



REVISTA DE GASTROENTEROLOGÍA DE MÉXICO

www.elsevier.es/rgmx



ORIGINAL ARTICLE

Endoscopic submucosal dissection as treatment for early gastric cancer: Experience at two centers in Lima, Peru[☆]



J.A. Chirinos Vega^{a,*}, G. Vargas^b, C. Alcántara^b, J. Zapata^b

^a Departamento de Gastroenterología, Clínica Angloamericana, Lima, Peru

^b Servicio Gastroenterología, Hospital Nacional Arzobispo Loayza, Lima, Peru

Received 16 June 2017; accepted 5 October 2017

Available online 4 April 2018

KEYWORDS

Gastric cancer;
Submucosal
endoscopic dissection

Abstract

Introduction and aims: The aim of the present study was to evaluate the feasibility of endoscopic submucosal dissection (ESD) and determine the clinical and pathologic characteristics of early gastric cancers and premalignant lesions treated with that technique at the *Hospital Nacional* of the Department of Health and a private clinic in Lima, Peru.

Materials and methods: A descriptive study of all pre-malignant and malignant gastric lesions treated with ESD at the Gastroenterology Service of the *Hospital Arzobispo Loayza* and the *Clínica Angloamericana* was conducted within the time frame of January 2012 and January 2017.

Results: A total of 13 lesions were resected through ESD: 8 adenocarcinomas (61.53%), 3 adenomas with high-grade dysplasia (23%), and 2 adenomas with low-grade dysplasia (15.38%). Twelve lesions (92.3%) were located in the lower third of the stomach. Slightly elevated lesions (Paris classification IIa) (4 lesions, 30.76%) and mixed slightly elevated lesions with a depressed component (IIa + IIc) (4 lesions, 30.76%) predominated. The mean size of the resected specimens was 35 mm. Complete resection of all lesions was achieved in 11 cases (84.6%) and en bloc resection was carried out in 11 cases (84.6%). Resection was curative in 6 cases (75%), from the total of 8 resected adenocarcinomas. One case of perforation was the only complication reported (7.6%) and it was surgically resolved.

Conclusions: The feasibility and efficacy of ESD for the treatment of early gastric cancer was demonstrated at two healthcare centers in Lima, Peru. The complication rate was similar to that reported in the international medical literature.

© 2018 Asociación Mexicana de Gastroenterología. Published by Masson Doyma México S.A. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

[☆] Please cite this article as: Chirinos Vega JA, Vargas G, Alcántara C, Zapata J. Disección submucosa endoscópica como tratamiento de cáncer gástrico temprano: experiencia en 2 centros de Lima, Perú. *Revista de Gastroenterología de México*. 2018;83:393–399.

* Corresponding author. Clínica Anglo Americana, Calle Alfredo Salazar 350, San Isidro 15073, C.P. 15036, Lima, Peru. Phone: +51957668855. E-mail address: juanochirinos@hotmail.com (J.A. Chirinos Vega).

PALABRAS CLAVE

Cáncer gástrico;
Disección
endoscópica
submucosa

Disección submucosa endoscópica como tratamiento de cáncer gástrico temprano: experiencia en 2 centros de Lima, Perú

Resumen

Introducción y objetivos: El objetivo del estudio fue evaluar la factibilidad de la disección endoscópica submucosa (DES) y determinar las características clínico-patológicas de los cánceres gástricos tempranos y lesiones premalignas tratados con esta técnica en un Hospital Nacional del Ministerio de Salud y en una clínica particular en Lima, Perú.

Materiales y métodos: Estudio descriptivo de todas las lesiones gástricas malignas y premalignas tratadas con DES en el Servicio de Gastroenterología del Hospital Arzobispo Loayza y la Clínica Angloamericana desde enero de 2012 a enero de 2017.

