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WJH mainly publishes articles reporting research results and findings obtained in the field of hepatology and covering a wide range of topics including chronic cholestatic liver diseases, cirrhosis and its complications, clinical alcoholic liver disease, drug induced liver disease autoimmune, fatty liver disease, genetic and pediatric liver diseases, hepatocellular carcinoma, hepatic stellate cells and fibrosis, liver immunology, liver regeneration, hepatic surgery, liver transplantation, biliary tract pathophysiology, non-invasive markers of liver fibrosis, viral hepatitis.

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Case Control Study

Outcomes of endoscopic submucosal dissection in cirrhotic patients: First American cohort

Robert Luke Pecha, Fares Ayoub, Ankur Patel, Abdullah Muftah, Michael W Wright, Mai A Khalaf, Mohamed O Othman

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Abstract

BACKGROUND

Among patients with cirrhosis and pre-malignant or early malignant mucosal lesions, surgical intervention carries a much higher bleeding risk. When such lesions are discovered, endoscopic submucosal dissection (ESD) may offer curative therapy with lower risks than surgery and improved outcomes compared to traditional endoscopic resection.

AIM

To evaluate the outcomes of ESD in patients with cirrhosis.

METHODS

Patients with cirrhosis undergoing ESD between July 2015 and August 2022 were retrospectively matched in 1:2 fashion to controls based on lesion location, size, and anticoagulation use. Procedural outcomes were compared between groups.

RESULTS

A total of 64 Lesions from 59 patients were included (16 cirrhosis, 43 control).

There were no differences in patient or lesion characteristics between groups. En bloc and curative resection was achieved in 84.21%, 78.94% of the cirrhosis group and 88.89%, 68.89% of controls, respectively, with no significant differences. Cirrhotic patients had significantly higher rates of intra-procedural coagulation grasper use for control of bleeding (47.37% *vs* 20%; $P = 0.02$). There were otherwise no significant differences in adverse event rates. In the 29 patients with follow up, we found higher rates of recurrence in the cirrhosis group compared to controls (40% *vs* 5.26%; $P = 0.019$), however this effect did not persist on multivariable analysis controlling for known confounders.

CONCLUSION

ESD may be safe and effective in patients with cirrhosis. Most procedure related outcomes were not significantly different between groups. Intra-procedural bleeding requiring use of the coagulation grasper use was expectedly higher in the cirrhosis group given the known effects of liver disease on hemostasis.

Key Words: Endoscopic submucosal dissection; Cirrhosis; Advanced polypectomy; Intraprocedural bleeding; Colon cancer

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Core Tip: In our 1:2 matched case control study comparing patients with and without cirrhosis undergoing endoscopic submucosal dissection, we found that cirrhotic patients required higher rates of intraprocedural coagulation graspers use, and had higher rates of lesion recurrence among those with follow-up endoscopy.

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INTRODUCTION

For many patients with decompensated cirrhosis, liver transplant remains the only hope for long-term survival. However, prior to consideration for liver transplant, patients must undergo rigorous testing including colonoscopy and imaging to rule out malignancy. A dilemma can arise, as an extra-hepatic malignancy may be a disqualifying condition for transplant, and surgery in cirrhotic patients frequently has a mortality > 50% in patients who have a model for end stage liver disease score above 20[1,2]

Endoscopic submucosal dissection (ESD) is a minimally invasive technique that allows for endoscopic removal of pre-malignant or malignant lesions with superficial submucosal invasion. The procedure involves a submucosal injection of solution to lift the tumor base, followed by endoscopic dissection beneath the tumor margins until the tumor is removed. This technique has been utilized with a goal of curative resection for esophageal, gastric, and colorectal lesions. ESD offers advantages over other endoscopic resection techniques as tumors can be removed en-bloc allowing for margin evaluation, increased dissection depth and fewer tumor size limitations. While the outcomes of ESD are well described in non-cirrhotic patients, its safety and efficacy among patients with cirrhosis is less clear[3]. The main aim of this study is to evaluate the safety and efficacy of ESD in patients with cirrhosis.

