

# Endoscopic Doppler probe ultrasonography for detecting blood flow at post-endoscopic submucosal dissection ulcers of the stomach ▶



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## Bibliography

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## ABSTRACT

**Background and study aims** The rate of early rebleeding after endoscopic submucosal dissection (ESD) for early gastric cancer ranges from 5% to 38%, despite application of preventive methods. Post-ESD rebleeding may be caused by “invisible” vessels that may not be detectable using ultrasonographic techniques. Recently, Doppler probe ultrasonography (DOP) has been used in endoscopy. Because little is known about the usefulness of DOP for decreasing the post-ESD rebleeding rate, we performed a preliminary case series study.

**Patients and methods** Twelve patients underwent DOP for post-ESD ulcer evaluation after visible vessel coagulation. In this study, the novel DOP system used in the vascular surgery department was used. DOP-positive invisible vessels were shown as a pulse wave on the monitor.

**Results** No (0%) cases of post-ESD rebleeding occurred. Twenty invisible vessels were detected, and 13 were subjected to additional coagulation up to a depth of 3 mm. Mean DOP procedure time was 11.6 minutes (range: 8–18 minutes). In these latter cases, disappearance of the Doppler pulse wave was confirmed. No early rebleeding or other adverse events were experienced.

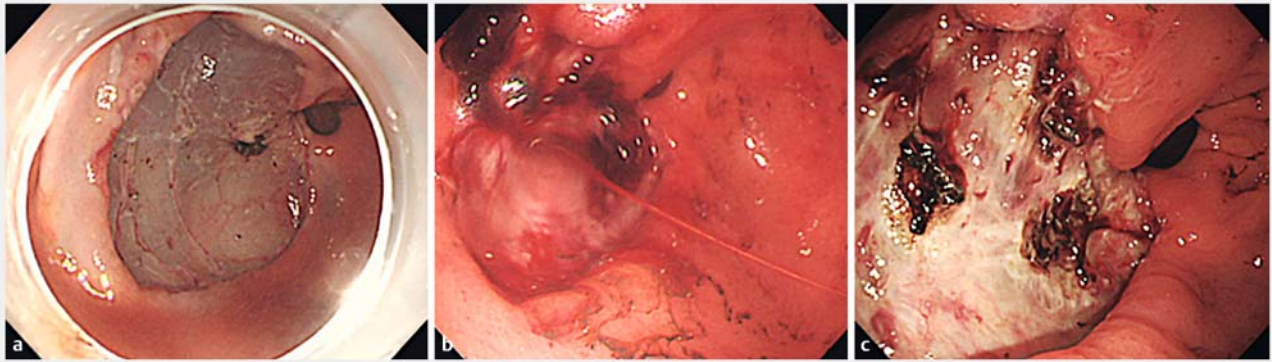
**Conclusion** DOP is a safe and feasible method for detecting invisible vessels in post-ESD ulcers. Further investigation of the clinical relevance is warranted.

## Introduction

Endoscopic submucosal dissection (ESD) is an established treatment for early gastrointestinal cancer in Japan. However, this procedure is associated with postoperative bleeding rates of approximately 5% to 38% [1, 2]. Coagulation of nonbleeding visible vessels (NBVVs) has been identified as a useful and safe method for decreasing the rate of early rebleeding [3–5]. However, 7% of patients bleed despite coagulation of NBVVs [6]. Invisible vessels (IVs) are related to early rebleeding, and usefulness, such as mapping method and observation of post-ESD ulcer using magnification function scope, has been reported [6, 7]. In addition, in our experience, early rebleeding may occur from IVs that could not be detected immediately after ESD

(▶ **Fig. 1a**, ▶ **Fig. 1b**, ▶ **Fig. 1c**). Consequently, it is important to detect IVs.