Resultados: Se resecaron un total de 13 lesiones con DES: 8 adenocarcinomas (61.53%), 3 adenomas con displasia de alto grado (23%) y 2 adenomas con displasia de bajo grado (15.38%). Doce lesiones (92.3%) se localizaron en el tercio inferior gástrico. Predominaron las lesiones plano elevadas (Ila de París; 4 lesiones, 30.76%) y las mixtas plano elevadas con componente deprimido (Ila + IIc; 4 lesiones, 30.76%). La media de tamaño del espécimen resecado fue de 35 mm. Se consiguió resección completa, del total de lesiones, en 11 casos (84.6%), y resección en bloque en 11 casos (84.6%). En 6 casos (75%), de un total de 8 adenocarcinomas resecados, se observó una resección curativa. Se reportó una complicación (7.6%) la cual fue perforación y se resolvió por cirugía.

Conclusiones: En 2 centros de Lima, Perú, se demostró la factibilidad y eficacia de la DES para el tratamiento del cáncer gástrico precoz, con una tasa de complicaciones similar a la descrita en la literatura internacional.

© 2018 Asociación Mexicana de Gastroenterología. Publicado por Masson Doyma México S.A. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction and aims

Early gastric cancer is a malignant tumor confined to the mucosa or submucosa, with or without lymph node metastasis. Endoscopic submucosal dissection (ESD) is an advanced endoscopic technique developed at the end of the 1990s in Japan that enables *en bloc* resection, regardless of the size of the lesion.^{1,2} Unlike mucosectomy, ESD makes *en bloc* resection possible, allowing better pathologic evaluation of the surgical specimen, a greater number of complete resections, and less premalignant and malignant local gastric lesions.^{3,4}

Endoscopic therapy for early gastric cancer is indicated in carcinomas with close to 0% risk for lymph node metastasis. Initial studies determined that intramucosal differentiated carcinomas (cT1a) smaller than 2 cm, that had no ulceration, met those criteria. Later studies found that the risk for lymph node metastasis was extremely low (under 1%) in the following lesions: 1) UL (-) cT1a differentiated carcinomas larger than 2 cm in diameter, 2) UL (+) cT1a differentiated carcinomas smaller than 3 cm in diameter, 3) UL (-) cT1a undifferentiated carcinomas smaller than 2 cm in diameter, and 4) tumors smaller than 3 cm involving the superficial submucosa with no lymphovascular infiltration (ly, v).⁵

The aim of the present study was to evaluate the feasibility of ESD and to determine the clinical and pathologic characteristics of early gastric cancers and premalignant lesions.

Materials and methods

A descriptive, case series study was conducted within the time frame of January 2012 and January 2017 in Lima, Peru, at two centers: the Health Department's *Hospital Arzobispo Loayza*, which is a national referral center for gastroenterology, and the *Clinica Anglo Americana*. All lesions were previously diagnosed through endoscopy with biopsy. The clinical and pathologic characteristics evaluated were: sex, age, macroscopic tumor size and type, tumor location, procedure duration, *en bloc* resection, complications, depth of invasion, compromised lateral margins, and histologic type. Tumor location was divided into upper, middle, and lower, according to the Japanese classification of gastric cancer.

En bloc resection was defined as that which made it possible to obtain the endoscopic specimen in a single piece with no fragmentation. Complete resection was defined as the entire removal of the cancer, leaving no neoplastic components in the lateral or vertical margins and with no lymphovascular invasion in the microscopic examination and when *en bloc* adenocarcinoma resection was: (I) predominantly differentiated, intramucosal, with no ulcer, disease-free lateral and vertical margins, regardless of lesion diameter; (II) lesion < than 3 cm, predominantly differentiated, intramucosal, and ulcerated; (III) lesion < 2 cm, predominantly undifferentiated, intramucosal, and non-ulcerated; or (IV) lesion < 3 cm, predominantly differentiated, up to submucosa 1 (less than 500 μ m). Curative

resection was considered when there was no lymphovascular invasion and lateral and vertical margins were lesion-free, according to expanded indications.⁵ Recurrence was defined as the reappearance of the cancer at the lesion site (local recurrence), synchronous or metachronous reappearance, or distant metastasis.

