

Updates in the Treatment of Superficial Gastric Neoplasms by Endoscopic Submucosal Dissection

Josue Aliaga Ramos^{1*}, Vitor N. Arantes²

¹Faculty of Medicine “Alberto Hurtado”, Cayetano Heredia Peruvian University, Digestive Endoscopy Unit of the San Pablo Clinic, Surco, Lima, Peru; Member of the Gastroenterology Society of Peru

²Endoscopy Unit, Alfa Institute of Gastroenterology, Federal University of Minas Gerais, Mater Dei Contorno Hospital, Belo Horizonte, Minas Gerais, Brazil

*Correspondence should be addressed to Vitor Arantes; arantesvitor@ufmg.br

Received date: December 09, 2020, **Accepted date:** January 25, 2021

Copyright: © 2021 Aliaga-Ramos J, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Summary

Gastric cancer is one of the neoplasms with the highest degree of mortality worldwide, responsible for more than 780,000 deaths in 2018 and whose incidence has been increasing over the last few years, mainly in Asian and Latin American countries.

The technological imaging advances in digestive endoscopy such as virtual chromoendoscopy and magnification associated with a systematic and comprehensive endoscopic examination of the entire gastric mucosa by a trained operator have optimized the early detection of pre-malignant and malignant lesions, which have favoured the high rate of curability through the use of endoscopic resection techniques such as endoscopic submucosal dissection (ESD).

ESD is one of the techniques in advanced therapeutic endoscopy that has revolutionized the management of early neoplasms of the gastrointestinal tract, demonstrating excellent results that are as equally efficient as surgery in the medium and long-term, but avoiding the post-operative morbi-mortality associated with surgical interventions and also presenting a low rate of adverse events in expert hands. This review has the objective to discuss the most recent advances in the management of superficial gastric neoplasms and to present an algorithm approach for these types of lesions.

Review

ESD is currently the first-line of treatment in the eradication of the pre-malignant and early malignant neoplasms, demonstrating in most studies, mainly from Asia, high rates of efficiency and safety in expert hands. This also reinforces the concept of early detection of pre-malignant and malignant lesions using virtual chromoendoscopy/endoscopic magnification techniques associated with a systematic and sequential revision, based on an endoluminal endoscopic anatomy [1-3].

For many years, gastrectomy has been considered the standard treatment for early gastric cancer, however it is associated with post-surgical morbidity and mortality, particularly high surgical risks patients. Japanese pioneers developed ESD as an alternative for the eradication of this

