Two Cases of 10 cm Circumferential Esophageal Endoscopic Submucosal Dissection and Subsequent Endoscopic and Medical Management

Ki-Yoon Kim, M.D.
Mentor: Gregory Haber, M.D.
Advanced Therapeutic Endoscopy Fellow
NYU Langone Health

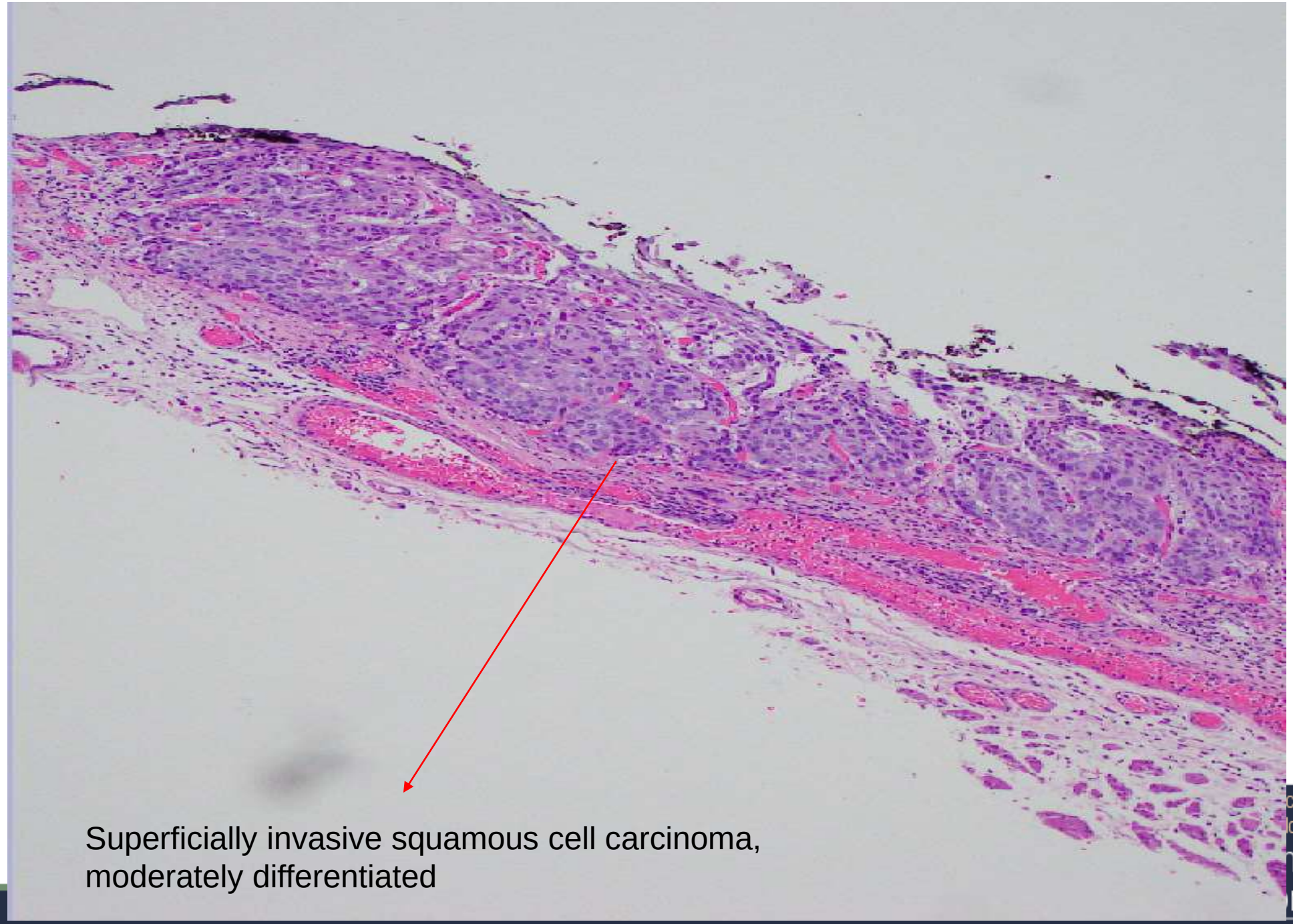
New York Society for Gastroenterology and Endoscopy
46th Annual New York Course