The endoscopes employed were: the standard FUJINON model EG-590WR endoscope with 0.4% of indigo carmine, and in some cases, the LASEREO model EG-L590Z magnification endoscope. Carbon dioxide instead of air was used in the procedures performed at the *Clínica Anglo Americana*. The ESD technique utilized consisted of the following steps: 1) marking the perimeter of the lesion; 2) submucosal injection to produce a submucosal buffering effect and to raise the lesion; 3) an incision outside of and surrounding the marked limits of the lesion; 4) submucosal dissection. In several cases, the surrounding incision was not initially complete, to maintain the tension of the specimen to be resected, and the submucosal dissection was progressively alternated with the incision. A model DH-11GZ transparent CAP was placed at the tip of the endoscope in the majority of cases. Isotonic saline solution and/or hyaluronic acid at 0.4% (Lagricel[®]) was injected to create a submucosal buffer. A small quantity of indigo carmine was mixed in all the solutions and injected with a 21 to 25-caliber needle. Circumferential incision and submucosal dissection were achieved with a variety of devices that included: a Hybrid knife-I, Flush knife BT-2, Hybrid knife T, and IT-knife-2. Immediate bleeding was that in which there was a descent in hemoglobin greater than 2 g/dl from the beginning of the procedure to 24 h after the procedure. Late bleeding was defined as clinical evidence of bleeding that required endoscopic treatment, such as hematemesis or melena, 0-30 days after the procedure.

Results

Clinical and pathologic characteristics

Within the time frame of January 2012 and January 2017, 13 early malignant and premalignant gastric lesions were treated through ESD in 13 patients (one lesion per patient). Ten (76.9%) of those procedures were performed at the *Hospital Nacional Arzobispo Loayza* and 3 (23%) were performed at the *Clínica Anglo Americana*, in Lima, Peru. Nine (69.2%) of the patients were women and 4 (30.76%) were men. Mean patient age was 70 years (range: 44-85 years). Mean lesion size was 35 mm (range: 20-50 mm). Twelve (92.3%) of the lesions were located in the lower region and one (7.6%) was in the middle region. [Tables 1 and 2](#) show the clinical and pathologic characteristics of the patients and [Figure 1](#) illustrates a case of ESD.

Endoscopic devices and injection solutions

The Hybrid knife-I was used in 8 cases (61.53%); the Flush knife BT-2 in 3 cases (23%); the Hybrid knife T in one case (7.7%), and the IT-knife-2 in one case (7.7%). To raise the lesions, physiologic saline serum was used in 2 cases (15.3%), methylene blue in 4 cases (30.7%), and hyaluronic acid in 7 cases (58.8%).

Table 1 Clinical and pathologic characteristics of the patients/lesions.

	Gastric lesions
<i>Patients/Lesions</i>	13/13
<i>Men (%), Women (%)</i>	4 (30.7), 9 (69.23)
<i>Mean age (range)</i>	70 (44-85)
<i>Location, n (%)</i>	
Middle	1 (7.6)
Lower	12 (92.3)
<i>Macroscopic type, n (%)</i>	
Ila + Ilc	4 (30.76)
Ila	4 (30.76)
0-Is	2 (15.38)
Ilc + Ila	1 (7.6)
Ilc	1 (7.6)
III + Ilc	1 (7.6)
<i>Lesion size, n (%)</i>	
< 20 mm	3 (23)
20-30 mm	5 (38.46)
> 30 mm	5 (38.46)
<i>Ulceration, n (%)</i>	
Absent	10 (76.92)
Present	3 (23)
<i>Procedure duration</i>	
Mean (range), min	109 (67-228)
<i>Complications, n (%)</i>	
Perforation	1 (7.6)
Immediate or late bleeding	0
Mortality	0

Table 2 Histopathologic characteristics of the patients.

