrointestinal hemorrhage over the course of fol-

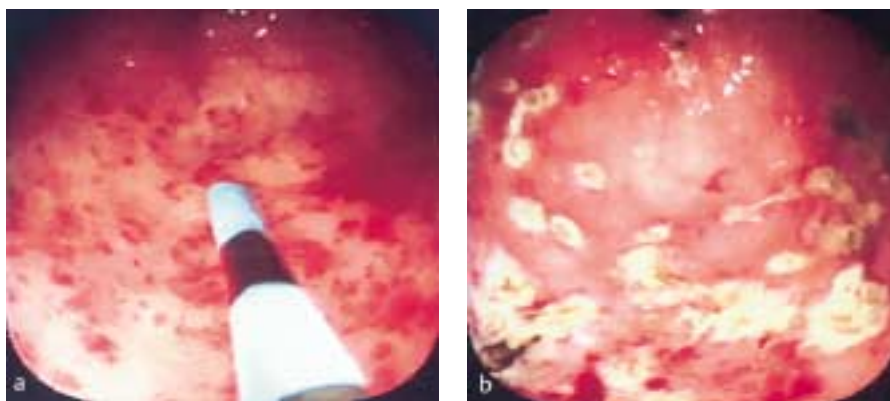


Figure 1 Typical appearance of watermelon stomach in a patient with portal hypertension. **a** Before treatment, **b** after treatment.

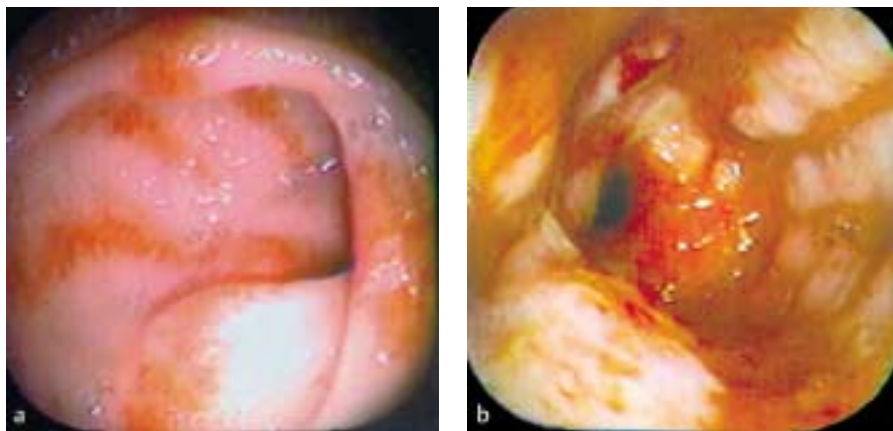


Figure 2 Typical appearance of watermelon stomach in a patient without portal hypertension. **a** Before treatment, **b** after treatment.

low-up was significantly lower than the number of packed red blood cell units transfused over the year prior to the first endoscopic treatment for the group without portal hypertension ($P=0.001$), while the group with portal hypertension showed a strong trend in this direction ($P=0.0625$). In similar fashion, the median number of hospitalizations for gastrointestinal hemorrhage during follow-up was significantly lower than the number of such hospitalizations in the year prior to first endoscopic treatment in the group without portal hypertension ($P=0.0014$), while those with portal hypertension demonstrated a trend ($P=0.3672$) in this direction. The number and size of lesions in those without portal hypertension often decreased markedly, while any change in the endoscopic appearance of those with portal hypertension was difficult to detect. Importantly, complete obliteration of endoscopic lesions was not achieved in any of the patients. This suggests that treatment is palliative, not curative, and that surveillance endoscopic treatment sessions will be required.