Cases

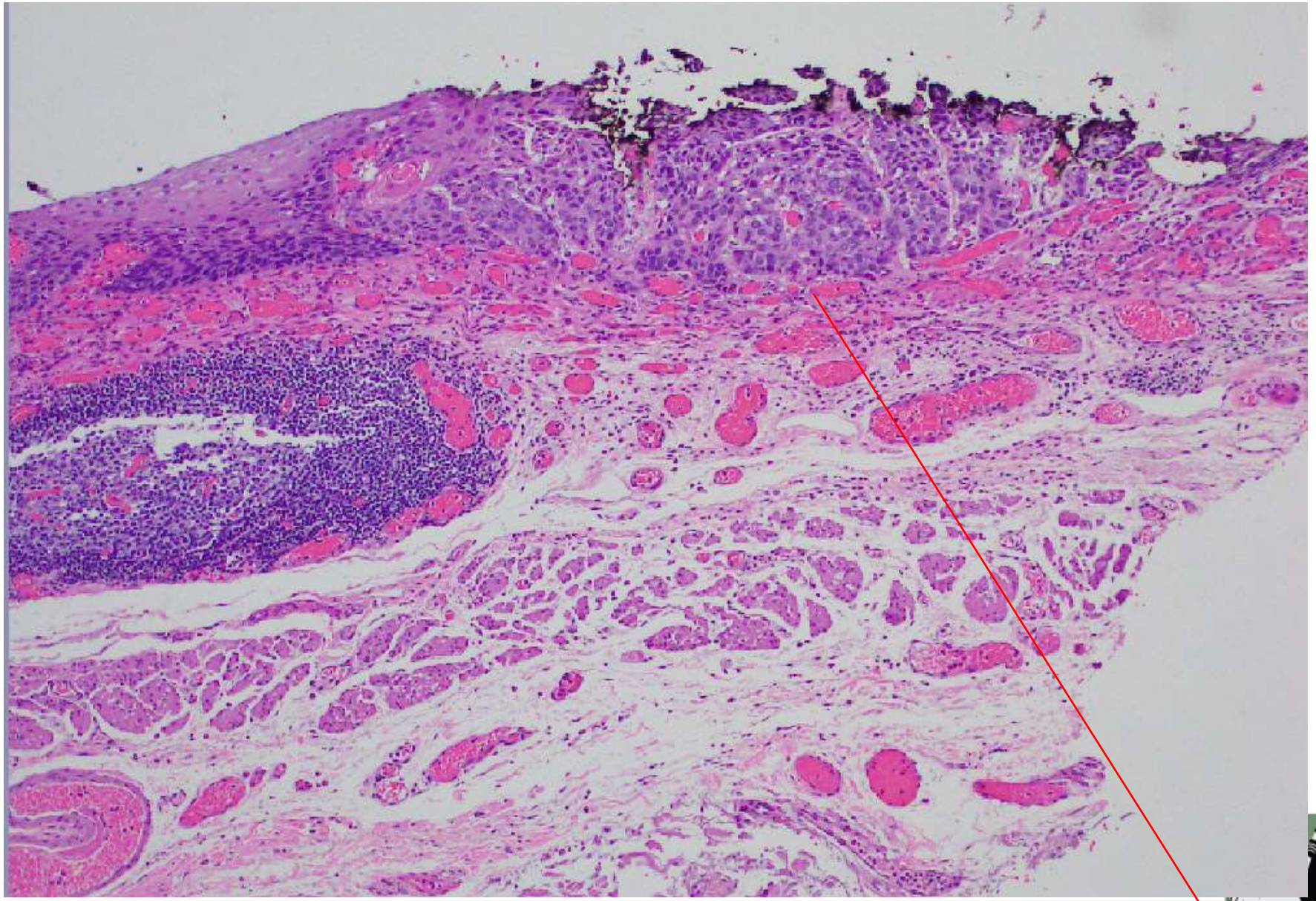
- 74 yo woman with severe PAD s/p stent with revascularization of superior femoral artery on plavix and afib on eliquis who presents with **esophageal SCC who presents for circumferential ESD.**
- 76 yo man who presents with **esophageal SCC for circumferential ESD.**
- Both patients had **en bloc, R0 resection of SCC resected in 10 cm segment, post ESD pura-stat application**
- Both started on **weekly prednisone taper starting at 50 mg qday.**