MATERIALS AND METHODS

Study design

This was a retrospective matched cohort study conducted at a tertiary referral center. All ESD procedures were performed by a single experienced endoscopist (M.O.). This retrospective study was approved by the Baylor College of Medicine Institutional Review Board (IRB H-39179). Patients above the age of 18 with cirrhosis undergoing ESD between July 2015 and August 2022 were identified from a prospectively maintained ESD database. Patients were considered to have cirrhosis based on physician documentation, supported by clinical, laboratory, imaging [computed tomography (CT), magnetic resonance imaging, ultrasound] and/or liver biopsy findings consistent with cirrhosis. Patients with a prior history of liver transplant were excluded from the study. Patients with cirrhosis were then matched in 2:1 fashion to a control group of patients without cirrhosis based on lesion location, size, and anticoagulation use. We collected clinical, demographic, and endoscopic data from the patients in both groups using chart review of the electronic medical record. Outcomes were then compared between groups.

ESD procedure

All procedures were completed using Pentax (Montvale, NJ) video endoscopes. Lesions were carefully examined under white light and enhanced imaging (Pentax iScan) to identify features suspicious for deep invasion. Once the decision to

perform ESD was taken, the periphery of the lesion was marked with the tip of the chosen resection knife using soft coagulation current. Then, a mucosal injection using a solution of 0.004% methylene blue mixed with Hespan (6% Hetastarch in 0.9% Sodium Chloride injection) was used to provide a submucosal lift and allow mucosal incision. In esophageal, gastric and small bowel lesions, 1 mL of 1:10000 epinephrine was added to each syringe of 10 mL of injection fluid to decrease the risk of bleeding. For mucosal incision and dissection, the operator used several knives throughout the timeline of the study, including the Dual Knife, SB Knife, IT Nano (Olympus, Center Valley, PA, United States), Hybrid T-type Knife (ERBE, Tubingen, Germany), ORISE Pro Knife (Boston Scientific, Marlborough, MA, United States) and the Speedboat RS2 Knife (Creo Medical, Chepstow, United Kingdom). To treat visible vessels in certain lesions, the Coagrasper Hemostatic Forceps (Olympus, Center Valley, PA, United States) was used. Several electrosurgical generator units were used throughout the study period. The VIO300D and VIO200D (ERBE, Tubingen, Germany) and the Beamer® CE200 (CONMED, Utica, NY, United States) were used with varying settings. A rigidizing overtube (Pathfinder, Neptube Medical, Burlingame, CA, United States) or the DiLumen traction device (Lumendi, Westport, CT, United States) was used in specific cases to provide stability during resection and allow ease of scope removal and re-insertion if required. Traction was used in some cases and included several methods such as clip and line, snare, rubber band, double clip or use of the DiLumen traction device.

RESULTS

Baseline patient and lesion characteristics

Table 1 summarizes patient and lesion characteristics between groups. A total of 59 patients undergoing 64 ESD procedures were eligible for inclusion, with 16 patients (19 procedures) included in the cirrhosis cohort. There were 45 procedures performed on the 43 control patients. Overall, the median age was 65 years (interquartile range: 58–72), 35.6% (21/59) were female, and 79.7% (47/69) were Caucasian. Patients were well-matched with regards to age, gender, race, blood thinner use, intraprocedural size, fibrosis, or location of lesions, without significant differences between groups.

In the cirrhotic patient group, 10 patients (62.5%) had Child-Pugh A cirrhosis, 3 (18.75%) had Child-Pugh B cirrhosis, 1 (6.25%) had Child-Pugh C cirrhosis, while 2 had unspecified Child scores. The majority of lesions were esophageal ($n = 10$, 52.63%), followed by colorectal ($n = 5$, 26.32%), gastric ($n = 3$, 15.79%), and duodenal ($n = 1$, 5.26%). The average intraprocedural lesion diameter was 39.2 ± 13.2 mm, and no patients in this cohort were using anticoagulants. Fibrosis was noted in 4 patients during dissection (25%), and 5 patients (26.32%) had Paris IIc lesions.