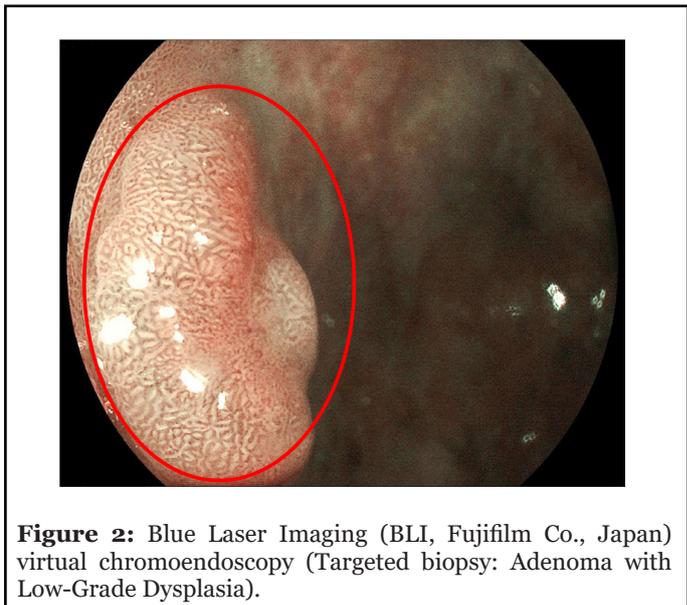
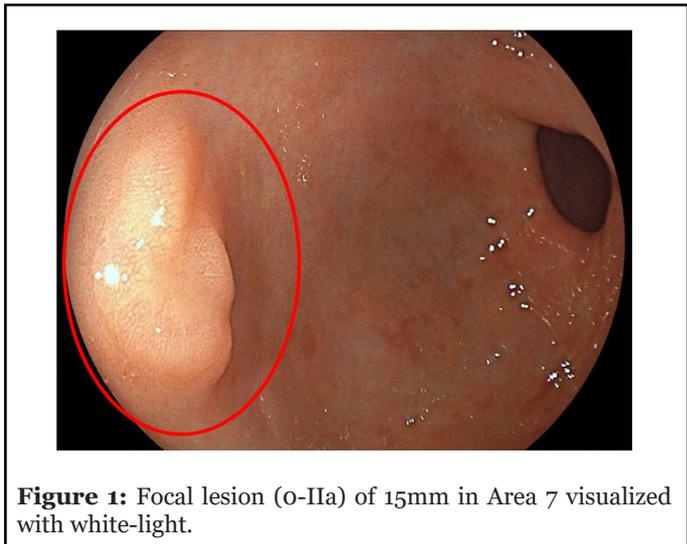
type of early gastric neoplasms with great advantages over conventional surgery, as demonstrated in different comparative studies [4-9]. Liu et al. [10] recently reported a meta-analysis in which they included 18 studies with 5,993 patients, observing the following benefits of ESD with respect to surgery: 1) shorter duration of the procedure (128.38 min; 95%CI: (-204.68, -52.09), $p=0.001$); 2) shorter hospital stay (7.13 days; 95%CI: (-7.98, -6.28), $p<0.00001$); 3) lower risk of death associated with the procedure (OR=0.21; 95%CI: (0.07, 0.68), $p=0.009$); 4) lower risk of complications (OR=0.47; 95%CI: (0.34, 0.63), $p<0.00001$) and 5) lower costs and better quality of life. Outcomes that are corroborated with those obtained by our research group. In order to obtain a high curative rate some principles should be followed: adequate selection of patients through a thorough evaluation of the lesions using enhanced imaging endoscopic techniques

such as virtual chromoendoscopy and magnification by an expert operator [11,12] ; precise tumor delineation in order to achieve a complete (R0) and en bloc resection of the target-lesion; preparation and fixation of the specimen for histological analysis by an experienced gastrointestinal pathologist and correct interpretation of the histological results in order to determine if a curative resection was obtained meeting the curability criteria proposed by the last Japanese guideline [13] .

It is essential to highlight the importance of endoscopic surveillance in all patients that undergoes gastric ESD aiming to detect local recurrences or metachronic lesions [14]. Emura et al. [15]. proposed a methodology for a high-quality upper gastrointestinal endoscopy with a systematic revision of the upper digestive tract defined as SACE (Systematic Alphanumeric Coded Endoscopy), establishing 28 areas of analysis, 21 of which belong to the stomach, in order to generate a complete and meticulous evaluation of the entire gastric mucosa detecting pre-malignant and early malignant lesions. In the aforementioned study, in 650 healthy volunteers used the SACE system and chromoendoscopy a rate of pre-malignant gastric lesions of 30% (195/650) was found, two of which were diagnosed as early gastric cancer and underwent successfully by ESD.

The Latin American experience in ESD is still limited due to the steep learning curve to master the technique, as well as the lack of training centers [16,17]. Recently Arantes et al. [18] reported one of the largest studies in Latin America including 103 ESD procedures for superficial gastric neoplasms, demonstrating an overall en-bloc resection rate of 96.3% with 97.1% (34/35) for pre-malignant lesions and 95.5% (43/45) for malignant lesions. Also, the study demonstrated complete resection (R0) rate of 92.5% with 94.2% (33/35) for pre-malignant lesions and 88.8% (40/45) for malignant lesions. Likewise, a global curative resection rate of 76% (32/42) was determined based on the expanded criteria proposed by the latest Japanese guidelines, with a rate of adverse events of only 2.5% (2/80), which demonstrates an excellent efficiency and safety profile of this resection endoscopic technique in expert hands. Furthermore, follow-up disclosed just one case of local recurrence (1.2%) and identified 3 cases of metachronic lesions (3.7%) during a mean surveillance period of 17 months, demonstrating the great benefits of curative resection for these types of lesions and the importance of annual surveillance to detect metachronous tumors. Another important finding to highlight in this study was that more than 80% of the resected lesions had a size ≥ 20 mm located mainly in the lower third of the stomach which were eradicated in an average procedure time of 107 minutes (SD \pm 51.6), demonstrating an interesting profile of clinical effectiveness. Of the 80 resected cases in the aforementioned study, 42 were

