Study Protocol

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Title: Efficacy and Safety of the RDI Mode in Endoscopic Submucosal Dissection: a Multicenter, Randomized Controlled Study

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Background and aim

Conventional white-light endoscopy (WLE) is hampered by insufficient contrast when attempting to identify deep vessels and active bleeding sites; visibility drops further when blood pools or spurts obscure the field, resulting in significantly lower hemostatic efficiency. Red dichromatic imaging (RDI), a novel image-enhanced endoscopic modality, has recently been shown to improve the visualization of deep-lying vessels and bleeding points, shorten hemostasis time and potentially increase overall procedural efficiency.

Although retrospective series have suggested that RDI may facilitate intra-operative bleeding control and better delineation of the submucosal plane during endoscopic submucosal dissection (ESD), high-level evidence from multicenter, randomized, controlled trials (RCTs) is lacking. No study has yet demonstrated superiority over WLE with respect to critical endpoints such as en-bloc resection rate, procedure time, complication rate and operator mental workload.

We therefore designed a multicenter RCT to systematically compare the efficacy and safety of full-procedural RDI with conventional WLE during ESD.

Methods

Study design: a multicenter, randomized controlled clinical trial.

Location: The Sixth Affiliated Hospital, Sun Yat-sen University, Guangdong Provincial Hospital of Chinese Medicine, Guangdong Second Provincial General Hospital

The inclusion criteria:

① Age ≥ 18 years.

② Early gastric cancer or precancerous lesions, early esophageal cancer or precancerous lesions, or early colorectal cancer/polyps that meet ESD indications.

③ ESD procedure to be performed at a participating center.

④ Lesion diameter 20–60 mm.

⑤ Written informed consent provided voluntarily.

The exclusion criteria:

① Foreigners.

② Severe coagulopathy (platelet count $<50\times10^9$/L or INR >1.5), significant cardiopulmonary disease, or any other contraindication to endoscopic therapy.

③ Imaging evidence of distant metastasis or lymph-node metastasis.

Intervention

Patients who met the inclusion and exclusion criteria were randomly assigned to either the RDI group or the conventional white-light endoscopy (WLE) group. In the RDI group, the submucosal dissection was performed entirely under RDI mode (white-light mode was allowed only for observation and marking). In the WLE group, the entire ESD procedure was completed with white-light mode without switching to RDI. All ESD procedures were performed by experienced endoscopists (≥300 previous ESD cases and formal RDI training, with ≥20 ESD cases performed under RDI mode).

Outcome parameters

The primary outcome parameter is the mean resection speed (mm^2/min) achieved with RDI versus conventional WLE during ESD.

The secondary outcome parameters are: complete resection (R0) rate, en-bloc resection rate, resection margin, number of intra-procedural bleeding episodes, intra-procedural blood loss, intra-procedural hemostasis time, other intra-procedural adverse events, and post-procedural adverse events.

The results will be analyzed in full analysis set, per-protocol set and safety set.

After the overall analysis, all data will be stratified by lesion location and analyzed separately for esophageal, gastric, and colorectal subgroups.

Definitions

The mean resection speed is the result of resection area divided by the resection time. The resection area is defined as the area on the specimen-fixation board. The resection time is defined as the time from the first mucosal incision to complete dissection of the lesion. Adverse events included bleeding, perforation, infection, and so on, mentioned by Cotton et al. (Gastrointest Endosc. 1994;40:514-518).

Sample Size

Based on a pilot study of 20 cases at our center, the mean resection speed in the RDI group was 27.2 ± 9.8 mm^2/min versus 21.1 ± 12.2 mm^2/min in the white-light group.

Assuming H_0: no difference in mean resection speed between the two groups, and setting α = 0.05 and power = 0.90, the required sample size is 71 lesions per arm (142 total).

Allowing for a 10 % dropout rate, we plan to enroll 79 lesions per arm, yielding 158 lesions in total (each lesion requiring ESD is counted as one case, even if multiple lesions occur in the same patient).

Randomization

Stratified randomization by center. Random numbers generated in Excel by an independent statistician; sequentially numbered, sealed, opaque envelopes prepared and held by the third party. The envelopes constitute the allocation sequence; random numbers remain concealed from patients and endoscopists until the envelope is opened immediately before allocation.

Blinding

Patients will be blinded; operators and video reviewers cannot be blinded; pathologists will remain blinded.

Statistical analysis

All analyses were performed with SPSS version 26. Baseline characteristics were examined to assess balance across concentration groups. Normally distributed continuous variables are presented as mean ± SD and compared between groups using independent-samples t-tests; non-normally distributed continuous variables are expressed as median (interquartile range) and compared with the Wilcoxon rank-sum test. Categorical rates were compared using the χ^2 test. A two-sided $P < 0.05$ was considered statistically significant.