Doppler probe ultrasonography (DOP) was recently introduced to the field of endoscopy [8]. Briefly, DOP is used to evaluate blood flow and can thus detect IVs in the gastrointestinal tract that could potentially cause bleeding [9]. One previous report described the effectiveness of DOP in terms of decreasing the gastric ulcer rebleeding rate [10]. However, that report did not sufficiently demonstrate the efficacy of DOP for detection of IVs in post-ESD ulcers. Furthermore, the limitations of prior DOP devices with respect to the fixed depth of signal detection have prevented identification of blood flow below a depth of 1.5 mm [11]. Moreover, some Doppler models produce an audible output but do not have a visual display [12]. To address



► **Fig. 1** A representative case of early rebleeding from a post-endoscopic submucosal dissection (ESD) ulcer. **a** Immediately after ESD, no obvious sites of bleeding stigmata are visible via endoscopy. **b** Rebleeding from the post-ESD ulcer occurred 12 hours after ESD. Emergency endoscopy revealed spurting bleeding from the center of the ulcer. **c** Additional coagulation was performed and no signs of bleeding were observed immediately after ESD, suggesting presence of an invisible artery.

these limitations, we conducted this preliminary study to explore the impact and safety of DOP with a new system, which includes a high-quality audio and visual monitor display, for detection of IVs at the post-ESD ulcers of the stomach.

## Patients and methods

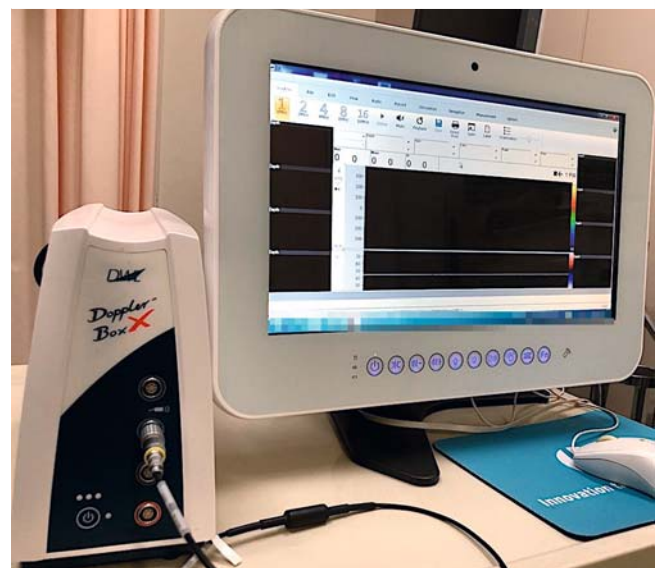
### Patients

From June 2019 to August 2019, 12 patients underwent ESD for early gastric cancer at St. Luke's International Hospital in Tokyo, Japan. DOP was performed to evaluate post-ESD ulcers in these patients. The study protocol was approved by the ethics committee at our hospital (19-R151). We received approval from the clinical ethics committee regarding use of DOP for post ESD ulcers and received informed consent directly from the patients prior to hemostatic treatment.

### Doppler probe ultrasonography methods

The Doppler Box DOP system (Compumedics, DWL, Germany; ► **Fig. 2**) and probe are marketed for use in vascular surgery departments [13]. The 16-MHz Doppler probe has a length and diameter of 2 m and 1 mm, respectively, and is reusable after gas sterilization or high-level liquid disinfection. The monitor includes a center screen that displays pulse waves and eight screens that display different scan depths. This system has a high-definition-compatible screen and produces a high-quality audible signal.