adenocarcinomas (52.5%), 22 were low-grade dysplasia (27.5%), 13 were high-grade dysplasia (16.3%) and 3 were neuroendocrine tumours (3.8%). Likewise, it was observed that 78.5% (33/42) had only intramucosal invasion (T1a) and 21.3% presented submucosal invasion (T1b): 3 cases (7.1%) to superficial submucosa (SM1) and 6 cases (14.2%) to deep submucosa (SM2). In accordance with international oncological guidelines, most non-curative cases (6/10) underwent surgical treatment (gastrectomy). The remaining patients were considered unfit for surgery and underwent endoscopic follow-up and no relapse was noticed during the average follow-up of 22.5 months. Figures 1-3 show a representative case of early detection and characterization of a superficial gastric neoplasm, using virtual chromoendoscopy techniques/endoscopic magnification, also Figures 4-8 detail the main steps of the endoscopic submucosal dissection performed for the eradication of this lesion.



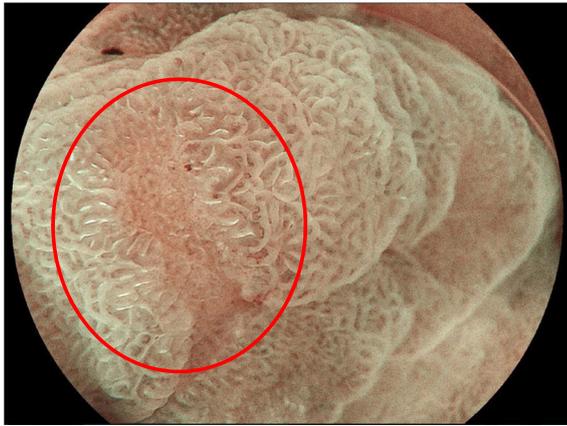


Figure 3: Endoscopic magnification / BLI (Note “light blue crest”, irregularity of the microsurface and demarcation line).

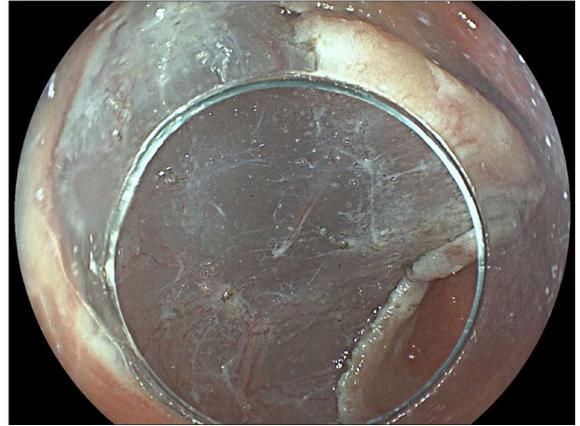


Figure 6: Submucosal dissection with a nice plane of dissection obtained with submucosal injection of teardrops sodium hyaluronate.

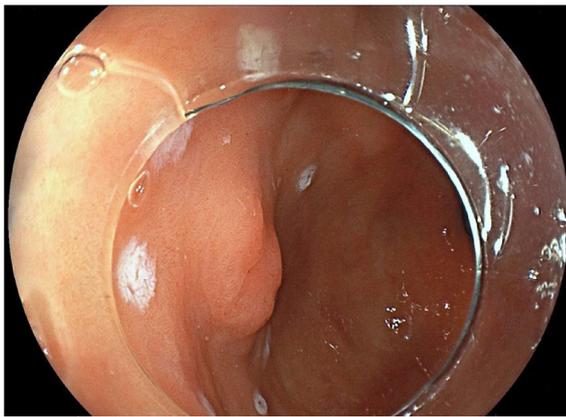


Figure 4: Demarcation of limits.