In the non-cirrhotic group, the majority of lesions were esophageal ($n = 24$, 53.33%), followed by colorectal ($n = 13$, 28.89%), gastric ($n = 6$, 13.33%), and duodenal ($n = 2$, 4.44%). The average diameter of the lesions was 43.4 ± 20.5 mm, and 7 patients (15.5%) were using anticoagulation. Fibrosis was noted in 14 patients during dissection (31.11%), and 12 patients (26.67%) had Paris IIc lesions.

Between group comparison

There was a significantly higher rate of intraprocedural bleeding requiring coagulation grasper use in the cirrhosis cohort compared to the control group (47.37% *vs* 20%; $P = 0.026$). Additionally, coagulation grasper use was more frequently used for colorectal lesions in the cirrhotic cohort (60% *vs* 0%; $P = 0.012$), stomach lesions (66.66% *vs* 33.33%; $P = 0.34$), and esophageal lesions (40% *vs* 29.17%; $P = 0.54$). Closure rates (63.16% *vs* 46.67%; $P = 0.23$) were comparable between cirrhotic patients and controls, respectively.

Among the 29 (49.1%) of patients with follow-up after the procedure, there was a significantly higher rate of recurrence in the cirrhosis group [4/10 (40%) *vs* 1/19 (5.26%), $P = 0.019$]. In the cirrhotic group, 3 of these recurrences occurred in the same patient with esophageal squamous cell carcinoma, while the fourth recurrence occurred in a patient with esophageal adenocarcinoma. The single recurrence in the non-cirrhotic group occurred in a patient with esophageal adenocarcinoma. Between the cirrhotic and non-cirrhotic groups, there were no significant between-group differences in en-bloc (84.21% *vs* 88.89%; $P = 0.61$), R0 resection (78.94% *vs* 68.89%; $P = 0.41$), procedure mean duration (89.32 min *vs* 97.62 min; $P = 0.52$). Among adverse events, there was no significant difference in overall adverse event rates (21.05% *vs* 12.5%; $P = 0.30$), surgery for any cause (10.52% *vs* 9.76%; $P = 0.83$), admission (36.84% *vs* 57.78%; $P = 0.13$), or delayed bleeding (5.26% *vs* 11.11%; $P = 0.46$) between the cirrhotic and non-cirrhotic cohorts (**Table 2**).

Multivariate analysis

Increased rates of lesion recurrence after ESD have been associated with larger size of lesion, and the presence of scar, as well as incomplete resection and piecemeal resections[4,5]. As there was (LP1) a difference in bleeding rates between the cirrhotic and non-cirrhotic cohorts, but no difference in incomplete or piecemeal resections, we performed a multivariate regression analysis adjusting for lesion size, bleeding requiring coagulation grasper use and fibrosis noted during the resection. After controlling for these variables, there was no significant association between cirrhosis and an increased rate of lesion recurrence (**Table 3**).

DISCUSSION

The majority of studies evaluating ESD in cirrhosis have come from non-western populations, and both causes of cirrhosis and rates of gastric cancer among other malignancies vary widely between the East and the West[6-8]. In this

Table 1 Baseline characteristics of the cirrhotic and non-cirrhotic cohorts, *n* (%) / mean \pm SD

	Cirrhosis (16 patients, 19 procedures)	Controls (43 patients, 45 procedures)	<i>P</i> value
Age (yr)	66.38 \pm 8.08	64.81 \pm 11.50	0.57
Gender (male)	10 (62.50)	28 (65.12)	0.85
Race (white)	14 (87.5)	33 (76.74)	0.36
Anticoagulation (yes)	0	7 (15.5)	0.09
Intraprocedural diameter (mm)	39.21 \pm 13.21	43.44 \pm 20.49	0.34
Fibrosis (yes)	4 (25)	14 (31.11)	0.55
Location of lesion			
Colorectal	5 (26.32)	13 (28.89)	0.83
Stomach	3 (15.79)	6 (13.33)	0.80
Esophagus	10 (52.63)	24 (53.33)	0.96
Duodenum	1 (5.26)	2 (4.44)	0.89
Child Classification			
A	10 (62.5)		
B	3 (18.75)		
C	1 (6.25)		
Unspecified	2 (12.5)		
Paris IIc (depressed) lesion	5 (26.32)	12 (26.67)	0.98