Gastric lesions	n (%)
Premalignant lesions	
Total	5
<i>Resection</i>	
En bloc	5 (100)
R 0	5 (100)
<i>Histologic type</i>	
Adenoma with high-grade dysplasia	3 (60)
Adenoma with low-grade dysplasia	2 (40)
Gastric cancer	
Total	8
<i>Resection</i>	
En bloc	6 (75)
R 0	6 (75)
Curative	6 (75)
<i>Histologic type</i>	
Well differentiated adenocarcinoma	8 (100)
Non-differentiated adenocarcinoma	0
<i>Depth of invasion</i>	
Mucosa (M)	5 (62.5)
Submucosa (SM1)	1 (12.5)
Submucosa (SM2)	2 (25)

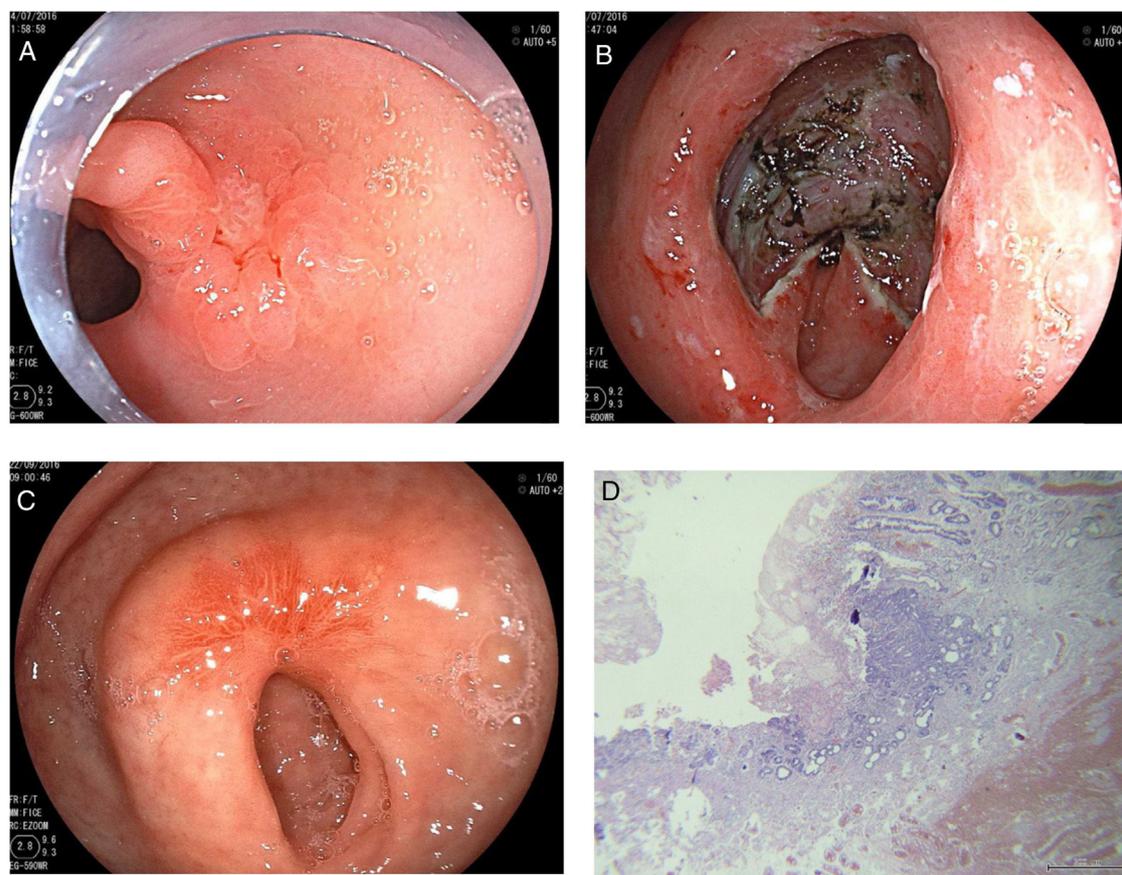


Figure 1 Endoscopic submucosal dissection (ESD) of pre-pylorus lesion. A) Slightly depressed lesion with 2-cm elevated edges, poorly defined edges, and irregular surface. B) Final result of the submucosal dissection. C) ESD scar 8 weeks after the procedure. D) Intramucosal well differentiated adenocarcinoma with disease-free surgical edges.

