Evaluation of the visibility of bleeding points using red dichromatic imaging in endoscopic hemostasis for acute GI bleeding (with video)

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Background and Aims: We aimed to clarify whether red dichromatic imaging (RDI), a new type of image-enhanced endoscopy, improves the visibility of bleeding points in acute GI bleeding (AGIB) compared with white-light imaging (WLI).

Methods: Images and videos of bleeding points acquired with WLI and RDI during endoscopic hemostasis for AGIB were retrospectively compared. In images, the color difference between bleeding points and surrounding blood was analyzed. In videos, 4 expert and 4 trainee endoscopists evaluated the visibility on a scale of 1 (undetectable) to 4 (easily detectable). Furthermore, the correlation between the color difference and visibility score was evaluated.

Results: We analyzed 64 lesions. The color difference was significantly higher in RDI (13.11 ± 4.02) than in WLI (7.38 ± 3.68, $P < .001$). The mean visibility score for all endoscopists was significantly higher in RDI (3.12 ± .51) compared with WLI (2.72 ± .50, $P < .001$); this was also observed in experts (3.18 ± .51 vs 2.79 ± .54, $P < .001$) and trainees (3.05 ± .54 vs 2.64 ± .47, $P < .001$). The color difference and visibility score were moderately correlated for all endoscopists ($\gamma = .56$, $P < .001$) and for experts ($\gamma = .53$, $P < .001$) and trainees ($\gamma = .57$, $P < .001$).

Conclusions: RDI improves the visibility of bleeding points in AGIB compared with WLI. RDI can help endoscopists at all levels of experience to recognize bleeding points by enhancing the color contrast relative to surrounding blood. (Gastrointest Endosc 2022;95:692-700.)

Acute GI bleeding (AGIB) is one of the most commonly encountered conditions in emergency medicine and a cause of significant morbidity and mortality.[1-3] Endoscopic hemostasis is the criterion standard for therapeutic management of AGIB.[4-6] Although several techniques and devices have been developed for endoscopic treatment of AGIB,[7,8] it remains challenging for endoscopists to accurately detect bleeding points and achieve hemostasis.

Abbreviations: AGIB, acute GI bleeding; ESD, endoscopic submucosal dissection; NBS, National Bureau of Standards; RDI, red dichromatic imaging; ROI, region of interest; WLI, white-light imaging.

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This video can be viewed directly from the GIE website or by using the QR code and your mobile device. Download a free QR code scanner by searching "QR Scanner" in your mobile device's app store.

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Red dichromatic imaging (RDI; Olympus Co, Tokyo, Japan) is a type of image-enhanced endoscopy that uses lights of 3 wavelengths: 540, 600, and 630 nm.[9] It is newly equipped in the latest endoscopic system (EVIS X1; Olympus Co) since 2020 in Europe and Asia. This system can be used with any compatible endoscope, including those already on the market; thus, RDI can be used at no additional cost for extra equipment. Although RDI has been reported to be useful for identifying vessels or bleeding points during endoscopic submucosal dissection (ESD),[10-12] effectiveness of this image-enhanced endoscopy technique in AGIB has not been thoroughly investigated.[13,14] The main mechanism of RDI, enabling the distinct visualization of bleeding points, relies on the difference in hemoglobin absorption in 600 nm (amber-colored) and 630 nm (red-colored). Because hemoglobin strongly absorbs light at 600 nm, reflected light is greatly attenuated in bleeding points with higher concentrations of hemoglobin compared with that in surrounding diluted blood. In contrast, hemoglobin absorbs light weakly at 630 nm, and the reflected light is weakly attenuated, regardless of hemoglobin concentration (Fig. 1). Thus, when observing bleeding using RDI, bleeding points appear orange in contrast to the surrounding yellow color. We speculated that RDI provides a greater color difference between bleeding points and surrounding blood compared with white-light imaging (WLI), and this difference may allow easier detection of bleeding points.

In this study, we aimed to investigate whether RDI improves the visibility of bleeding points in AGIB compared with WLI by analyzing the color difference between bleeding points and surrounding blood and visibility scores evaluated by endoscopists. We further attempted to interpret the efficacy of RDI according to the experience of endoscopists and bleeding pattern.

METHODS

Subjects and study design

In this single-center, retrospective study, consecutive patients who underwent endoscopic hemostasis for active (oozing or pulsatile) AGIB between January 2019 and January 2020 were enrolled. For the purpose of this study, a prototype endoscope equipped with RDI (mode 1) was used for all patients suspected to have AGIB, except when a prototype endoscope or light source was unavailable.

We evaluated images and videos of bleeding points acquired with WLI and RDI just before the hemostasis procedure at the same time point. We excluded cases in which images or videos were not obtained from a similar distance and/or angle in both WLI and RDI. This study was approved by the Institutional Review Board (R-19-117) of the National Hospital Organization Tokyo Medical Center and was performed in accordance with the revised version of the Declaration of Helsinki.

Endoscopic procedure

Endoscopic hemostasis was performed using prototype endoscopes (GIF-Y0043, GIF-Y0058, and PCF-Y0029-I; Olympus Co, Tokyo, Japan). These endoscopes had the feature of RDI in addition to regular specifications of production endoscopes (GIF-Q260J, GIF-2TQ260M, and PCF-Q260JI; Olympus Co). In these prototype endoscopes, WLI and RDI modes could be switched by pressing the button on the control head of the endoscope. We observed bleeding points using both WLI and RDI, and an image was captured in each modality just before the hemostasis procedure. A fitted disposable transparent hood was attached for all procedures. Hemostasis procedures were performed through soft coagulation using a Coagrasper (Olympus Co), or argon plasma coagulation with an electrosurgical generator (VIO300D; Erbe, Tübingen, Germany), or clipping. All endoscopies were performed with the patient under moderate sedation (intravenous administration of pethidine and/or midazolam). We recorded all procedures using video processors (EVIS Lucera Elite system; Olympus Co).