We evaluated post-ESD ulcers using the following procedure. A water-jet scope (GIF-Q260J or GIF-2TQ260M; Olympus Corp., Tokyo, Japan) attached to a transparent hood was used; the specific scope was selected according to the endoscopist's preference. After routine coagulation of the NBVVs, the Doppler probe was pushed to the post-ESD ulcer at an angle of 60° and maneuvered mainly around the pigmented spots and NBVV to detect the whole ulcer. The Doppler pulse wave was observed to shift depending on the speed and direction of the blood flow relative to the probe. Blood flow sites were observed at depths of 0.5 to 5 mm. Once IVs were detected, additional

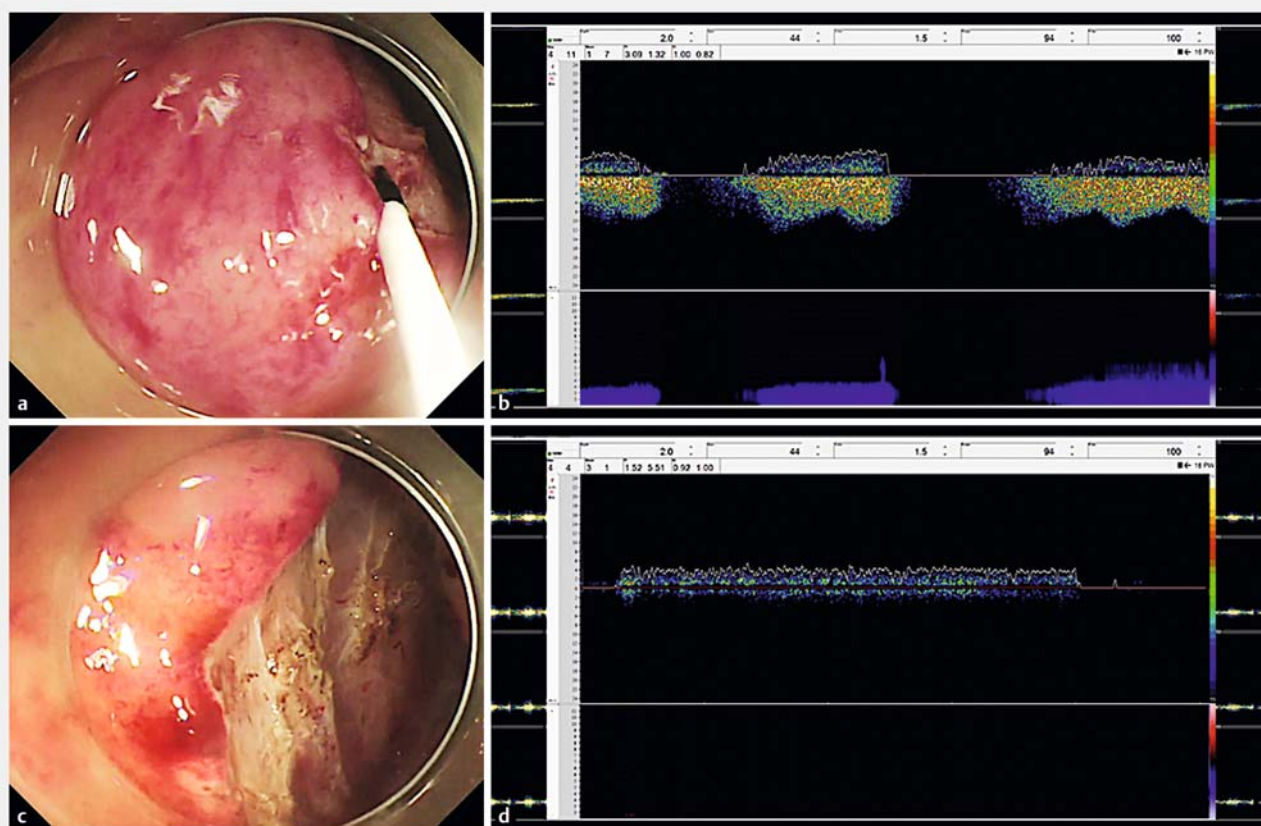


► **Fig. 2** The Doppler-BOX 16-MHz pulse-wave system with a reusable doppler probe and monitor. The Doppler probe ultrasonography (DOP) output signal is both visual and audible. Reproduced with permission from Compumedics, Inc.