first United States retrospective matched cohort study of 16 cirrhotic patients matched to 43 controls, we found that ESD was safe and effective, with comparable outcomes between groups. Expectedly, we found a significantly higher rate of intra-procedural bleeding requiring coagulation grasper use in patients with cirrhosis, without an increased rate of post-procedural adverse events such as delayed bleeding. Recurrence was noted to be higher in the cirrhotic cohort on univariate analysis, and the majority of recurrences in the cirrhosis cohort were limited to a single patient. After adjusting for known confounders recurrence rates were comparable between groups.

The principal complications associated with ESD are bleeding and perforation. Bleeding rates in ESD have been reported as 3.4%-7.2% for gastric procedures, 3.1%-22% for duodenal lesions, and may be as high as 13% for colonic lesions, although these results have varied greatly across studies[9-12]. Perforation rates similarly vary depending on location with the highest reported rates of 33% for duodenal lesions, 4.5% for gastric lesions, and 10% for colorectal lesions, though only a small number of perforations require surgical repair, approximately 0.5%[13-15].

While the complications of ESD are relatively well described in non-cirrhotic patients, there is an ongoing question about its safety and efficacy among cirrhotics. This is particularly important given the well-described dysregulation of primary and secondary hemostasis among cirrhotics that may put patients at higher risk for bleeding[16]. One study by Soh *et al*[17] evaluated 1267 colonic polypectomies and concluded that patients with Child-Pugh B or C were at higher risk for both immediate and delayed bleeding compared to Child-Pugh A patients (17.5% *vs* 6.3% and 4.4% *vs* 0.7%, respectively)[17]. Two studies evaluating short-term outcomes evaluating gastric ESD among patients with cirrhosis have found that there was no difference in outcomes between cirrhotics and non-cirrhotics, though these were small studies from Japan and may not apply to a western population[18,19]. A third small study from Korea evaluated long-term outcomes of matched cohorts with and without cirrhosis who had undergone ESD for early gastric cancer, and found no significant differences in bleeding, perforation risks, *en-bloc*, or complete resection rates, but found that the cirrhosis cohort had significantly higher rates of recurrence[20]. Other small studies have evaluated primarily gastric and esophageal ESD in cirrhotic and have found similar findings, with no significant difference in bleeding[12,21,22]. One meta-analysis that included 319 patients who underwent ESD evaluated outcomes among patients with cirrhosis who underwent both EMR or ESD and reported pooled data[23]. Delayed (LP1) bleeding, perforation, and short-term mortality were equivalent, but rates of immediate bleeding between cirrhosis and non-cirrhosis patients were significantly different [13.3% *vs* 5.2%, relative risk 1.57 (95%CI: 1.2-2.1)].

Overall, adverse event rates in our study are similar to those reported in the literature, with delayed bleeding rates in our cirrhotic and noncirrhotic cohorts of 5.26% and 11.11%, respectively. However, higher bleeding rates requiring coagulation grasper use in the cirrhotic group suggests that coagulopathy plays a significant intraprocedural role. Notably, our cirrhotic cohort was primarily composed of Child-Pugh a cirrhotic, likely under-estimating bleeding risk compared to patients with more advanced decompensated cirrhosis. Large perforations were not seen in our cohort, but three patients had pneumoperitoneum or pneumomediastinum, and one micro-perforation was noted in the non-cirrhotic cohort without significant between-group differences.