In cases of lower AGIB, polyethylene glycol solution or enema was administered before colonoscopy based on the endoscopist's discretion. The quality of bowel preparation was assessed by an examiner according to the extent of mucosal visualization after suctioning the fluid residue, using the Aronchick Bowel Preparation Scale[15]: excellent, 95% mucosal visualization; good, 90%-95% mucosal visualization; fair, 80%-90% mucosal visualization; and poor, <80% mucosal visualization.

Evaluation of the color difference

We evaluated the color difference between bleeding points and surrounding blood for WLI and corresponding RDI images. The color difference was assessed by comparing the color values of the region of interest (ROI) for bleeding points and surrounding blood using Adobe Photoshop Elements 2020 (Adobe Systems Inc, San Jose, Calif, USA). We defined a single region inside the bleeding points and 3 regions within the surrounding blood as the ROI of bleeding points and surrounding blood, respectively. Details of the ROI settings are shown in Figure 2. The color values were determined by average color values in ROI (350 dpi, 24 × 24 pixels) based on the Commission Internationale d'Eclairage $L^*a^*b^*$ (where L^* is black/0 to white/+100, a^* is green/–128 to red /+127, and b^* is blue/–128 to yellow /+127) color space.[16] The color difference was quantified by the equation $\Delta E = [(\Delta L)^2 + (\Delta a)^2 + (\Delta b)^2]^{1/2}$. Moreover, the color difference was converted and expressed according to the National Bureau of Standards (NBS) units using the formula NBS units = $\Delta E \times .92$[17] to objectify the levels of perceived color change through visual inspection. NBS units classified color difference as follows: 0 to 1.5 = trace, 1.5 to 3.0 = noticeable, 3.0 to 6.0 = appreciable, 6.0 to 12.0 = much, and >12.0 = very much.

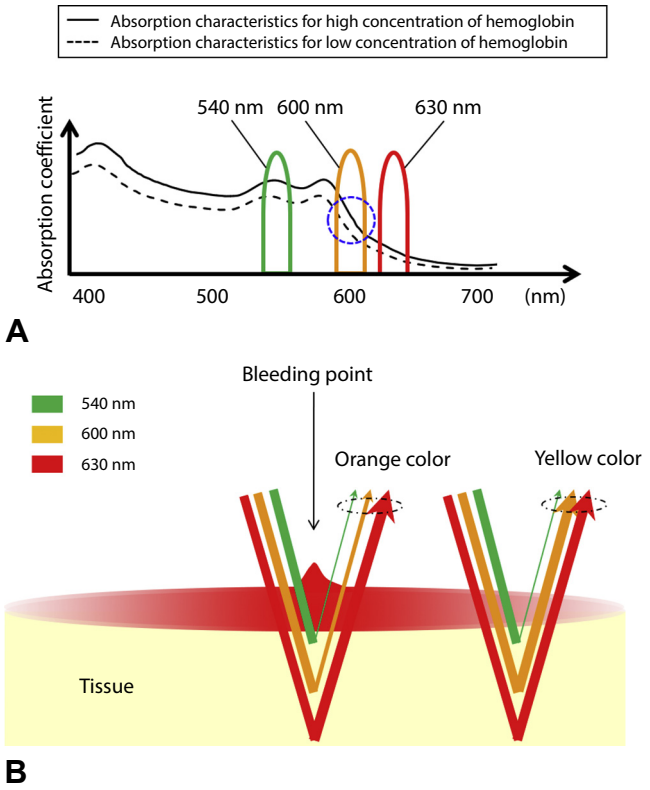

Figure 1. Mechanism of red dichromatic imaging (RDI) for enhancing the visualization of bleeding points. **A,** RDI consists of 3 types of illumination with wavelengths of 540, 600, and 630 nm. Of these 3 wavelengths, 600 nm highlights different concentrations of hemoglobin the most. **B,** The green light at 540 nm is strongly absorbed by hemoglobin, and the reflected light is mostly attenuated regardless of hemoglobin concentration. The amber light at the 600-nm wavelength is strongly absorbed by hemoglobin, and the reflected light is greatly attenuated in bleeding points with higher concentrations of hemoglobin compared with that in the surrounding area. The red light at the 630-nm wavelength is weakly absorbed by hemoglobin, and reflected light is hardly attenuated regardless of hemoglobin concentration. With this difference in hemoglobin absorption between 600 nm and 630 nm, RDI provides a contrast between the orange color of bleeding points and yellow color in the surrounding area of diluted blood.

We compared color difference and NBS units between WLI and RDI. A similar evaluation was conducted for bleeding patterns: oozing and pulsatile bleeding.

Evaluation of the visibility score

Eight endoscopists, 4 experts (performed >5000 endoscopies) and 4 trainees (performed <1000 endoscopies), evaluated the visibility of bleeding points using WLI and RDI in the videos (Video 1, available online at www.giejournal.org). All endoscopists had the experience with RDI in <10 endoscopies. The visibility was evaluated on a 4-point scale (4, easily detectable; 3, reasonably detectable; 2, barely detectable; and 1, undetectable). This scale was determined by referring to published studies[18-20] that evaluated the endoscopic visibility of colorectal polyps, because no study as yet has evaluated the visibility of bleeding points. All videos were viewed in a random order (each video included a lesion viewed with a single modality) on the same computer monitor (535 × 313 mm). None of the evaluators viewed any of the videos before the study, and the endoscopists were blinded to each other's score.

Visibility scores and the distribution of the WLI and RDI scores of all endoscopists, experts and trainees, were evaluated and compared for both modalities. Furthermore, the interobserver agreement of the visibility score for all endoscopists, experts and trainees, was evaluated using weighted kappa values. Scores and weighted kappa values were also analyzed according to the bleeding pattern: oozing and pulsatile.

Correlation between the color difference and visibility score

To assess the contribution of contrast in color difference for recognition of bleeding points, we evaluated the correlation between the color difference and visibility score for all endoscopists, experts and trainees. The correlation was also assessed according to the bleeding patterns: oozing and pulsatile bleeding.