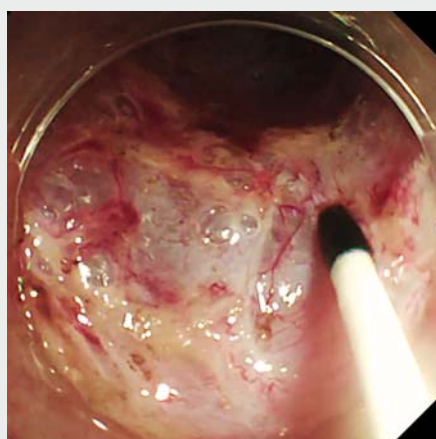
coagulation was performed (HDB2418W, Pentax Co, Japan) to a maximum depth of 3 mm. The subsequent disappearance of the corresponding Doppler pulse wave was then confirmed (► **Fig. 3a**, ► **Fig. 3b**, ► **Fig. 3c**, ► **Fig. 3d** and ► **Video 1**). IVs with a depth of >3 mm were considered subserosal blood flow and were not coagulated [12].

### Follow-up after ESD

On the first day after the procedure, a second look was performed to evaluate post-ESD ulcers without reference to the DOP findings. Additional coagulation was performed at the sites of exposed vessels.



► **Fig. 3** **a** Detection of a Doppler probe ultrasonography (DOP)-positive vessel at the post-ESD ulcer. The Doppler probe was maneuvered while observing the blood flow. **b** Visual graphic display of the three positive Doppler waves corresponding to the vessel. The blood flow velocity (cm/s) and time (s) are plotted on the Y axis and X axis, respectively. The blood flow depth (2.0 mm) is indicated at the upper left of the plot. **c** Performance of additional coagulation for the vessel. **d** The Doppler wave disappeared after additional coagulation of the vessel.



► **Video 1** We report a case using DOP for post-ESD ulcer.

## Endpoints and statistical analysis

The primary study endpoint was the post-ESD rebleeding rate. IV detection rate, procedure time, and adverse events (AEs) were measured as the secondary endpoints. The definition of early rebleeding was a lesion requiring hemostasis within 7 days after ESD. The IVs were divided into two groups according to a depth of  $\leq 3$  or  $> 3$  mm. Procedural duration was defined as total time required for the DOP examination and subsequent coagulation. AEs were evaluated according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0 [14].

Statistical analyses were performed using JMP, version 14 (SAS Institute, Inc., Cary, North Carolina, United States). The patient age and procedural duration are reported as means  $\pm$  standard deviations.

## Results

Characteristics and study findings of the 12 patients who underwent DOP are presented in ► **Table 1**. Mean age was  $65.5 \pm 12$  years old. Mean post-ESD ulcer size was  $36 \text{ mm} \times 30 \text{ mm}$  (range:  $345\text{--}1802 \text{ mm}^2$ ). Two patients (No. 11 and 12) had

► **Table 1** Summary of the study results.

No.	Age	Sex	Location	Type	Size	NBVV	IV (≤3 mm)	IV (>3 mm)	Procedure time (min)	Additional coagulation in second look	Antithrombotic agents	Early re-bleeding
1	70	F	U, LC	IIc	32×21	3	2	2	18	–	–	–
2	61	M	U, LC	IIc	52×32	4	2	1	15	–	–	–
3	68	F	M, LC	IIc	34×30	2	0	2	12	–	–	–
4	66	M	A, GC	IIc	23×15	3	0	0	8	–	–	–
5	63	M	M, PW	IIc	38×34	2	2	0	8	–	–	–
6	49	M	M, LC	IIc	38×30	3	2	0	8	–	–	–
7	69	M	L, GC	IIc	36×30	3	1	0	10	–	–	–
8	54	M	U, GC	IIc	35×30	1	0	0	10	–	–	–
9	72	M	M, AW	IIc	34×20	2	1	1	14	–	–	–
10	45	M	A, GC	IIc	26×20	1	1	0	10	–	–	–
11	80	M	L, LC	IIc	33×26	3	2	0	11	–	+	–
12	90	F	A, AW	IIa	42×x32	3	0	1	10	+	+	–

NBVV, non-bleeding visible vessels; IV, invisible vessel; U, upper third; L, lower third; LC, lesser curvature; M, middle third; A, anterior; PW, posterior wall; GC, greater curvature; AW, anterior wall

used antithrombotic agents (low-dose aspirin in both cases). A total of 30 NBVVs were initially detected and coagulated in the 12 patients.

