內視鏡背景黏膜換皮術預防早期食道鱗癌經內視鏡完整切除後之異時性復發～一隨機分配前瞻試驗

Endoscopic Background Mucosal Resurfacing to Prevent Metachronous Recurrence of Superficial Esophageal Squamous Cancer After Curative Endoscopic Submucosal Dissection: A Randomized Pilot Study

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Background: Metachronous recurrence frequently develops in patients with superficial esophageal squamous cell carcinomas (ESCCs) after curative endoscopic submucosal dissection (ESD), especially in those with multiple (>10) small Lugol-voiding lesions (LVLs) over the esophageal background mucosa (i.e. speckled pattern). We conducted a randomized controlled trial to investigate whether endoscopic radiofrequency ablation (RFA) for esophageal background mucosal resurfacing (EBMR) can decrease the rate of metachronous neoplasia.

Methods: Patients who received curative ESD and whose Lugol staining showed a speckled pattern over the background mucosa were randomly assigned in a 1:1 ratio to either receive RFA (EBMR group) or endoscopic surveillance alone (control group). EBMR with RFA was performed with a balloon device for circumferential ablation of the total esophageal mucosa 2–3 months after ESD. The primary outcome was the metachronous recurrence of squamous neoplasia during a 5-year follow-up period. The secondary outcomes were major adverse events.

Figure 1. The study protocol, following the recommendations of the CONSORT statement.