Statistical analysis

Quantitative data are presented as mean and standard deviation. The color difference and visibility scores were compared between WLI and RDI using the Wilcoxon rank sum test, and the proportion of visibility score was compared using the χ^2 test. To determine the interobserver agreement for the visibility score, weighted Cohen kappa values for pairs of assessors were calculated and averaged over all possible pairs.[21-23] Agreement was assessed according to the kappa value as follows: <.20, slight; .21 to .40, fair; .41 to .60, moderate; .61 to .80, substantial; and >.81, excellent.[24] The degree of correlation between the color difference and visibility scores was evaluated using the Spearman's correlation coefficient, in which values of <.3 denoted a weak correlation, .3 to .7 a moderate correlation, and >.7 a strong correlation.[25] A $P < .05$ was considered to indicate statistical significance. All statistical analyses were performed using JMP version 16.0 (SAS Institute Inc, Cary, NC, USA).

RESULTS

Subjects

Between January 2019 and January 2020, 73 patients with 75 lesions underwent endoscopic hemostasis for AGIB. However, because of the exclusion of inappropriate videos or images and cases wherein a conventional endoscope without RDI was used, 64 lesions in 62 patients were finally evaluated in this study (Fig. 3).

Characteristics of patients, lesions, and endoscopic procedures are shown in Table 1. The mean patient age was 77. 2 ± 12.2 years (range, 44-96). Nine patients (14.1%)

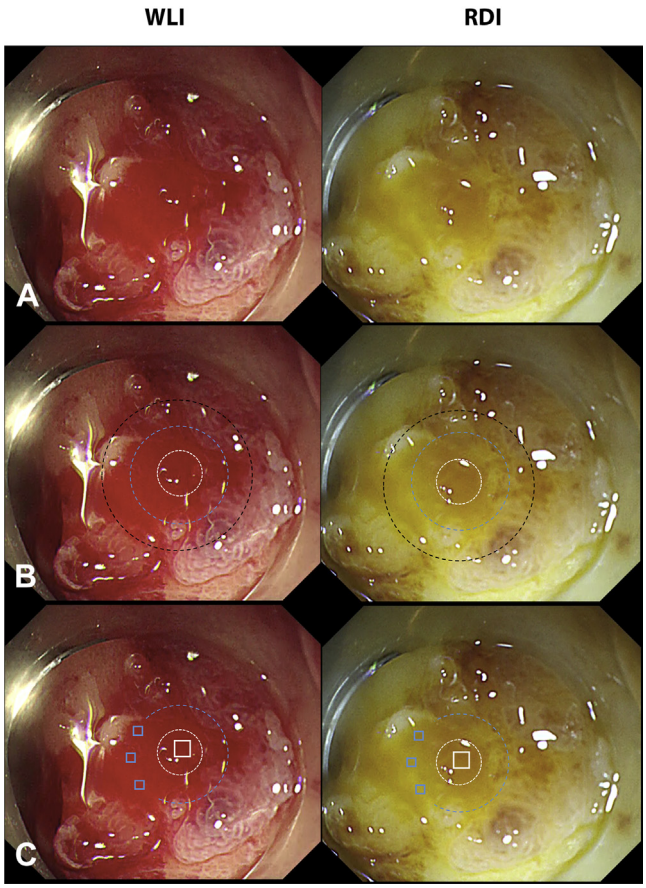

Figure 2. Protocol for defining the region of interest (ROI) in bleeding points and surrounding blood. **A,** A representative case with pulsatile bleeding of the gastric ulcer. **B,** First, an endoscopist determines a margin (*white dotted line*) among the bleeding point and surrounding blood using the video as a reference. A second endoscopist independently confirms the boundary. Assuming the area of surrounding blood as a circle centered at the bleeding point (*black dotted line*), a concentric circle half the size of surrounding blood (*blue dotted line*) is drawn. **C,** A single region is defined to the center of the bleeding point (*white box*; ROI of bleeding points), and 3 regions are positioned at approximately equal intervals on the concentric circle inside the surrounding blood (*blue boxes*; ROI of surrounding blood), avoiding areas with halation or excess brightness or darkness. Each ROI is set roughly in the same regions in both white-light imaging and red dichromatic imaging

were taking antiplatelet drugs, whereas 12 (18.8%) were on anticoagulant drugs. Of 64 lesions, 41 presented as upper AGIB and 23 as lower AGIB. Of the 64 lesions, the most frequent bleeding sources were peptic ulcers in 46 (71.9%) followed by other benign lesions in 12 (18.8%). The remaining lesions were gastric cancer in 1 (1.6%) and iatrogenic causes in 5 (7.8%). Bleeding pattern was oozing in 36 lesions (56.3%) and pulsatile in 28 (43.7%). Soft coagulation using hemostatic forceps (51/64, 79.7%) was the most used procedure of hemostasis.

Evaluation of the color difference

Table 2 shows the color difference and NBS units between bleeding points and surrounding blood in WLI and RDI for all lesions. The color difference was significantly higher in RDI (13.11 ± 4.02) than in WLI (7.38 ± 3.68, $P < .001$). NBS units were a grade higher for RDI categorized as "very much," whereas WLI was categorized as "much." The color difference and NBS units in WLI and RDI according to the bleeding pattern are shown in Supplementary Table 1 (available online at www.giejournal.org). For oozing bleeding, the color difference was significantly higher in RDI (14.02 ± 3.44) than in WLI (6.84 ± 3.63, $P < .001$). NBS units were a grade higher for RDI categorized as "very much," whereas those for WLI were categorized as "much." For pulsatile bleeding, the color difference was also significantly higher in RDI (11.94 ± 4.46) than in WLI (8.07 ± 3.71, $P < .001$), although NBS units were categorized as "much" in both WLI and RDI.