Case Video

Video

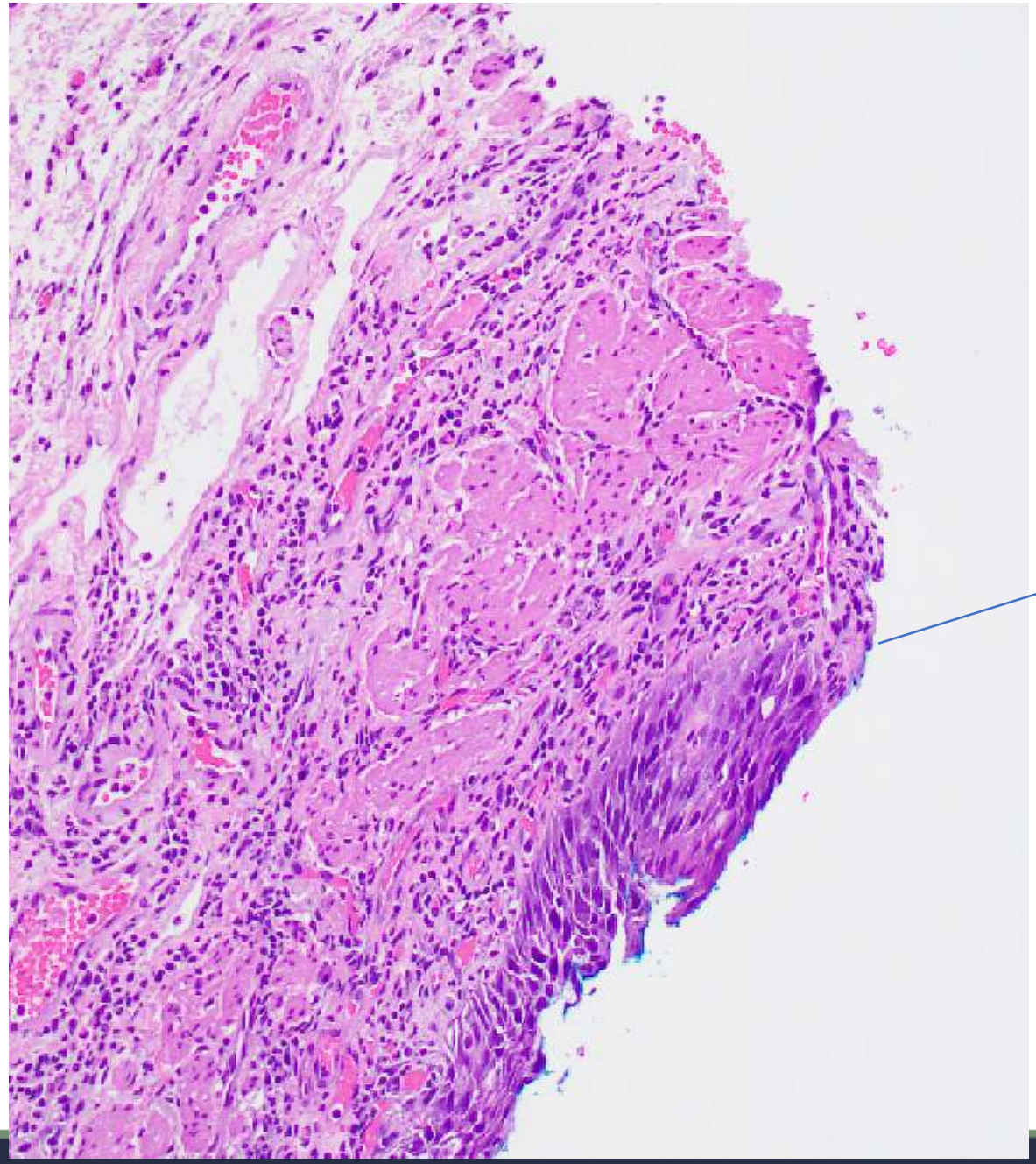


Superficially invasive squamous cell carcinoma,
moderately differentiated



New York Society for Gastroenterology and Endoscopy
46th Annual New York Course

Superficially invasive squamous cell carcinoma, moderately differentiated



HGD at mucosal margin

Endoscopic and Medical Management Post Circumferential ESD

Esophagus (2019) 16:1–24
https://doi.org/10.1007/s10388-018-0641-9

SPECIAL ARTICLE

Esophageal cancer practice guidelines 2017 edited by the Japan Esophageal Society: part 1