Table 2 Procedural outcomes of cirrhotic and non-cirrhotic cohorts, *n* (%)

	Cirrhosis (16 patients, 19 procedures)	Controls (43 patients, 45 procedures)	<i>P</i> value
Primary outcomes			
En bloc resection	16 (84.21)	40 (88.89)	0.61
R0 resection	15 (78.94)	31 (68.89)	0.41
Curative resection	14 (73.68)	29 (64.44)	0.47
Procedure duration (mean \pm SD; min)	89.32 \pm 40.61	97.62 \pm 57.3	0.52
Follow-up	10 (52.63)	19 (42.22)	0.44
Recurrence	4 (40)	1 (5.26)	0.019
Adverse events			
Any adverse event	4 (21.05)	5 (12.5)	0.30
Surgery for any cause	2 (10.52)	4 (9.76)	0.83
Admitted	7 (36.84)	26 (57.78)	0.13
Pneumoperitoneum/pneumomediastinum	1 (5.26)	2 (4.44)	0.89
Micro-perforation	0	1 (2.22)	1.00
Delayed bleeding (yes)	1 (5.26)	5 (11.11)	0.46
Procedural characteristics			
Closure (yes)	12 (63.16)	21 (46.67)	0.23
Use of traction (yes)	1 (5.26)	3 (6.67)	0.83
Use of a stabilization device (yes)	4 (21.05)	3 (6.67)	0.09
Use of coagrasper (yes)	9 (47.37)	9 (20)	0.026
Coagrasper use by location			
Colorectal	3 (60)	0	0.012
Stomach	2 (66.66)	2 (33.33)	0.34
Esophagus	4 (40)	7 (29.17)	0.54
Duodenum	0	0	

Table 3 Multivariate regression analysis

Risk of recurrence at follow up	Odds ratio	Robust standard error	<i>P</i> value	Lower bound of 95%CI	Upper bound of 95%CI
Lesion size in mm	1.03	0.19	0.103	0.99	1.06
Cirrhosis	13.77	18.95	0.057	0.92	204.47
Bleeding requiring coagulation grasper use	0.51	0.057	0.554	0.056	4.66
Presence of fibrosis	0.73	0.90	0.802	0.06	8.25

Lesion recurrence (or residual neoplasia) after ESD can occur and is influenced by several factors. Primarily, piecemeal resection, poor differentiation, and positive/indeterminate vertical margin have been identified as the strongest risk factors in a recent large multicenter analysis[24]. While overall follow up rates were low, we found no significant association between cirrhosis and disease recurrence after multivariate analysis. The relatively low follow up rate is most likely due to our status as a tertiary referral center where many patients are referred from distant locations and often choose to return to their referring physician for surveillance endoscopy locally.

Our study is limited by a small study size, the retrospective nature of the study, and by the limited long-term follow-up. Our cirrhotic cohort was primarily composed of Child-Pugh class a cirrhotic, likely underestimating bleeding risk in higher-risk cirrhotic patients. All procedures were performed at a tertiary academic center by an experienced endoscopist, limiting generalizability. Future studies should focus on larger cohort sizes with higher numbers of patients with advanced cirrhosis and long-term follow-up.

CONCLUSION

In this first United States retrospective matched cohort study of 16 cirrhotic patients matched to 43 controls, we found that ESD may be safe and effective in patients with cirrhosis. Most procedure related outcomes were not significantly different between groups. Intra-procedural bleeding requiring use of the coagulation grasper use was expectedly higher in the cirrhosis group given the known effects of liver disease on hemostasis.

FOOTNOTES

Author contributions: Pecha RL, Ayoub F performed study conceptualization, data collection, statistical analysis, drafted and revised the manuscript; Khalaf MA performed study conceptualization, data collection; Patel A, Muftah A, Wright MW performed data collection; Othman MO performed study conceptualization, drafted and revised the manuscript.