Evaluation of the visibility score

Table 3 shows the mean visibility score in WLI and RDI and the interobserver agreement among endoscopists for all lesions. The mean score among all endoscopists was significantly higher for RDI (3.12 ± .51) than for WLI (2.72 ± .50, $P < .001$). In experts, the mean score was significantly higher in RDI (3.18 ± .51) than in WLI (2.79 ± .54, $P < .001$). In trainees, the mean score was also significantly higher in RDI (3.05 ± .54) than in WLI (2.64 ± .47, $P < .001$). The interobserver agreement for the visibility score was substantial among all endoscopists (mean weighted kappa, .65; range, .55-.78) and experts (mean weighted kappa, .66; range, .55-.75) but was moderate among trainees (mean weighted kappa, .59; range, .56-.62).

The mean visibility score in WLI and RDI and interobserver agreement among endoscopists according to the bleeding pattern are shown in Supplementary Table 2 (available online at www.giejournal.org). The mean visibility scores for oozing bleeding were significantly higher in RDI than in WLI for all endoscopists (2.88 ± .38 vs 2.47 ± .32, $P < .001$), experts (2.97 ± .38 vs 2.51 ± .32, $P < .001$), and trainees (2.80 ± .43 vs 2.43 ± .34, $P < .001$). Similarly, the mean visibility scores for pulsatile bleeding were significantly higher in RDI than in WLI for all endoscopists (3.42 ± .50 vs 3.04 ± .51, $P < .001$), experts (3.46 ± .52 vs 3.16 ± .55, $P < .001$), and trainees (3.38 ± .50 vs 2.91 ± .49, $P < .001$). For oozing bleeding, there was a moderate interobserver agreement on the visibility scores for all endoscopists (mean weighted kappa, .52; range, .42-.68), experts (mean weighted kappa, .50; range, .45-.60), and trainees (mean weighted kappa, .46; range, .42-.50). Pulsatile bleeding had substantial interobserver agreement on visibility scores among all endoscopists (mean weighted kappa, .68; range, .49-.84) and experts (mean weighted kappa, .71; range, .56-.84) but only moderate agreement in trainees (mean weighted kappa, .60; range, .49-.74).

Figure 4 shows the distribution of visibility scores in WLI and RDI in all lesions. No bleeding point was scored as 1 (undetectable) on visibility in either WLI or RDI. The

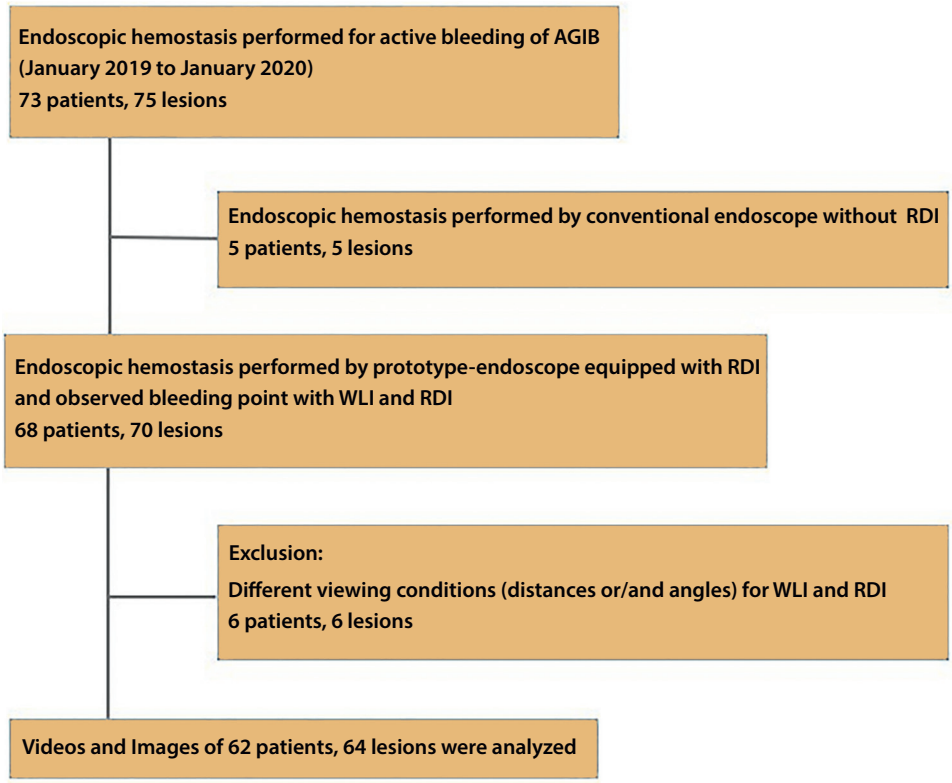

Figure 3. Flowchart of this study. *AGIB*, Acute GI bleeding; *WLI*, white-light imaging; *RDI*, red dichromatic imaging.

proportion of visibility scores 3 or 4 (reasonably or easily detectable) in RDI (79.9%) was significantly higher than that in WLI (57.7%, $P < .001$) for all endoscopists, experts (84.8% vs 60.5%, $P < .001$), and trainees (75.0% vs 54.7%, $P < .001$).

The distribution of visibility scores in WLI and RDI according to bleeding pattern are shown in Supplementary Figure 1 (available online at www.giejournal.org). The proportion of visibility score 3 or 4 in RDI for oozing bleeding was significantly higher than that in WLI for all endoscopists (71.9% vs 42.0%, $P < .001$), experts (79.2% vs 45.2%, $P < .001$), and trainees (64.6% vs 38.9%, $P < .001$). Correspondingly, the proportion of visibility score 3 or 4 for pulsatile bleeding in RDI was significantly higher than in WLI for all endoscopists (90.1% vs 77.7%, $P < .001$), experts (92.0% vs 80.3%, $P = .01$), and trainees (88.4% vs 75.0%, $P = .01$).