Histologic evaluation and macroscopic tumor type

Of the 13 resected lesions, 8 (61.53%) were well-differentiated adenocarcinomas; 5 (38.46%) were adenomas, of which 3 (23%) had high-grade dysplasia and 2 (15.38%) had low-grade dysplasia. Regarding macroscopic appearance, 4 (30.76%) lesions were described as II-a; 4 (30.76%) lesions as IIa + IIc; 2 (15.38%) lesions as 0-I; one (7.69%) lesion as IIc + IIa; one (7.69%) lesion as IIc; and one (7.69%) lesion as III + IIc. Only 3 (23%) lesions presented with ulceration.

Cure rate and complications

ESD was indicated for 6 (75%) of the 8 patients with gastric cancer according to the expanded criteria for the submucosal dissection and 2 (25%) of the cancer patients underwent the procedure because they met the absolute criteria for submucosal dissection described by Oda et al.⁴ One patient with lesion ulceration had submucosal involvement (SM1) and met the cure criteria. *En bloc* resection was achieved in all the premalignant lesions (5 lesions) and in 6 of the 8 adenocarcinomas (75%). Two (25%) of the 8 adenocarcinomas required hybrid resection (submucosal dissection and snare resection).

Of the 8 patients diagnosed with adenocarcinoma, curative resections were achieved in 6 patients (75%) with gastric adenocarcinoma. The depths of invasion found were: 2 patients with SM2 submucosal invasion and one patient with SM1 submucosal invasion. The remaining 5 patients were diagnosed with adenocarcinoma limited to the mucosa. There were no neoplastic lesions found at endoscopy performed in the patients diagnosed with adenocarcinoma at the follow-up at 6 months. Mean procedure duration was 109 min (range: 67-228 min). The muscularis propria layer was damaged in one of the cases, with no air observed in the abdominal cavity, and was resolved through the placement of 3 endoclips. Perforation was reported in one patient and it was surgically resolved, because technical endoscopic difficulties did not allow adequate closure of the defect. The patient had favorable progression. No deaths were reported (Table 3).

Discussion and conclusions

The first case report of submucosal dissection of early gastric cancer in Peru was presented by Vargas et al.⁶ in 2012, with no others reported in the country since then.

The incidence of lymph node metastasis was studied by Gotoda et al., who analyzed more than 5,000 gastrec-

Table 3 Characteristics of the study patients.