Early rebleeding did not occur in any cases (0%). Although there was no bleeding, prophylactic coagulation was performed in a very small vessel in one patient (No. 12). After coagulating the NBVVs, DOP detected 20 IV sites in the 12 post-ESD ulcers. Of these, 13 IVs with depths ≤3 mm were detected in eight patients, while seven IVs with depths >3 mm were detected in five patients. We performed coagulation of the 13 IV sites at depths ≤3 mm, with a mean procedural duration of 11.6 ± 4.6 minutes (range: 8–18 minutes). No adverse events related to the DOP were observed.

## Discussion

Our study findings revealed that DOP is a feasible method for detecting IVs in post-ESD ulcers and preventing early rebleeding from these lesions.

Post-ESD ulcers may rebleed, leading to serious complications such as hemorrhagic shock. Increasing use of antithrombotic drugs may further increase risk of rebleeding. As noted above, we experienced rebleeding after NBVV coagulation, which we attributed to presence of IVs. Therefore, we performed a preliminary study to demonstrate the feasibility of a novel DOP system for preventing early rebleeding and detecting IVs in post-ESD ulcers. Notably, we detected 13 IVs with depths ≤3 mm in two-thirds of our patient sample. After coagulation, none of these cases experienced rebleeding, and only one required additional coagulation after a second look. Although the procedural duration was influenced by the size of

the post-ESD ulcer and the requirement for additional coagulation, this variable was gradually reduced as the clinicians became more familiar with the procedure.

Compared to previous DOP systems, the DOP system used in this study is novel, as it assesses blood flow at multiple depths and provides high-quality audio and video outputs. In contrast, the Doppler US unit used by Uedo (VTI Endoscopic Doppler System, Vascular Technology Inc., Nashua, New Hampshire, United States) had three fixed preset depths: from the surface to 1.5, 4, and 7 mm and lacked a video display [11]. Similarly, the VTI Endoscopic Doppler System (Vascular Technology, Inc., Lowell, Massachusetts, United States) described by Richard produced only an audible signal and was not accompanied by a visual monitor display [12]. The observation range of the above system is limited due to fixed depths. In addition, because blood flow is sensed by sound, the depth is not known, and blood flow outside the stomach wall (>3 mm) may be sensed.

In this study, the DOP system used in the vascular surgery department was considered to have a high ability to detect blood flow. However, one visible vessel was considered DOP-negative. The Doppler wave was easier to detect near 60° and may be related to the angle between the Doppler probe and vessels. This issue should be investigated in future studies. An earlier study reported a reduction in frequency of post-hemostatic rebleeding from 26% to 11% by performing a hemostasis procedure on the DOP-positive in advance among patients with severe non-variceal upper gastrointestinal bleeding [10, 15]. Other reports suggested that it is less costly and more useful (14% lower rebleeding rate) than traditional endoscopic visual assessment for the management of severe non-variceal upper gastrointestinal bleeding [16]. DOP is considered to be useful



not only for post-ESD ulcers, but also gastrointestinal bleeding in general.

## Conclusion

This preliminary study revealed the safety and feasibility of a novel DOP system for detection of IVs in post-ESD ulcers. In the future, to describe the effectiveness of DOP, a controlled study with a sufficient number of patients will be needed.

In conclusion, this novel DOP system provides a safe and feasible method for detecting IVs in post-ESD ulcers. A further investigation of the clinical relevance is warranted.

## Competing interests

The authors declare that they have no conflict of interest.

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