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REFERENCES

- Martin P, DiMartini A, Feng S, Brown R Jr, Fallon M. Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Hepatology* 2014; **59**: 1144-1165 [PMID: 24716201 DOI: 10.1002/hep.26972]
- Teh SH, Nagorney DM, Stevens SR, Offord KP, Therneau TM, Plevak DJ, Talwalkar JA, Kim WR, Kamath PS. Risk factors for mortality after surgery in patients with cirrhosis. *Gastroenterology* 2007; **132**: 1261-1269 [PMID: 17408652 DOI: 10.1053/j.gastro.2007.01.040]
- Draganov PV, Aihara H, Karasik MS, Ngamruengphong S, Aadam AA, Othman MO, Sharma N, Grimm IS, Rostom A, Elmunzer BJ, Jawaide SA, Westerveld D, Perbtani YB, Hoffman BJ, Schlachterman A, Siegel A, Coman RM, Wang AY, Yang D. Endoscopic Submucosal Dissection in North America: A Large Prospective Multicenter Study. *Gastroenterology* 2021; **160**: 2317-2327.e2 [PMID: 33610532 DOI: 10.1053/j.gastro.2021.02.036]
- Ryu DG, Kim SJ, Choi CW, Park SB, Nam HS, Lee SH, Hwang SH. Local Recurrence after Endoscopic Submucosal Dissection of Early Gastric Cancer. *J Clin Med* 2023; **12** [PMID: 36902804 DOI: 10.3390/jcm12052018]
- Ohata K, Kobayashi N, Sakai E, Takeuchi Y, Chino A, Takamaru H, Kodashima S, Hotta K, Harada K, Ikematsu H, Uraoka T, Murakami T, Tsuji S, Abe T, Katagiri A, Hori S, Michida T, Suzuki T, Fukuzawa M, Kiriya S, Fukase K, Murakami Y, Ishikawa H, Saito Y. Long-term Outcomes After Endoscopic Submucosal Dissection for Large Colorectal Epithelial Neoplasms: A Prospective, Multicenter, Cohort Trial From Japan. *Gastroenterology* 2022; **163**: 1423-1434.e2 [PMID: 35810779 DOI: 10.1053/j.gastro.2022.07.002]
- Sitarz R, Skierucha M, Mielko J, Offerhaus GJA, Maciejewski R, Polkowski WP. Gastric cancer: epidemiology, prevention, classification, and treatment. *Cancer Manag Res* 2018; **10**: 239-248 [PMID: 29445300 DOI: 10.2147/CMAR.S149619]
- Zhai M, Long J, Liu S, Liu C, Li L, Yang L, Li Y, Shu B. The burden of liver cirrhosis and underlying etiologies: results from the global burden of disease study 2017. *Aging (Albany NY)* 2021; **13**: 279-300 [PMID: 33436531 DOI: 10.18632/aging.104127]
- Cheemerla S, Balakrishnan M. Global Epidemiology of Chronic Liver Disease. *Clin Liver Dis (Hoboken)* 2021; **17**: 365-370 [PMID: 33436531 DOI: 10.18632/aging.104127]