Correlation between color difference and visibility score

Figure 5 shows the correlation between the color difference and visibility score in all lesions. A moderate correlation was observed between the color difference and the visibility score among all endoscopists ($\gamma = .56$, $P < .001$), experts ($\gamma = .53$, $P < .001$), and trainees ($\gamma = .57$, $P < .001$).

The correlation between the color difference and the visibility score according to bleeding pattern is shown in Supplementary Figure 2 (available online at www.giejournal.org). For oozing bleeding, a strong correlation was observed in all endoscopists ($\gamma = .76$, $P < .001$), experts ($\gamma = .76$, $P < .001$), and trainees ($\gamma = .71$, $P < .001$). In contrast, the correlation for pulsatile bleeding was moderate in all endoscopists ($\gamma = .60$, $P < .001$), experts ($\gamma = .55$, $P < .001$), and trainees ($\gamma = .62$, $P < .001$).

DISCUSSION

This is the first detailed study to demonstrate the usefulness of RDI for visualizing bleeding points in AGIB supported by an objective evaluation of the color difference. A few studies that discussed the use of RDI mostly focused on the treatment of intraprocedural bleeding in ESD.[10-12] AGIB is a common condition and is often encountered in daily medical practice. Hence, we believe this novel image-enhanced endoscopy technique will have wide applicability globally.

The promising outcome of our study was that the efficacy of RDI was not dependent on the experience of the endoscopists. The visibility score was significantly higher in RDI than in WLI regardless of the assessor (experts and trainees) or the bleeding pattern. Also, the correlation between visibility score and color difference was similar between experts and trainees. The enhanced contrast in the color difference with RDI appears to be useful for

TABLE 1. Characteristics of patients (n = 62), lesions (n = 64), and endoscopic procedures

Characteristics	Value
Patient characteristics	
Age, y	77.2 ± 12.2
Sex	
Male	40 (62.5)
Female	22 (34.4)
Antithrombotic therapy	
Antiplatelets	9 (14.1)
Anticoagulants	12 (18.8)
Hemoglobin level on the day of endoscopy, g/dL	8.9 ± 2.8
Lesion characteristics	
Location	
Upper	41 (64.1)
Lower	23 (35.9)
Etiology	
Peptic ulcer	46 (71.9)
Gastric ulcer	22
Duodenal ulcer	9
Gastrojejunal anastomic ulcer	1
Rectal ulcer	14
Other benign lesion	12 (18.8)
Mallory-Weiss syndrome	3
Gastric angiectasia	1
Duodenal angiectasia	2
Colonic angiectasia	3
Colonic diverticular bleeding	3
Malignant tumor	1 (1.6)
Gastric cancer	1
Iatrogenic cause	5 (7.8)
Postgastric biopsy sampling	1
Postgastric ESD	1
Postcolonic ESD/EMR	3
Bleeding pattern	
Oozing	36 (56.3)
Pulsatile	28 (43.7)
Bowel preparation in lower acute GI bleeding	
Methods	
Polyethylene glycol solution	14 (66.7)
Enema	7 (33.3)
Quality/Aronchick score	
Excellent	0 (0)
Good	3 (14.3)
Fair	15 (71.4)
Poor	3 (14.3)
Endoscopic procedures	
Endoscopist	
Expert	37 (61.2)
Nonexpert	27 (38.8)
Procedure of hemostasis	
Soft coagulation	51 (79.7)
Argon plasma coagulation	7 (10.9)
Clipping	6 (9.4)
Successful hemostasis	64 (100)
Adverse events	0 (0)

Values are mean ± standard deviation, n, or n (%).
ESD, Endoscopic submucosal dissection.

TABLE 2. Color difference and NBS units between bleeding points and surrounding blood with WLI and RDI in all lesions

	WLI	RDI	*P* value
Δ*E*	7.38 ± 3.68	13.11 ± 4.02	<.001
NBS units/rating criteria	6.79 ± 3.39/ much	12.06 ± 3.70/very much	

Values are mean ± standard deviation.
NBS, National Bureau of Standards; *ΔE*, color difference; *WLI*, white-light imaging; *RDI*, red dichromatic imaging.

recognition of bleeding points regardless of the endoscopists' experience. Furthermore, the assessors in our study had the experience of <10 endoscopies using RDI, suggesting it would not take long to get accustomed to observation with RDI. Ultimately, we expect an accurate hemostasis with better visualization of bleeding points using RDI would enable a safer procedure, avoiding adverse events such as perforation. Moreover, the anticipated improvement on the time of the hemostasis procedure could eventually lead to a lower threshold for performing emergent endoscopy.

With respect to bleeding pattern, Yorita et al[11] reported in their subjective evaluation of gastric ESD that RDI improved the visibility of bleeding points in cases with oozing bleeding. In our study of AGIB, bleeding points appeared to be more recognizable by endoscopists and revealed greater color difference relative to surrounding blood in RDI compared with WLI, not only for oozing

TABLE 3. Mean visibility score of bleeding points with WLI and RDI and interobserver agreement among endoscopists in all lesions

	Mean visibility score			Interobserver agreement
	WLI	RDI	*P* value	Mean weighted kappa (range)
All endoscopists	2.72 ± .50	3.12 ± .51	<.001	.65 (.55-.78)
Experts	2.79 ± .54	3.18 ± .51	<.001	.66 (.55-.75)
Trainees	2.64 ± .47	3.05 ± .54	<.001	.59 (.56-.62)

Values are mean ± standard deviation unless otherwise defined.
WLI, White-light imaging; *RDI*, red dichromatic imaging.