Yuko Kitagawa[1] · Takashi Uno[2] · Tsuneo Oyama[3] · Ken Kato[4] · Hiroyuki Kato[5] · Hirofumi Kawakubo[1] · Osamu Kawamura[6] · Motoyasu Kusano[6] · Hiroyuki Kuwano[7] · Hiroya Takeuchi[8] · Yasushi Toh[9] · Yuichiro Doki[10] · Yoshio Naomoto[11] · Kenji Nemoto[12] · Eisuke Booka[1] · Hisahiro Matsubara[13] · Tatsuya Miyazaki[7] · Manabu Muto[14] · Akio Yanagisawa[15] · Masahiro Yoshida[16]

Received: 19 August 2018 / Accepted: 22 August 2018 / Published online: 31 August 2018

Kitagawa et al *Esophagus* 2019

Endoscopic and Medical Management Post Circumferential ESD

"For a lesion involving ***≥ 3/4th of the esophageal circumference (MDC; Mucosal Defect Circumference), a preventive strategy against stenosis should be considered****, as such lesions are associated with a high risk of development of stenosis after ER."*

Kitagawa *Esophagus* 2019

Endoscopic and Medical Management Post Circumferential ESD

- **Katada et al. *GIE* 2003**
  - >3/4th circumferential EMR of 216 pts with esophageal CA
  - **13 of 216 patients** had post EMR stenosis
- **Ono et al. *Endoscopy* 2009**
  - >3/4th circumferential esophageal ESD of 6 pts with esophageal CA
  - **5 of 6 patients** had post ESD esophageal stenosis
- **Shi et al. *Endoscopy* 2014**
  - >3/4th circumferential esophageal ESD of 34 pts with esophageal CA
  - **32 of 34 patients** had post ESD esophageal stenosis
- **Meta-analysis of Katada, Ono, and Shi**
  - Risk ratio of stenosis in >3/4th circumferential endoscopy resection
  - **30.93 [95% CI: 18.85–50.76, p < 0.001]**

Katada *GIE* 2003
Ono *Endoscopy* 2009
Shi *Endoscopy* 2014
Kitagawa *Esophagus* 2019

Endoscopic and Medical Management Post Circumferential ESD

"There is strong evidence to recommend any one of the ***prophylactic balloon dilatation, local steroid injection, or oral steroid administration*** *for the prevention of stenosis after endoscopic treatment (Rate of consensus: 90% [18/20], strength of evidence: A)."*

Kitagawa et al *Esophagus* 2019

Prophylactic Endoscopy Balloon Dilation

- **Inoue et al. *Stomach Intestine* 2009**
  - Prophylactic EBD with 18-20 mm CRE balloon after circumferential ESD
  - **Every 1-3 days** for median number of **35 procedures over 100 days**
  - Prevented stenosis in **all 6 patients**
- **Ezoe et al. *J. Clin. Gastroenterol.* 2011**
  - Prophylactic EBD among patients with > 3/4th circumferential EMR/ESD.
  - Weekly CRE dilation with 18-20 mm
  - Incidence of stenosis in prophylactic EBD vs control **(59% vs. 92%)**
  - Duration of EBD in prophylactic vs control group **(29 days vs. 78 days)**
- **Limitations**
  - Frequent procedures, cumulative risks of perforation, financial burden
  - **Inferior to oral steroid therapy**

Inoue Stomach Intestine 2009
Ezoe J. Clin. Gastroenterol 2011
Hikichi J Clin Med 2021