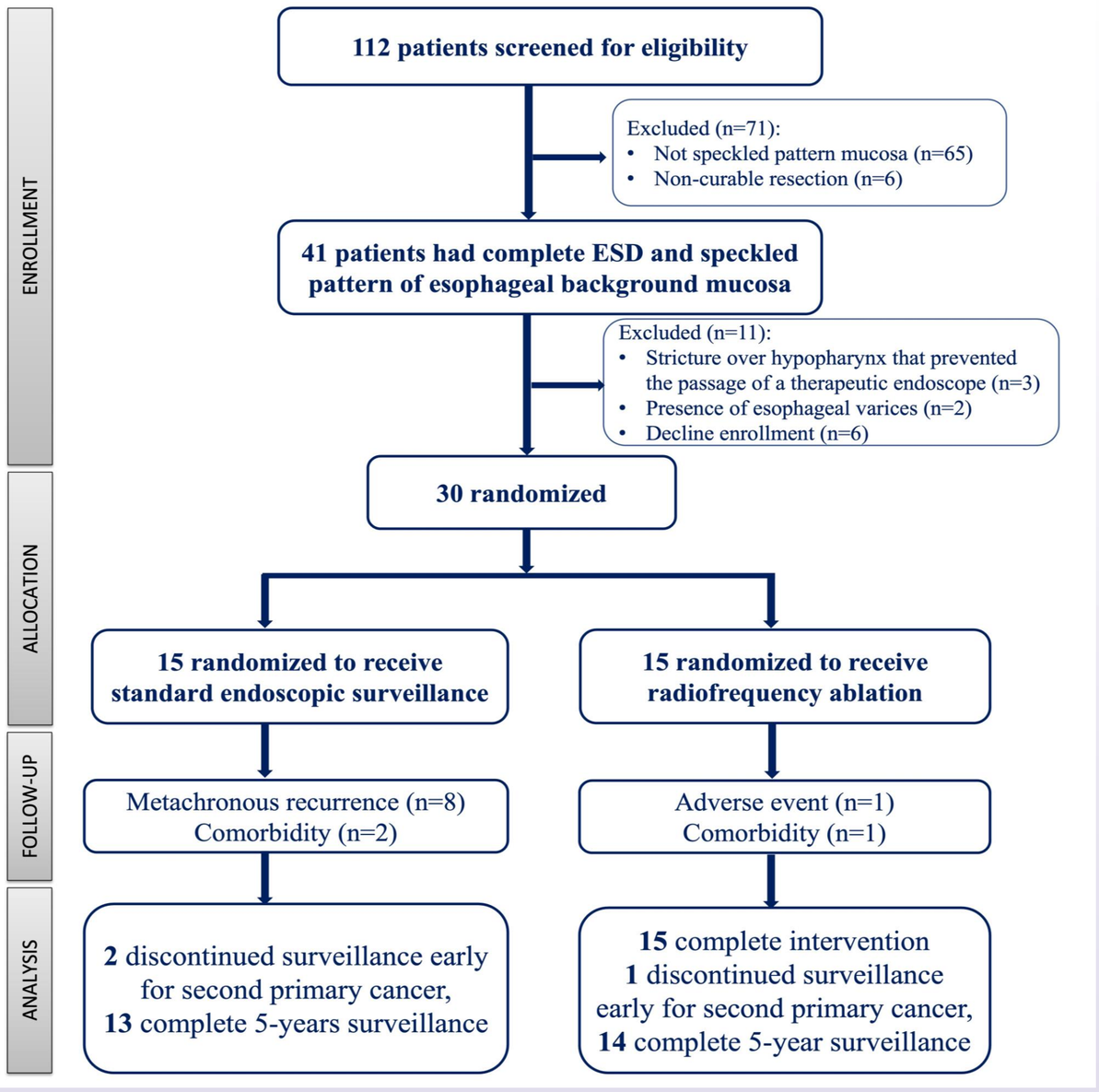

Table 1. Primary and secondary outcomes

	EBMR group (n=15)	Control group (n=15)	P value
Metachronous recurrences	0 (0%)	8 (53%)	0.002
Episodes of metachronous recurrent, median (range), per-patient	0	1 (0-3)	
Total lesions of metachronous recurrence, per-group	0	13	
Peak pain scale, median (range)	4 (2-7)	-	
Adverse events, Stenosis	1	0	

