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## Endless Challenges in Overcoming Complications Associated with Endoscopic Submucosal Dissection

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See “Effectiveness of Autologous Platelet-Rich Plasma for the Healing of Ulcers after Endoscopic Submucosal Dissection” by Eunju Jeong, In kyung Yoo, Ozlem Ozer Cakir, et al., on page 472-478.

Endoscopic submucosal dissection (ESD) has now been accepted as a nearly perfected method of endoscopic resection of gastrointestinal neoplasms. After the first report on this ground-breaking procedure published in 2001, this procedure have been improved to accomplish safer and more effective treatment at each step owing to the development of electro-surgical knives, electro high-frequency generators, injection agents, and improved strategies.<sup>1,2</sup> Presently, curative resection can be achieved for challenging lesions that were treated by radical resection a decade ago. However, some unresolved complication remain associated with this procedure, including postoperative bleeding. Even though various risk factors of postoperative bleeding including patient comorbidities and tumor location and size have been revealed, a major cause of postoperative bleeding after ESD is an artificial postoperative ulcer caused by ESD itself.<sup>3</sup> From this point of view, prophylactic treatments for the postoperative ulcer have been major concerns for postoperative bleeding prevention after ESD, especially in the stomach.

Possible approaches to prevent postoperative bleeding after gastric ESD can be categorized into three groups. The first ap-

proach is controlling the pH in the stomach using gastric acid inhibitors. Since the establishment of ESD, gastric acid inhibitors have been prescribed as treatments for postoperative ulcers because a lower pH not only damages the ulcer bed tissue by activating pepsin but also inhibits platelet aggregation in exposed vessels. Histamine H<sub>2</sub>-receptor blockers (H<sub>2</sub>Bs) were key drugs in the early days of gastric ESD usage. Subsequently, proton pump inhibitors gradually replaced H<sub>2</sub>Bs owing to their strong suppressive effect on gastric acid secretion.<sup>4</sup> Recently, the efficacy of potassium-competitive acid blockers for the prevention of postoperative bleeding has been reported.<sup>5</sup> Thus, controlling pH is a well-known and well-accepted approach to prevent postoperative bleeding after gastric ESD.

The second approach is shielding postoperative ulcers from physical or chemical stimuli with agents or materials. Mucosal protectants are conventional agents that are used to shield postoperative ulcers; although their effects are limited, they have been prescribed in combination with gastric acid inhibitors. Recently, polyglycolic acid (PGA) sheet use initiated a new era for the shielding of postoperative ulcers.<sup>6</sup> Although shielding postoperative ulcers with PGA or other emerging materials can be a promising approach to prevent postoperative bleeding after gastric ESD, deployment methods of PGA sheets still require improvement.

The last potential approach is accelerating the healing process of postoperative ulcers. As mentioned above, gastric acid inhibitors and mucosal protectants are preferable for postoperative ulcer healing. However, these compounds do not accelerate the ulcer healing process but merely prevent delays in healing. In that sense, no methods have been developed that

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accelerate the ulcer healing process itself. Jeong et al. demonstrated the possibility of using autologous platelet-rich plasma to accelerate the healing process of postoperative ulcers.<sup>7</sup> Although this trial, which included a very small number of patients, suggested the possibility of using the third approach to prevent postoperative bleeding, no significant improvements in clinical outcomes were observed.

Additionally, this prophylactic treatment, in combination with others, can be applied to postoperative ulcers after ESD in other gastrointestinal sites. This approach may be effective not only to prevent postoperative bleeding but also to delay the formation of perforations and postoperative strictures. Undoubtedly, although these attempts may overcome complications associated with ESD, further accumulation of evidence on the efficacy of these approaches is required. The vigorous challenges faced by endoscopists will never end until the next ground-breaking procedure is developed.

#### Conflicts of Interest

The authors have no financial conflicts of interest.

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