Steroid Injection Therapy

- **Hanaoka Endoscopy 2012**
  - "Gold Standard," one-time triamcinolone injection immediately after ESD
  - **25-gauge needle with 5 mg/ml triamcinolone**
  - Inject into submucosal tissue of the ulcer bed in 0.5–1.0mL increments (20–40 punctures).
  - Initially margins of the ulcer followed by linear injections distal to proximal side of the ulcer margin, avoiding muscle layers
  - In patients with > 3/4th esophageal circumferential resection (but not fully circumferential), stenosis rate in treatment vs control **(10% vs. 66%, respectively).**

Hanaoka *Endoscopy* 2012

Oral Steroid Therapy

- **Yamaguchi *et al. GIE* 2011**
  - **PO Prednisolone 30 mg per day** starting on the third day after ESD
  - Titrated in weekly decrements of 5 mg per day, discontinued after eight weeks.
  - Among patients with > 3/4 MDC, including total MDC, the incidence of stricture lower with PO prednisolone compared with prophylactic EBD **(5.3% vs. 31.8%, respectively).**

Yamaguchi *GIE* 2011

Endoscopic and Medical Management Post Circumferential ESD

- **Japan Clinical Oncology Study Group (JCOG) RCT for PO steroid vs steroid injection**
  - Hanoka's regimen for steroid injection
  - Yamaguchi's regimen for oral steroid administration
- **Eligibility of cases**
  - Squamous cell carcinoma (SCC) lesions with more than 1/2 circumference but less than the total circumference
  - SCC lesions with less than 5 cm in longitudinal diameter
  - The enrollment of cases completed, results pending

Kitagawa et al *Esophagus* 2019

Acknowledgements

- **Gregory Haber, M.D.**
- **Lauren Khanna, M.D.**
- **Tamas Gonda, M.D.**
- **Janec Eileen, M.D.**
- **Jonathan Cohen, M.D.**
- **NYSGE**
- **NYU Gastroenterology**

Alternative Methods of Stricture Prevention

Table 1. Prevention of stricture after endoscopic submucosal dissection for esophageal for esophageal squamous cell carcinoma.

Prophylactic EBD	
Steroid therapy	Steroid injection therapy (ex. TA) Oral steroid administration (ex. PSL) Other steroid administration: combination of TA injection with oral PSL, TA injection with PGA, TA injection with EBD, TA-filling method
Drugs other than steroids	Botulinum toxin injection therapy Oral tranilast
Tissue shielding method	PGA sheet Carboxymethyl cellulose sheet
Regenerative medicine	Autologous oral mucosal epithelial cell sheet transplantation, et al.
Stent placement	Temporary metal stent placement, bioabsorbable stent placement

EBD, endoscopic balloon dilation; TA, triamcinolone acetate; PSL, prednisolone; PGA, polyglycolic acid.

Steroid Therapy

Table 2. Comparative studies of steroid therapy in the prevention of stricture after endoscopic submucosal dissection for esophageal squamous cell carcinoma, mainly compared with no therapy or prophylactic endoscopic balloon dilation.

Author	Year	Study Design	Protocol Therapy	Mucosal Deffect Circumference	Case Numbers (Protocol: Control)	Incidence of Stricture (Protocol vs. Control)	*p*-Value *1
Hashimoto [21]	2011	Retrospective, historical control	TA injection	>3/4	21:20 (untreated)	19% vs. 75%	<0.001
Yamaguchi [16] *2	2011	Retrospective, historical control	Oral PSL for eight weeks	>3/4	19:22 (prophylactic EBD) *3	5.3% vs. 31.8%	0.03
Isomoto [22] *2	2011	Retrospective, historical control	Oral PSL for eight weeks	Total circumference	4:3 (prophylactic EBD)	50% vs. 100%	N.S.
Hanaoka [23]	2012	Prospective, historical control	TA injection	>3/4	30:29 (untreated)	10% vs. 66%	<0.001
Takahashi [24]	2012	Prospective, randomized	TA injection	Lesion > 2/3	16:16 (untreated) *4	62.5% vs. 87.5%	0.22
Sato [25]	2013	Prospective, historical control	Oral PSL for eight weeks + prophylactic EBD	Total circumference	10:13 (prophylactic EBD) *5	100% vs. 100%	N.S.
Mori [26]	2013	Prospective, randomized	① TA gel + prophylactic EBD ② TA injection + prophylactic EBD	>2/3	20:21 (①:②)	N/A *6	N/A
Kadota [27]	2016	Retrospective	① TA injection + Oral PSL for eight weeks ② TA injection	>3/4	29:53:33 (①:②: untreated)	41% vs. 43% Vs. 67% (①:②: untreated)	0.073 (① vs. untreated) 0.046 (② vs. untreated)
Nagami [28]	2017	Retrospective, matched	TA injection	>2/3	37:37 (untreated)	18.9% vs. 45.9%	0.016
Zhou [29]	2017	Retrospective	Oral PSL for 12 weeks	>3/4 *7	13:10 (untreated)	23.1% vs. 80%	<0.05
Iizuka [30]	2018	Retrospective, historical control	① Oral PSL for 18 weeks (±TA injection) *8 ② Oral PSL for eight weeks (±TA injection) *8	Total circumference	11:11 (①:②)	36.4% vs. 82%	0.04
Chu [31]	2019	Retrospective	TA injection + Oral PSL for eight weeks	>2/3	34:36 (untreated)	14.7% vs. 52.8%	0.001
Pih [32]	2019	Retrospective	① Oral PSL ② TA injection	>3/4	25:6:22 (①: ②: untreated)	20% vs. 33.3% vs. 50% (①:②: untreated)	0.037 (① vs. untreated) 0.046 (①+② vs. untreated)