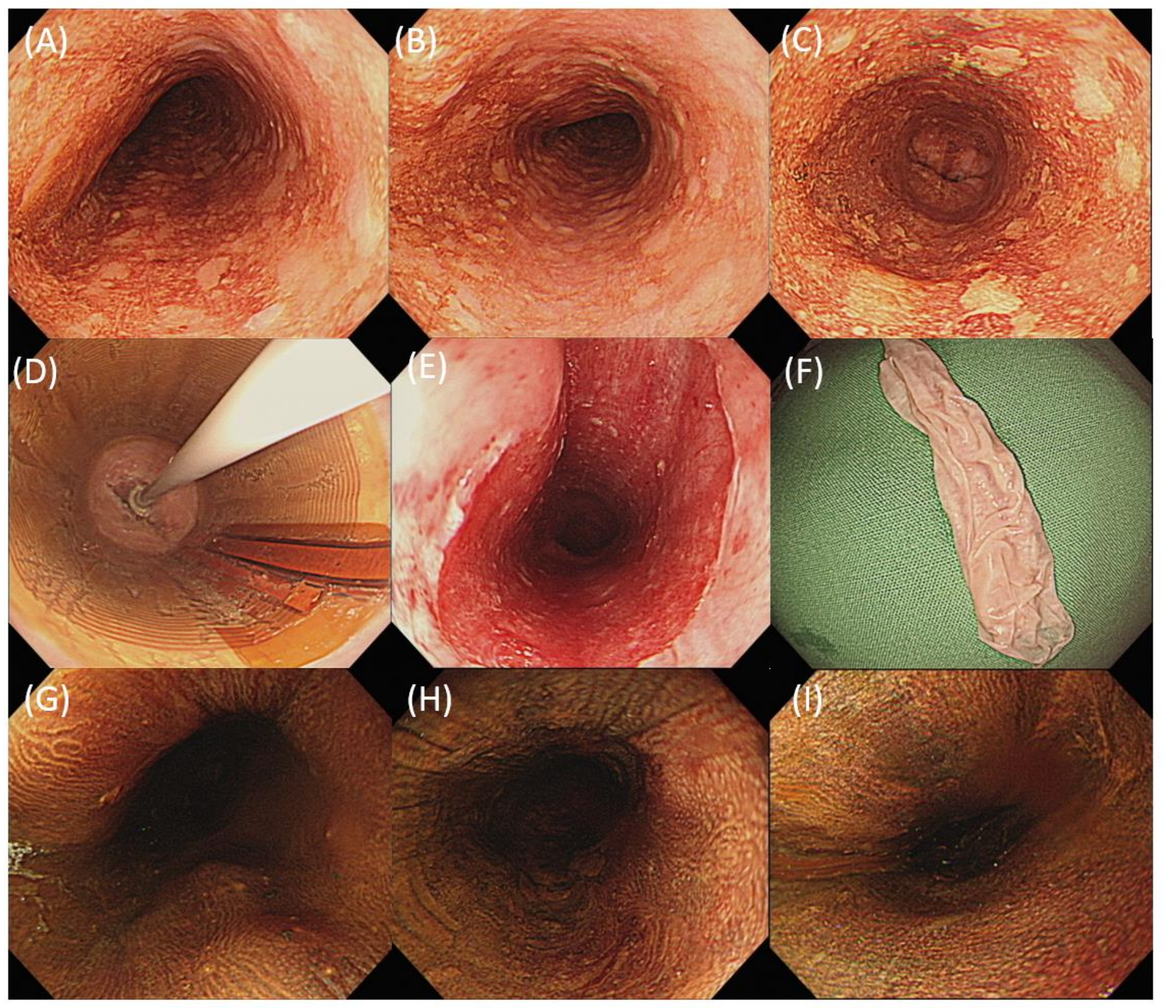

Figure 2. Representative case of esophageal background mucosal resurfacing (EBMR) with balloon-based endoscopic radiofrequency ablation. Before EBMR, Lugol chromoendoscopy showed multiple small Lugol-voiding lesions (LVLs) over the entire esophageal background mucosa (A–C). EBMR was performed to ablate the entire esophageal mucosa from the upper to lower esophagus (D). After single ablation, we attached a transparent hood at end of endoscope to remove coagulum (E). The coagulum of the entire esophageal epithelium was removed (F). Three months after EBMR, Lugol chromoendoscopy showed no residual LVLs over the esophageal background (G–I).

Results: Of 112 patients screened, 30 were randomized to receive EBMR (n=15) or surveillance (n =15). The mean procedure time of EBMR was 30.7 min (range: 25–40 min). One patient developed post-RFA stenosis, which resolved after 3 sessions of endoscopic dilation. EBMR reduced the risk of metachronous recurrence (0% in the EBMR group vs. 53% in the control group, p = 0.001), with the number needed to treat being 1.9. Reversal of the Lugol staining speckled pattern to only a few LVLs occurred in all patients and persisted for at least 5 years in the ablation group. A total of 13 metachronous lesions developed in eight patients (53%) in the control group.

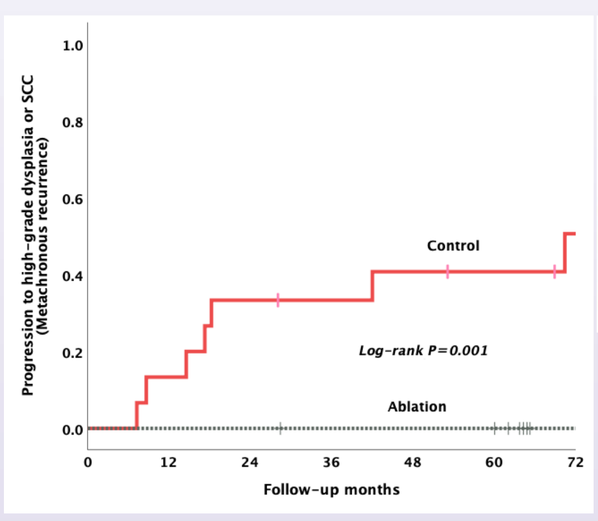

Figure 3. Progression from speckled background to high-grade dysplasia or squamous cell carcinomas.

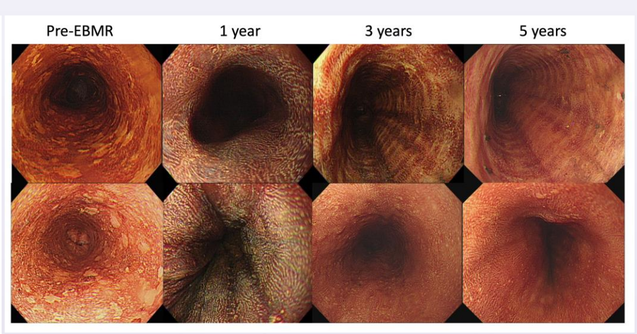

Figure 4. Durability of EBMR. Upper and lower panels contain endoscopic images of Lugol chromoendoscopy before EBMR and later images after EBMR, respectively, for two representative cases. Lugol staining still showed no LVLs over the background mucosa at 5-year follow-up.

Conclusion: In this randomized trial of patients with multiple small LVLs over the esophageal background after curative ESD, EBMR with balloon-type RFA is a promising and safe procedure for preventing metachronous recurrence over 5 years of follow-up. Clinical trial registration number: NCT03183115.