- 34136143 DOI: [10.1002/cld.1061](https://doi.org/10.1002/cld.1061)]
- 9 **Inoue H**, Minami H, Kaga M, Sato Y, Kudo SE. Endoscopic mucosal resection and endoscopic submucosal dissection for esophageal dysplasia and carcinoma. *Gastrointest Endosc Clin N Am* 2010; **20**: 25-34, v [PMID: [19951792](https://pubmed.ncbi.nlm.nih.gov/19951792/) DOI: [10.1016/j.giec.2009.08.005](https://doi.org/10.1016/j.giec.2009.08.005)]
- 10 **Rahmi G**, Hotayt B, Chaussade S, Lepilliez V, Giovannini M, Coumaros D, Charachon A, Cholet F, Laquière A, Samaha E, Prat F, Ponchon T, Bories E, Robaszekiewicz M, Boustière C, Cellier C. Endoscopic submucosal dissection for superficial rectal tumors: prospective evaluation in France. *Endoscopy* 2014; **46**: 670-676 [PMID: [24977400](https://pubmed.ncbi.nlm.nih.gov/24977400/) DOI: [10.1055/s-0034-1365810](https://doi.org/10.1055/s-0034-1365810)]
- 11 **Kim YJ**, Kim ES, Cho KB, Park KS, Jang BK, Chung WJ, Hwang JS. Comparison of clinical outcomes among different endoscopic resection methods for treating colorectal neoplasia. *Dig Dis Sci* 2013; **58**: 1727-1736 [PMID: [23385636](https://pubmed.ncbi.nlm.nih.gov/23385636/) DOI: [10.1007/s10620-013-2560-x](https://doi.org/10.1007/s10620-013-2560-x)]
- 12 **Bialek A**, Pertkiewicz J, Karpińska K, Marlicz W, Bielicki D, Starzyńska T. Treatment of large colorectal neoplasms by endoscopic submucosal dissection: a European single-center study. *Eur J Gastroenterol Hepatol* 2014; **26**: 607-615 [PMID: [24743502](https://pubmed.ncbi.nlm.nih.gov/24743502/) DOI: [10.1097/MEG.0000000000000079](https://doi.org/10.1097/MEG.0000000000000079)]
- 13 **Lee EJ**, Lee JB, Lee SH, Kim DS, Lee DH, Youk EG. Endoscopic submucosal dissection for colorectal tumors--1,000 colorectal ESD cases: one specialized institute's experiences. *Surg Endosc* 2013; **27**: 31-39 [PMID: [22729707](https://pubmed.ncbi.nlm.nih.gov/22729707/) DOI: [10.1007/s00464-012-2403-4](https://doi.org/10.1007/s00464-012-2403-4)]
- 14 **Pérez-Cuadrado-Robles E**, Quénéhervé L, Margos W, Moreels TG, Yeung R, Piessevaux H, Coron E, Jouret-Mourin A, Deprez PH. ESD versus EMR in non-ampullary superficial duodenal tumors: a systematic review and meta-analysis. *Endosc Int Open* 2018; **6**: E998-E1007 [PMID: [30083591](https://pubmed.ncbi.nlm.nih.gov/30083591/) DOI: [10.1055/a-0579-9050](https://doi.org/10.1055/a-0579-9050)]
- 15 **Oda I**, Saito D, Tada M, Iishi H, Tanabe S, Oyama T, Doi T, Otani Y, Fujisaki J, Ajioka Y, Hamada T, Inoue H, Gotoda T, Yoshida S. A multicenter retrospective study of endoscopic resection for early gastric cancer. *Gastric Cancer* 2006; **9**: 262-270 [PMID: [17235627](https://pubmed.ncbi.nlm.nih.gov/17235627/) DOI: [10.1007/s10120-006-0389-0](https://doi.org/10.1007/s10120-006-0389-0)]
- 16 **O'Leary JG**, Greenberg CS, Patton HM, Caldwell SH. AGA Clinical Practice Update: Coagulation in Cirrhosis. *Gastroenterology* 2019; **157**: 34-43.e1 [PMID: [30986390](https://pubmed.ncbi.nlm.nih.gov/30986390/) DOI: [10.1053/j.gastro.2019.03.070](https://doi.org/10.1053/j.gastro.2019.03.070)]
- 17 **Soh H**, Chun J, Hong SW, Park S, Lee YB, Lee HJ, Cho EJ, Lee JH, Yu SJ, Im JP, Kim YJ, Kim JS, Yoon JH. Child-Pugh B or C Cirrhosis Increases the Risk for Bleeding Following Colonoscopic Polypectomy. *Gut Liver* 2020; **14**: 755-764 [PMID: [31816672](https://pubmed.ncbi.nlm.nih.gov/31816672/) DOI: [10.5009/gnl19131](https://doi.org/10.5009/gnl19131)]