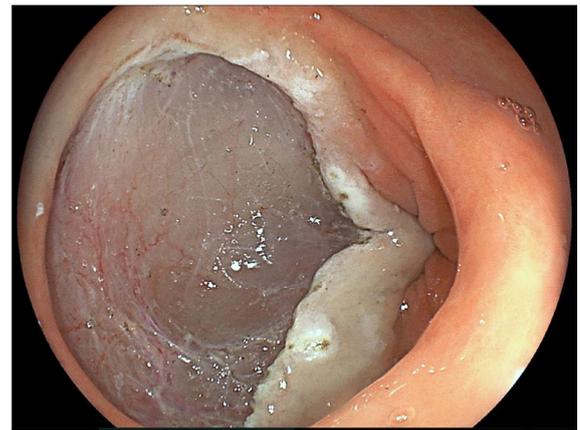


Figure 7: En-bloc resection was achieved without damage to muscularis propria.

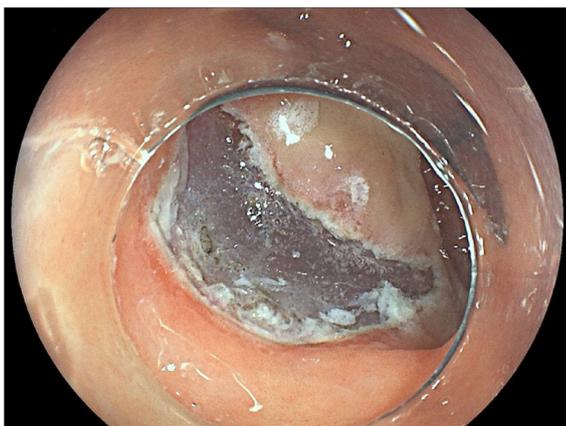


Figure 5: Incision of the mucosa.



Figure 8: Resected specimen fixed for histology that disclosed adenoma with low grade dysplasia and free margins (R0 resection).

A critical step for the execution of ESD is the creation of a submucosal cushion. For this effect, the research team of this study used 0.4% sodium hyaluronate teardrops for submucosal injection (*Adaptis Fresh*[®], Legrand Laboratory, Brazil). Although there is currently not enough scientific evidence to support the off-label use of this substance for submucosal injection in gastric ESD, the same research group recently published a study in which the benefits of the use of this substance were demonstrated with an optimal safety profile, presenting promising results, and appearing as an excellent alternative in the Western countries that have no access to *Muco Up*[®], which is only available in Japan [19].

In conclusion our research group reaffirms the importance of high-quality endoscopy examination in all patients with the objective of detecting pre-malignant or early malignant lesions, and the fundamental role of ESD in providing an effective and minimally invasive therapeutic approach to gastric neoplastic lesions, preserving the organ and the quality of life of the affected patients.