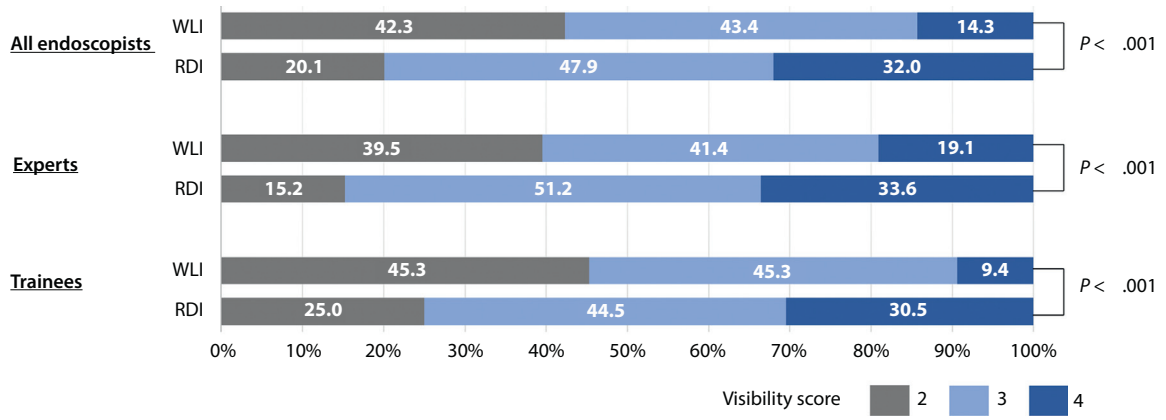

Figure 4. Distribution of the visibility score of bleeding points with WLI and RDI in all lesions. *WLI*, White-light imaging; *RDI*, red dichromatic imaging.

bleeding but also for pulsatile bleeding. However, RDI seemed especially effective for oozing bleeding from the perspective of color difference. The color difference expressed in NBS units yielded by RDI was categorized as "very much," a grade higher than WLI ("much") for oozing bleeding, whereas NBS units were categorized as same rating criteria ("much") in WLI and RDI for pulsatile bleeding. In addition, the correlation between the color difference and visibility score was strongly observed for oozing bleeding ($\gamma = .76$), whereas the correlation for pulsatile bleeding was moderate ($\gamma = .60$).

When observing oozing bleeding with WLI, the exact bleeding points are often difficult to detect because the blood flows slowly with scarce morphologic change. Therefore, it is presumed that the enhanced color contrast provided with RDI is particularly effective for oozing bleeding. In fact, this may be of more importance in intraprocedural bleeding during ESD than AGIB because more precise hemostasis is required in the former even with minor oozing bleeding. When hemostasis must be repeated because of inaccuracy, the tissue becomes carbonized, leading to reduced visibility of the submucosal layer and intraoperative perforation or delayed perforation because of hypercoagulability.[26,27]

For pulsatile bleeding, we sometimes encounter AGIB with the bleeding point buried under pooled blood, especially when persistent bleeding occurs at the gravity side or in a narrow space, such as the colon. In such circumstances, we observe the bleeding point in similar shades of red with pooled blood in WLI even when flushing with the water-jet function. However, RDI may facilitate clear visibility of bleeding points by showing the difference in hemoglobin concentration between the thick undiluted blood flowing from the bleeding points and the water-diluted blood around it. For instance, Saino et al[28] presented a case of colonic diverticular bleeding in which RDI clearly demarcated active bleeding from the responsible diverticulum among massive blood pooling. Thus, enhancement with a greater color difference between bleeding points and surrounding blood in RDI likely contributes to easier identification of bleeding points regardless of the bleeding pattern.

RDI has 3 modes (modes 1-3) that can be switched by pressing the button on the processor (EVIS X1). Going from mode 1 to mode 3, there is an increase in deep vessel enhancement level. Mode 1 can be useful in the observation of bleeding areas in AGIB, as shown in our study, or intraprocedural bleeding in ESD[10-12] and peroral endoscopic myotomy.[29] Mode 2 enhances deep blood vessels more clearly than mode 1 and is used for the detection of deep blood vessels during early local injection in ESD or peroral endoscopic myotomy.[29,30] Mode 2 also predicts the depth of esophageal varices and red color signs.[31,32] Mode 3 enhances both superficial and deep

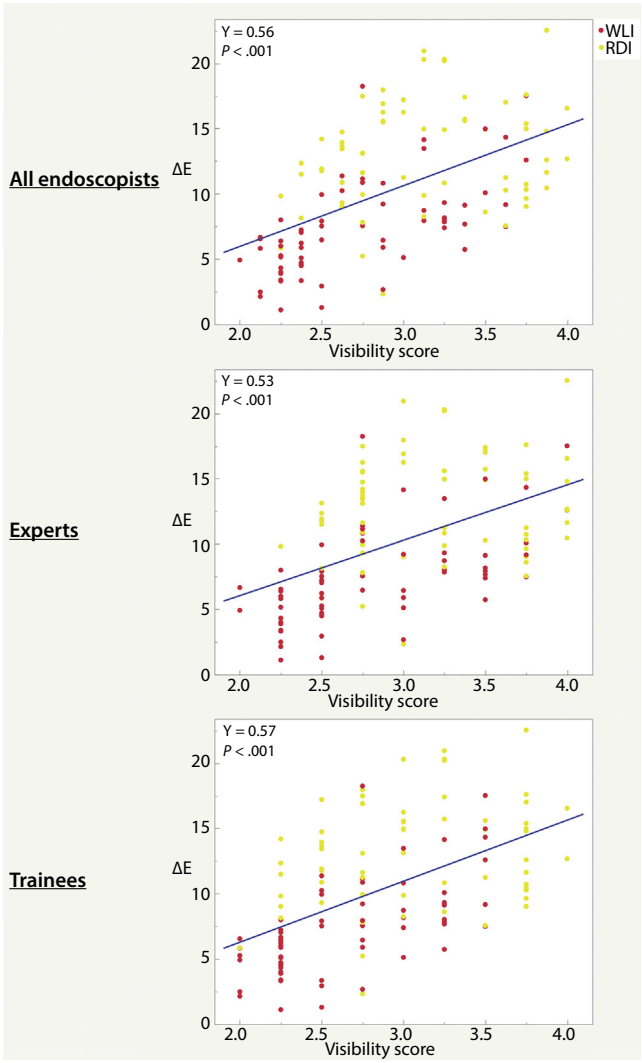

Figure 5. Correlation between the color difference and visibility score in all lesions. *WLI*, White-light imaging; *RDI*, red dichromatic imaging.

vessels. Deep blood vessels appear green, and shallow blood vessels appear red. Mode 3 is reported to be useful in assessing the severity of inflammation using the deep vascular pattern in patients with ulcerative colitis.[33] Although RDI is expected to support endoscopic treatments or diagnoses by using each mode depending on the situation, as described above, the role of each mode still requires further clarification in future studies.