No.	Age (years)	Sex	Location (third)	Macroscopic type	Lesion size	Ulceration	Complications	Type of resection	Histologic type	Depth of invasion	Endoscopic knife	Site
1	70	W	Lower	Ila+Ilc	35x35 mm	Yes	No	En bloc	Well differentiated adenocarcinoma	Mucosa	IT-Knife 2	HNAL
2	44	W	Lower	Ila+Ilc	50x40 mm	No	No	En bloc	Well differentiated adenocarcinoma	Mucosa	Hybrid knife I	HNAL
3	65	W	Lower	Ila	41x18 mm	No	No	En bloc	Well differentiated adenocarcinoma	Mucosa	Hybrid knife I	HNAL
4	60	M	Lower	0-Is	37x30 mm	Yes	No	En bloc	Tubulovillous adenoma with low-grade dysplasia	Mucosa	Hybrid knife I	HNAL
5	75	W	Lower	Ila	25x15 mm	Yes	No	En bloc	Tubular adenoma with low-grade dysplasia	Mucosa	Hybrid knife I	HNAL
6	78	W	Lower	Ila	45x30 mm	No	No	En bloc	Adenoma with high-grade dysplasia	Mucosa	Hybrid knife I + REM	HNAL
7	85	M	Lower	Ilc	35x20 mm	No	No	En bloc	Adenoma with high-grade dysplasia	Mucosa	Hybrid knife I + REM	HNAL
8	83	W	Lower	Ila	20x20 mm	No	Perforation	Hybrid	Well differentiated adenocarcinoma	Submucosa (SM2)	Hybrid knife I	HNAL
9	75	W	Lower	Ilc+Ila	35x20 mm	No	No	En bloc	Well differentiated adenocarcinoma	Mucosa	Hybrid knife T	HNAL
10	63	W	Middle	0-Is	26x32 mm	No	No	En bloc	Well differentiated adenocarcinoma	Submucosa (SM1)	Flush knife	<i>Clínica Anglo Americana</i>
11	66	W	Lower	Ila+Ilc	31x30 mm	No	No	En bloc	Tubular adenoma with high-grade dysplasia	Mucosa	Flush knife	<i>Clínica Anglo Americana</i>
12	77	M	Lower	Ila+Ilc	20x20 mm	No	No	Hybrid	Well differentiated adenocarcinoma	Submucosa (SM2)	Flush knife	<i>Clínica Anglo Americana</i>
13	77	M	Lower	III+ Ilc	35x23 mm	No	Microperforation	En bloc	Well differentiated adenocarcinoma	Mucosa	Hybrid knife T	HNAL

^a Note: Case 13 had muscle layer damage, with no observed complete continuity solution and no apparent leakage of air into the abdominal cavity that was resolved through endoclip placement.

tomies with D2 lymph node dissection. That study published both the absolute and expanded criteria for ESD of early gastric cancer lesions. According to those criteria, lymph node metastasis incidence is below 1%.⁷ In our study, 3 patients had submucosal invasion: one patient up to SM1 and 2 patients to SM2. In the patient with SM1, conservative treatment was decided upon, given that all the Godota criteria were met: well differentiated lesion smaller than 3 cm (it measured 1.2 cm in diameter and only 300 μ m in depth).

The importance of early gastric cancer diagnosis is that if the lesion is resected and meets the curative criteria defined by Oda et al.,⁴ 5-year survival can be greater than 95%, similar to that for surgery.⁵ Fukunaga et al. demonstrated greater survival (97.1 vs 85.8%; $p = 0.01$) and fewer adverse effects (6.8 vs 28.4%; $p < 0.01$) in patients that underwent ESD, compared with those that had surgery in a study that evaluated follow-up at 5 years in patients with differentiated early gastric cancer according to the expanded criteria.⁸ The incidence of gastric cancer recurrence after submucosal dissection has been reported at 0-1%.⁹ In our population, curative resection (6 out of 8 patients diagnosed with adenocarcinoma) was 75%, which is close to that reported in the international literature. We believe that was due to the experience of the endoscopist in performing the procedure and the adequate patient selection which was carried out following the Godota criteria, as well as working in two well-equipped endoscopic centers with the necessary resources for resolving any immediate complication and a team skilled in performing advanced endoscopic therapy.

Serious complications of the ESD procedure are bleeding and perforation, and incidence of the latter is 0-5%. Oka et al. reported the incidence of perforation at 9.7%, when ESD was performed in cases of non-ulcerated lesions.¹⁰ In our study on 13 patients, there was only one perforation and it was not resolved endoscopically (7.6%). Despite having detected the defect during the procedure, endoscopic closure was not achieved, due to technical difficulties. The patient progressed favorably after the surgery.