References

1. Banks M, Graham D, Jansen M, Gotoda T, Coda S, Di Pietro M, et al. British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. *Gut.* 2019 Sep 1;68(9):1545-75.
2. Icaza-Chávez ME, Tanimoto MA, Huerta-Iga FM, Remes-Troche JM, Carmona-Sánchez R, Ángeles-Ángeles A, et al. Mexican Consensus on Detection and Treatment of Early Gastric Cancer. *Journal of Gastroenterology of Mexico.* 2020 Jan 1; 85 (1): 69-85.
3. Pimentel-Nunes P, Libânio D, Marcos-Pinto R, Areia M, Leja M, Garrido M, et al. Management of epithelial precancerous conditions and lesions in the stomach (maps II): European Society of gastrointestinal endoscopy (ESGE), European Helicobacter and microbiota Study Group (EHMSG), European Society of pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. *Endoscopy.* 2019;51(4):365-88.
4. Li H, Feng LQ, Bian YY, Yang LL, Liu DX, Huo ZB, et al. Comparison of endoscopic submucosal dissection with surgical gastrectomy for early gastric cancer: an updated meta-analysis. *World Journal of Gastrointestinal Oncology.* 2019 Feb 15;11(2):161-71.
5. Abdelfatah MM, Barakat M, Ahmad D, Ibrahim M, Ahmed Y, Kurdi Y, et al. Long-term outcomes of endoscopic submucosal dissection versus surgery in early gastric cancer: a systematic review and meta-analysis. *European Journal of Gastroenterology & Hepatology.* 2019 Apr 1;31(4):418-24.
6. Gu L, Khadaroo PA, Chen L, Li X, Zhu H, Zhong X, et al. Comparison of long-term outcomes of endoscopic submucosal dissection and surgery for early gastric cancer: a systematic review and meta-analysis. *Journal of Gastrointestinal Surgery.* 2019; 23:1493-501.
7. Shin DW, Hwang HY, Jeon SW. Comparison of endoscopic submucosal dissection and surgery for differentiated type early gastric cancer within the expanded criteria. *Clinical Endoscopy.* 2017 Mar;50(2):170-8.
8. Lee S, Choi KD, Han M, Na HK, Ahn JY, Jung KW, et al. Long-term outcomes of endoscopic submucosal dissection versus surgery in early gastric cancer meeting expanded indication including undifferentiated-type tumors: a criteria-based analysis. *Gastric Cancer.* 2018 May;21(3):490-9.
9. Hahn KY, Park CH, Lee YK, Chung H, Park JC, Shin SK, et al. Comparative study between endoscopic submucosal dissection and surgery in patients with early gastric cancer. *Surgical Endoscopy.* 2018 Jan;32(1):73-86.
10. Liu Q, Ding L, Qiu X, Meng F. Updated evaluation of endoscopic submucosal dissection versus surgery for early gastric cancer: A systematic review and meta-analysis. *International Journal of Surgery.* 2020 Jan 1;73:28-41.
11. Yao K, Nagahama T, Matsui T, Iwashita A. Detection and characterization of early gastric cancer for curative endoscopic submucosal dissection. *Digestive Endoscopy.* 2013 Mar;25:44-54.
12. Nakamura M, Shibata T, Tahara T, Yoshioka D, Okubo M, Mizoguchi Y, et al. The usefulness of magnifying endoscopy with narrow-band imaging to distinguish carcinoma in flat elevated lesions in the stomach diagnosed as adenoma by using biopsy samples. *Gastrointestinal Endoscopy.* 2010 May 1;71(6):1070-5.
13. Ono H, Yao K, Fujishiro M, Oda I, Nimura S, Yahagi N, et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. *Digestive Endoscopy.* 2016 Jan;28(1):3-15.
14. Quea NR, Emura F, Bolaños FB, Arias YS, Suárez FA, Rivera AP. Effectiveness of systematic alphanumeric coded endoscopy for diagnosis of gastric intraepithelial neoplasia in a low socioeconomic population. *Endoscopy International Open.* 2016 Oct;4(10):E1083-9.
15. Emura F, Mejía J, Mejía M, Osorio C, Hernández C, González I, et al. Effectiveness of systematic chromoendoscopy for diagnosis of early cancer and gastric premalignant lesions: Results of two consecutive screening campaigns in Colombia (2006-2007). *Revista Colombiana de Gastroenterología.* 2010 Mar;25(1):18-28.

16. Arantes VN, Sanna MD, Alves JS, Milhomem-Cardoso DM, Maluf-Filho F. Is endoscopic submucosal dissection still limited to few tertiary centers in the West? Results from a national survey in Brazil. *Arquivos de Gastroenterologia*. 2020 Dec;57(4):477-83.

17. González N, Parra-Blanco A, Arantes V, Mönkemüller K. Current status of endoscopic submucosal dissection in Latin America. *Acta Gastroenterológica Latinoamericana*. 2016; 46 (3): 213-9.

18. Arantes V, Aliaga Ramos J, Pedrosa MS. Endoscopic submucosal dissection for superficial gastric neoplasms in two referral hospitals in Brazil: Can the Japanese and South Korean results be equaled? *Revista de Gastroenterologia de Mexico*. 2020; 20: 1-9.

19. Arantes V, Aliaga Ramos J, Abdul Rani R, Yoshida N. Off-label use of 0.4% sodium hyaluronate teardrops: a safe and effective solution for submucosal injection in gastric endoscopic submucosal dissection. *Endoscopy International Open*. 2020; 08(12): E1741-E1747.