This study has several limitations. First, this was a retrospective study with a small sample size, and the nonblinded manner of the study is subject to potential biases. As is typical for studies evaluating the impact of technologies in endoscopy, it is impossible to blind the endoscopist to the image modality. Therefore, potential bias in favoring the new technologies subconsciously may be present. Second, the visibility score used in our study is not validated, although an association between visibility score and color difference was seen. Additionally, the interobserver agreement based on weighted kappa values tended to be lower in trainees than in experts. One possible reason for this is that endoscopic experience or skills differed comparatively in the trainees (because of the learning curve), whereas experts had reached a certain level in endoscopic skills. Third, in calculating the color difference value, selection of the margin between the bleeding points and surrounding blood and setting of the ROI were dependent on the endoscopists. However, we avoided areas with colors that were out of the ordinary and used ROIs in 3 different locations in the surrounding blood. Fourth, the number of cases with lower AGIB was small, and thus our results cannot be generalized to all patients with AGIB. Finally, this study was performed with a review of videos and may not reflect real-time visibility during endoscopy. The endoscopic procedure is affected not only by the visibility of bleeding points but also by various factors such as location, sedation level, and endoscopist experience or technique. Therefore, a prospective randomized controlled trial evaluating outcomes such as the hemostasis time and frequency and number of tools used to achieve hemostasis in various clinical settings is warranted.

In conclusion, RDI improves the visibility of bleeding points in AGIB over WLI. RDI may enable endoscopists at all levels of experience to recognize bleeding points more easily by enhancing the color contrast relative to surrounding blood, regardless of the bleeding pattern.

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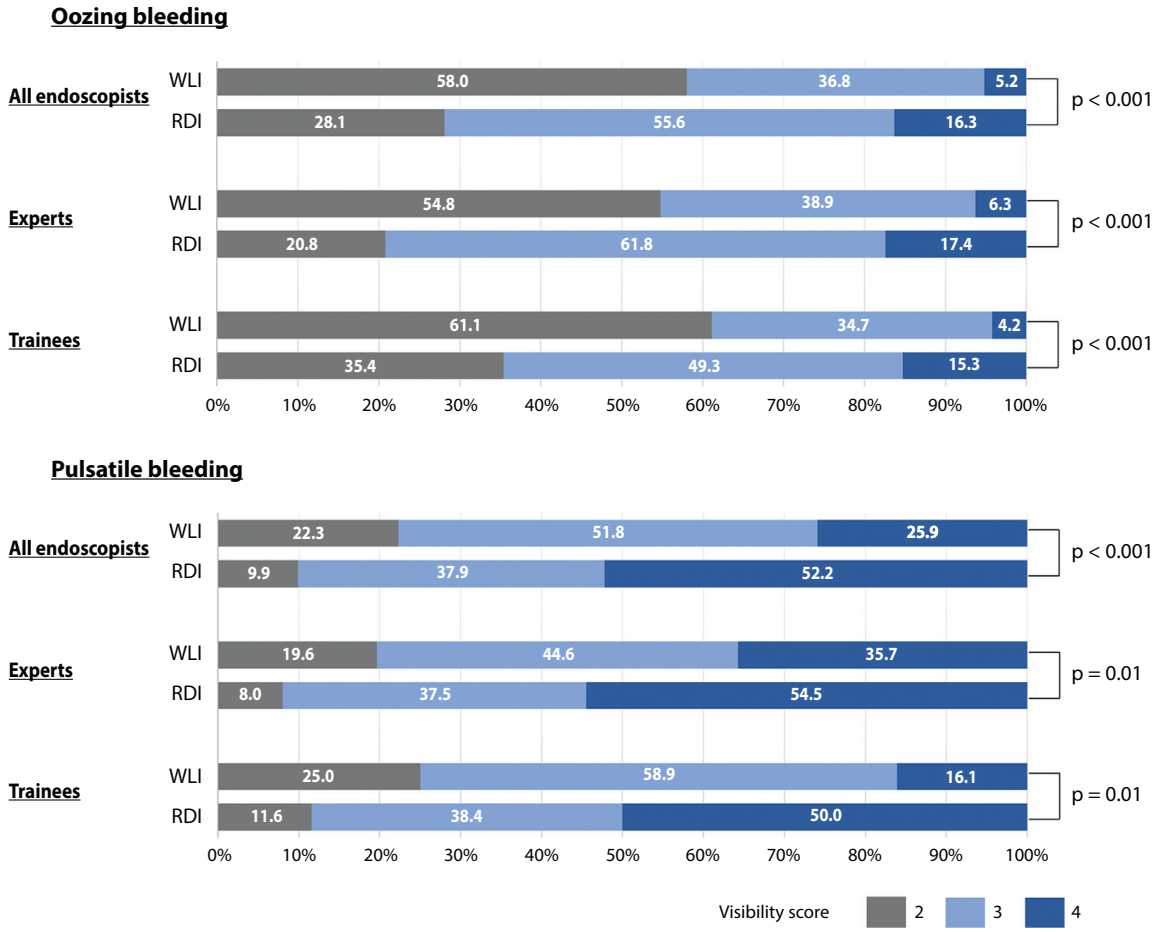
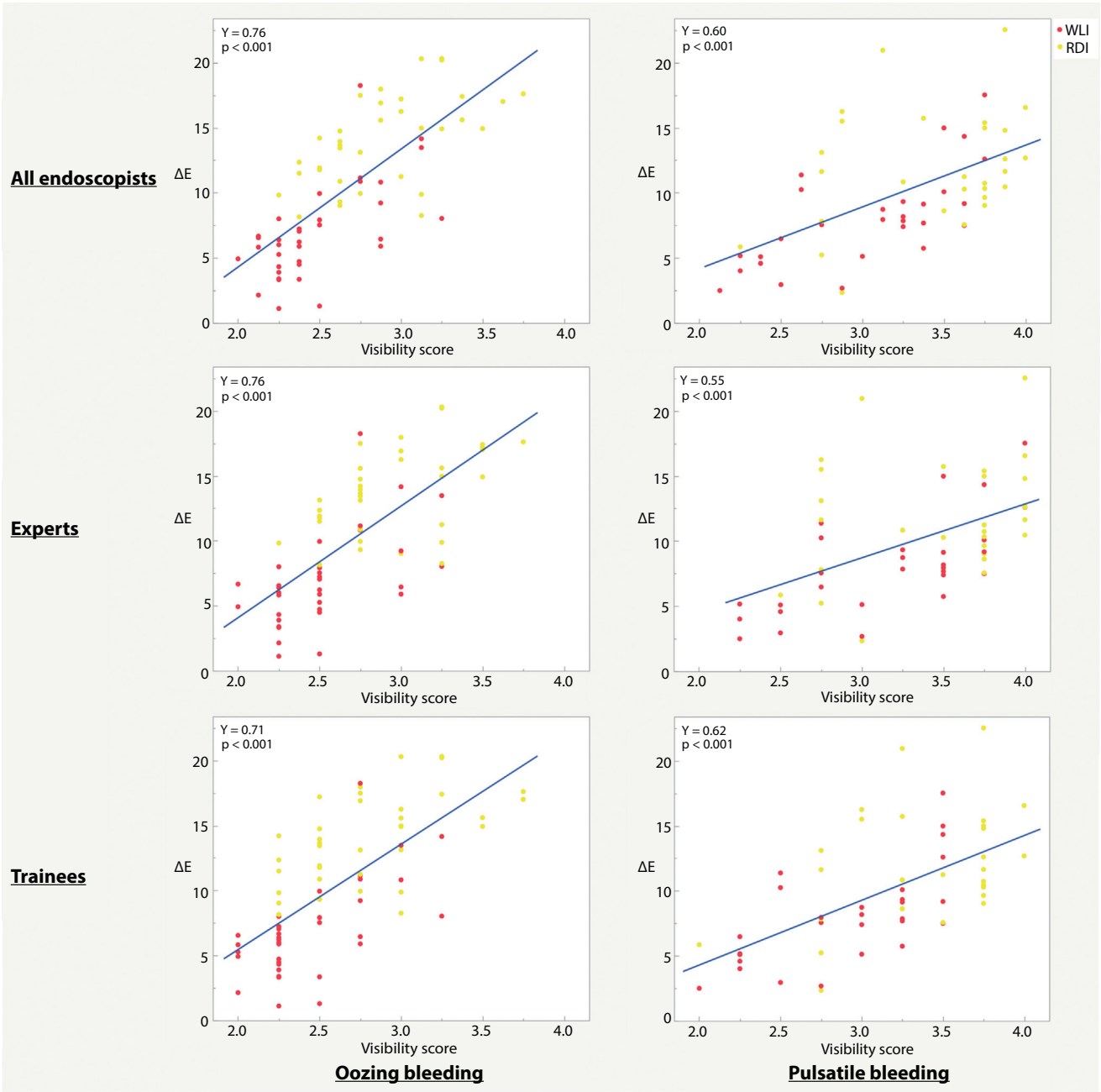