New York Society for Gastroenterology and Endoscopy
46th Annual New York Course

Hikichi J Clin Med 2021

Steroid Therapy in > 3/4th Circumference

Table 3. Effect of preventive steroid therapy after non-total circumferential endoscopic submucosal dissection for esophageal squamous cell carcinoma.

Author	Year	Study Design	Drugs	Dose	Timing of Intervention	Mucosal Defect Circumference	Incidence of Stricture
Steroid injection							
Hashimoto [21]	2011	Retrospective	TA	18–62 mg	Day 3, 7, 10 (3 times)	>3/4	19% (4/21)
Hanaoka [23]	2012	Prospective	TA	100 mg	Day 0	>3/4	10% (3/30)
Yamaguchi [33]	2013	Retrospective	TA	40 mg (<3 cm in longitudinal mucosal defect), 80 mg (≥ 3 cm)	Day 0 (>9/10 in circumference or ≥5 cm in longitudinal mucosal defect: additionally Day 21)	>3/4	4.3% (1/23)
Takahashi [24]	2015	Prospective, randomized	TA	40 mg	Day 0	>2/3 (lesion *)	45.5% (5/11)
Hanaoka [34]	2016	Retrospective	TA	50–100 mg	Day 0	>3/4	11.3% (13/115)
Kadota [27]	2016	Retrospective	TA	50 mg	Day 3, 7, 10 (three times) →Day 1 or Day 0 (once)	>3/4	36.2% (17/47)
Nagami [28]	2017	Retrospective	TA	80 mg	Day 0	>2/3	20.7% (12/58)
Iizuka [35]	2017	Retrospective	TA	40 mg	Day 0	>1/2	10.3% (3/29)
Nagami [36]	2018	Retrospective	TA	80 mg	Day 0	>2/3	16.8% (17/101)
Hashimoto [37]	2019	Retrospective	TA	40–100 mg (2nd session: 16–50 mg)	Day 0, 14 (two times)	>3/4	45.7% (16/35)
Oral steroid administration							
Yamaguchi [16]	2011	Retrospective	PSL	30 mg	Tapering gradually for eight weeks	>3/4	6.3% (1/16)
Yamaguchi [33]	2013	Retrospective	PSL	30 mg	Tapering gradually for 6–12 weeks	>3/4	10% (4/40)
Kataoka [38]	2015	Retrospective	PSL	30 mg	Tapering gradually for three weeks	>3/4	14.3% (2/14)
Modified or hybrid steroid therapy							
Kadota [27]	2016	Retrospective	TA + Oral PSL	TA: 50 mg PSL: 30 mg	TA: Day 3, 7, 10 (three times) →Day 1 or Day 0 (once) PSL: tapering gradually for eight weeks	>3/4	13.3% (2/15)
Nagami [39]	2016	Retrospective	TA injection + PGA	TA: 80 mg	Day 0	>5/6	25% (1/4)
Sakaguchi [40]	2016	Retrospective	TA injection + PGA	TA: 40 mg	Day 0	>3/4	11.1% (1/9)
Nakamura [41]	2017	Prospective	Pulse therapy	mPSL: 500 mg (intravenous administration)	Day 1, 2, 3 (three consecutive days)	>3/4	66.7% (6/9)
Shibagaki [42]	2018	Retrospective	TA filling method	TA: 80 mg	Day 1 and Day 7 and when mild stricture was found	>3/4	6.7% (1/15)
Shibagaki [43]	2020	Prospective	TA filling method	TA: 80 mg	Day 1 and Day 7 and when mild stricture was found	>3/4	5% (1/20)
Sakaguchi [44]	2020	Retrospective	TA injection + PGA	TA: 40 mg	Day 0	>3/4	18.9% (7/37)