Oka et al. described an incidence of bleeding of 22.6% for ulcerated lesions and 6.2% for non-ulcerated lesions. Likewise, lesion size and location were found to be risk factors for bleeding (lesions at the greater curvature tend to bleed more). In our experience, one third of the lesions were larger than 30 mm, but bleeding was not reported. Most likely that was due to the fact that both study sites had the necessary equipment for stopping immediate bleeding, such as Coagrasper forceps and other instruments, as well as having strict intra-procedural hemodynamic monitoring. The majority of lesions were located in the lower third of the stomach (92.3%) and were non-ulcerated lesions (76.9%), which could have reduced the risk for bleeding.

Our study is important because it is the first published case series on patients from 2 centers in Lima, Peru (the *Hospital Nacional* of the Health Department [MINSA, the Spanish acronym] and a private clinic) that demonstrates the feasibility and efficacy of the endoscopic technique in a larger number of cases with tumors of different sizes and locations, as well as a complication rate that coincided

with international experiences. One of the study's limitations was the reduced sample size and the short follow-up period. However, we believe it is relevant to communicate the advances made with this effective technique. More studies should be conducted to evaluate patient follow-up and assess disease recurrence.

In conclusion, ESD is an advanced endoscopic technique that enables early extraction of gastric cancer in a single specimen with no fragmentation, even in large or ulcerated lesions, favoring a lower rate of local disease recurrence and gastric cancer cure in selected cases. The procedure was performed at two centers in Lima and showed complete, curative, *en bloc* resection rates, together with complication rates similar to those reported in the international literature. Endoscopic submucosal dissection enables the reduction of surgery in selected patients with gastric cancer and paves the way for the detection of more cases of early gastric cancer through screening programs in Peru.

Ethical disclosures

Protection of human and animal subjects.

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data.

The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent.

The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Financial disclosure

No financial support was received in relation to this study.

Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Park YM, Cho E, Kang HY, et al. The effectiveness and safety of endoscopic submucosal dissection compared with endoscopic mucosal resection for early gastric cancer: A systematic review and metaanalysis. *Surg Endosc.* 2011;25:2666-77.
2. Hotta K, Oyama T, Akamatsu T, et al. A comparison of outcomes of endoscopic submucosal dissection (ESD) for early gastric neoplasms between high-volume and low-volume centers: Multicenter retrospective questionnaire study conducted by the Nagano ESD study group. *Intern Med.* 2010;49:253-9.

3. Emura F, Oda I, Ono H, et al. Disección endoscópica de la submucosa (DES). Un procedimiento superior a la mucosectomía para el tratamiento del cáncer gástrico temprano. *Rev Col Gastroenterol.* 2007;22:209–16.
4. Oda I, Gotoda T, Hamanaka H, et al. Endoscopic submucosal dissection for early gastric cancer: Technical feasibility, operation time and complications from a large consecutive series. *Dig Endosc.* 2005;17:54–8.
5. Ono H, Yao K, Fujishiro M, et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. *Dig Endosc.* 2016;28:3–15.
6. Vargas G, Chávez M, Sanchez V, et al. Tratamiento endoscópico de cancer gástrico temprano mediante disección endoscópica sub-mucosa (DES) usando el IT-KNIFE 2. *Rev Gastroenterol Perú.* 2012;32:297–302.
7. Gotoda T, Yanagisawa A, Sasako M, et al. Incidence of lymph node metastasis from early gastric cancer: Estimation with a large number of cases at two large centers. *Gastric Cancer.* 2000;3:219–25.
8. Fukunaga S, Nagami Y, Shiba M, et al. Long-term prognosis of expanded-indication differentiated-type early gastric cancer treated with endoscopic submucosal dissection or surgery using propensity score analysis. *Gastrointest Endosc.* 2017;85:143–52.
9. Gotoda T. Endoscopic resection of early gastric cancer. *Gastric Cancer.* 2007;10:1–11.
10. Oka S, Tanaka S, Kaneko I, et al. Advantage of endoscopic submucosal dissection compared with EMR for early gastric cancer. *Gastrointest Endosc.* 2006;64:877–83.