Supplementary Figure 1. Distribution of the visibility score of bleeding points with WLI and RDI according to the bleeding pattern. *WLI*, White-light imaging; *RDI*, red dichromatic imaging.



Supplementary Figure 2. Correlation between the color difference and visibility score according to bleeding pattern. *WLI*, White-light imaging; *RDI*, red dichromatic imaging.

SUPPLEMENTARY TABLE 1. Color difference and NBS units between bleeding points and surrounding blood with WLI and RDI according to the bleeding pattern

	WLI	RDI	*P* value
Oozing bleeding (n = 36)			
Δ*E*	6.84 ± 3.63	14.02 ± 3.44	<.001
NBS units/rating criteria	6.30 ± 3.34/much	12.90 ± 3.16/very much	
Pulsatile bleeding (n = 28)			
Δ*E*	8.07 ± 3.71	11.94 ± 4.46	<.001
NBS units/rating criteria	7.42 ± 3.41/much	10.98 ± 4.10/much	

Values are mean ± standard deviation.
NBS, National Bureau of Standards; Δ*E*, color difference; *WLI*, white-light imaging; *RDI*, red dichromatic imaging.

SUPPLEMENTARY TABLE 2. Mean visibility score of bleeding points with WLI and RDI and interobserver agreement among endoscopists according to the bleeding pattern

	Mean visibility score			Interobserver agreement
	WLI	RDI	*P* value	Mean weighted kappa (range)
Oozing bleeding (n = 36)				
All endoscopists	2.47 ± .32	2.88 ± .38	<.001	.52 (.42-.68)
Experts	2.51 ± .32	2.97 ± .38	<.001	.50 (.45-.60)
Trainees	2.43 ± .34	2.80 ± .43	<.001	.46 (.42-.50)
Pulsatile bleeding (n = 28)				
All endoscopists	3.04 ± .51	3.42 ± .50	<.001	.68 (.49-.84)
Experts	3.16 ± .55	3.46 ± .52	<.001	.71 (.56-.84)
Nonexperts	2.91 ± .49	3.38 ± .50	<.001	.60 (.49-.74)

Values are mean ± standard deviation unless otherwise defined.
WLI, White-light imaging; *RDI*, red dichromatic imaging.