- 18 **Kato M**, Nishida T, Hamasaki T, Kawai N, Yoshio T, Egawa S, Yamamoto K, Ogiyama H, Komori M, Nakahara M, Yabuta T, Nishihara A, Hayashi Y, Yamada T, Takehara T. Outcomes of ESD for patients with early gastric cancer and comorbid liver cirrhosis: a propensity score analysis. *Surg Endosc* 2015; **29**: 1560-1566 [PMID: [25294528](https://pubmed.ncbi.nlm.nih.gov/25294528/) DOI: [10.1007/s00464-014-3841-y](https://doi.org/10.1007/s00464-014-3841-y)]
- 19 **Choi YK**, Ahn JY, Kim DH, Jung KW, Na HK, Choi KD, Lee JH, Song HJ, Lee GH, Jung HY. Efficacy and safety of endoscopic submucosal dissection for gastric neoplasms in patients with compensated liver cirrhosis: a propensity score-matched case-control study. *Gastrointest Endosc* 2018; **87**: 1423-1431.e3 [PMID: [29410022](https://pubmed.ncbi.nlm.nih.gov/29410022/) DOI: [10.1016/j.gie.2018.01.035](https://doi.org/10.1016/j.gie.2018.01.035)]
- 20 **Kim SH**, Joo MK, Yoo AY, Kim SM, Kim WS, Lee BJ, Park JJ, Chun HJ, Lee SW. Long-term outcome of the endoscopic submucosal dissection of early gastric cancer: A comparison between patients with and without liver cirrhosis. *Oncol Lett* 2022; **24**: 404 [PMID: [36276485](https://pubmed.ncbi.nlm.nih.gov/36276485/) DOI: [10.3892/ol.2022.13524](https://doi.org/10.3892/ol.2022.13524)]
- 21 **Ahlenstiel G**, Hourigan LF, Brown G, Zanati S, Williams SJ, Singh R, Moss A, Sonson R, Bourke MJ; Australian Colonic Endoscopic Mucosal Resection (ACE) Study Group. Actual endoscopic versus predicted surgical mortality for treatment of advanced mucosal neoplasia of the colon. *Gastrointest Endosc* 2014; **80**: 668-676 [PMID: [24916925](https://pubmed.ncbi.nlm.nih.gov/24916925/) DOI: [10.1016/j.gie.2014.04.015](https://doi.org/10.1016/j.gie.2014.04.015)]
- 22 **Choe WH**, Kim JH, Park JH, Kim HU, Cho DH, Lee SP, Lee TY, Lee SY, Sung IK, Park HS, Shim CS. Endoscopic Submucosal Dissection of Early Gastric Cancer in Patients with Liver Cirrhosis. *Dig Dis Sci* 2018; **63**: 466-473 [PMID: [29282635](https://pubmed.ncbi.nlm.nih.gov/29282635/) DOI: [10.1007/s10620-017-4814-5](https://doi.org/10.1007/s10620-017-4814-5)]
- 23 **Chandan S**, Deliwala S, Khan SR, Ramai D, Mohan BP, Bilal M, Facciorusso A, Kassab LL, Kamal F, Dhindsa B, Perisetti A, Adler DG. Advanced Endoscopic Resection Techniques in Cirrhosis-A Systematic Review and Meta-Analysis of Outcomes. *Dig Dis Sci* 2022; **67**: 4813-4826 [PMID: [34993682](https://pubmed.ncbi.nlm.nih.gov/34993682/) DOI: [10.1007/s10620-021-07364-w](https://doi.org/10.1007/s10620-021-07364-w)]
- 24 **Santos-Antunes J**, Pioche M, Ramos-Zabala F, Cecinato P, Gallego Rojo FJ, Barreiro P, Félix C, Sferrazza S, Berr F, Wagner A, Lemmers A, Figueiredo Ferreira M, Albéniz E, Uchima H, Küttner-Magalhães R, Fernandes C, Morais R, Gupta S, Martinho-Dias D, Rios E, Faria-Ramos I, Marques M, Bourke MJ, Macedo G. Risk of residual neoplasia after a noncurative colorectal endoscopic submucosal dissection for malignant lesions: a multinational study. *Endoscopy* 2023; **55**: 235-244 [PMID: [35863354](https://pubmed.ncbi.nlm.nih.gov/35863354/) DOI: [10.1055/a-1906-8000](https://doi.org/10.1055/a-1906-8000)]



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