Discussion

The results of this study suggest that watermelon stomach has a distinct endoscopic appearance in patients with portal hypertension. As opposed to the classic appearance of watermelon stomach seen in patients without portal hypertension, patients with portal hypertension in the group studied here had more diffuse gastric lesions that were often actively bleeding. In contrast to other reports, gastric biopsy was not found to be useful in the present study in definitively establishing a diagnosis of watermelon stomach [26]. Gastric biopsy specimens were therefore not systematically obtained from patients in this study. In the group of patients studied, the diagnosis was based on a characteristic endoscopic appearance in the setting of overt or occult gastrointestinal hemorrhage. Although the interobserver reliability of endoscopic diagnosis was not formally assessed, there was general agreement amongst the endoscopic hemostasis group participating, based on informal review of the printed video images. Again in contrast to other reports, active or clinically significant gastric bleeding was very rarely seen in this study in patients with the classic endoscopic picture (i.e., mosaic or snakeskin pattern without discrete angiomas or a watermelon pattern) of portal hypertensive gastropathy in a large series of patients with severe upper gastrointestinal hemorrhage.

Despite the difference in endoscopic appearance, watermelon stomach patients with and without portal hypertension appeared to benefit from endoscopic intervention. Transfusion requirements and bleeding-related hospitalizations decreased, while hematocrits increased for patients in both groups during an extended post-treatment follow-up period.

There are several potential limitations to this study. The first stems from the fact that patients served as their own, historical, controls in the pre-test-post-test design. Without an independent control group, it was not possible to definitively establish a causal effect of the endoscopic intervention on the outcome. However, a randomized controlled trial of endoscopic therapy versus no therapy for watermelon stomach is unlikely to occur, due to the rarity of the disease and because failing to provide any endoscopic treatment might be deemed unethical.

Secondly, these findings might have occurred by chance, or might be due to other confounding factors such as the natural history of the disease, intervening medical therapy (such as iron replacement), incomplete collection of pretreatment utilization data, limited follow-up, and the degree to which the investigators assumed responsibility for clinical decision-making (i.e., when to transfuse or when to hospitalize) in these patients. However, there are no reports suggesting that gastrointestinal hemorrhage from watermelon stomach spontaneously resolves, nor have medical therapies alone been successful in controlling active bleeding or preventing rebleeding in this condition. In fact, many of the patients in the present study had been treated medically with beta-blockers, hormones, and/or iron replacement without response before the initiation of endoscopic therapy. None of the patients with portal hypertension was treated with any form of portosystemic shunt or liver transplantation during the study period. Thirdly, the efforts undertaken to collect pretreatment utilization data (e.g., units of blood transfused, bleeding-related hospitalizations) were extensive, but the demonstrated treatment effect may be conservative to the extent that data were missed. Fourthly, this group of patients represents the collective experience of an endoscopic hemostasis research group practicing in two tertiary referral centers. Selection bias is possible in that patients with severe disease (e.g., overt rather than occult gastrointestinal bleeding) are more likely to be referred to such centers. This is likely to be the setting in which these patients are seen and treated for the foreseeable future. General-

ization of the present results to the community setting may be questionable, due to variations in techniques of diagnosis and treatment. Generalization to patients with more advanced liver disease may not be possible, because all of the patients with portal hypertension in this study were clinically well compensated.

In summary, the groups of watermelon stomach patients with and without portal hypertension who were enrolled in this study were similar with regard to age, sex distribution, and clinical presentation. The endoscopic findings differed between groups in that portal hypertension patients were likely to have a greater number of antral lesions and active gastric bleeding. Bleeding from watermelon stomach was effectively palliated by endoscopic treatment – with reduced packed red blood cell transfusions, reduced bleeding-related hospitalizations, and increased hematocrit values – regardless of the presence of portal hypertension. On the basis of these findings and those of other investigators, it may be recommended that endoscopists should receive information about the endoscopic diagnosis and treatment of watermelon stomach. Consideration of palliative endoscopic treatment can also be recommended for all patients with upper gastrointestinal hemorrhage and/or iron deficiency anemia related to watermelon stomach, regardless of the presence or absence of portal hypertension.

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