TA, triamcinolone acetonide; PSL, prednisolone; PGA, polyglycolic acid; mPSL, methylprednisolone. The dose was shown in one session. Day 0 means immediately after ESD. * Lesion circumference (not mucosal defect circumference).

Gastroenterology and Endoscopy
46th Annual
New York Course

Hikichi J Clin Med 2021

Steroid Therapy in Full Circumferential Esophageal ESD

Table 4. Effect of preventive steroid therapy after total circumferential endoscopic submucosal dissection for esophageal squamous cell carcinoma.

Author	Year	Study Design	Drugs	Dose	Timing of Intervention	Incidence of Stricture
Steroid injection						
Yamaguchi [33]	2013	Retrospective	TA	80 mg	Day 0, 21	100% (4/4)
Takahashi [24]	2015	Prospective, randomized	TA	40 mg	Day 0	100% (5/5)
Hanaoka [34]	2016	Retrospective	TA	100 mg	Day 0	91.7% (11/12)
Miwata [45]	2016	Retrospective	PSL	N/A	Day 1	100% (6/6)
Hashimoto [37]	2019	Retrospective	TA	40–100 mg (second: 16–50 mg)	Day 0, 14 (two times)	80% (4/5)
Oral steroid administration						
Yamaguchi [16]	2011	Retrospective	PSL	30 mg	Tapering gradually for eight weeks	0% (0/3)
Isomoto [22]	2011	Retrospective	PSL	30 mg	Tapering gradually for eight weeks	50% (2/4)
Sato [25]	2013	Prospective	PSL	30 mg	Tapering gradually for eight weeks	100% (10/10)
Yamaguchi [33]	2013	Retrospective	PSL	30 mg	Tapering gradually for 8–18 weeks	27.3% (3/11)
Kataoka [38]	2015	Retrospective	PSL	30 mg	Tapering gradually for three weeks	33.3% (1/3)
Miwata [45]	2016	Retrospective	PSL	0.5 mg/kg	Tapering gradually 5 mg/week	100% (13/13)
Modified or hybrid steroid therapy						
Kadota [27]	2016	Retrospective	TA + Oral PSL	TA: 50 mg PSL: 30 mg	TA: Day 3, 7, 10 (three times) →Day 1 or Day 0 (once) PSL: tapering gradually for eight weeks	71% (10/14)
Nagami [39]	2016	Retrospective	TA injection + PGA	TA: 80 mg	Day 0	66.7% (4/6)
Sakaguchi [40]	2016	Retrospective	TA injection + PGA	TA: 40 mg	Day 0	50% (1/2)
Iizuka [30]	2018	Retrospective	Oral PSL ±TA injection	PSL: 30 mg TA: 80–120 mg	PSL: tapering gradually for eight weeks (TA injection: Day 0)	81.8% (9/11)
			Oral PSL ±TA injection	PSL: 30 mg TA: 80–120 mg	PSL: tapering gradually for 18 weeks (TA injection: Day 0)	36.4% (4/11)
Shibagaki [42]	2018	Retrospective	TA filling method	TA: 80 mg	Day 1 and Day 7 and when mild stricture was found	0% (0/7)
Kadota [46]	2020	Retrospective	TA + Oral PSL	TA: 50 or 100 mg PSL: 30 mg	TA: Day 0 PSL: tapering gradually for eight weeks	61.5% (16/26)

TA, triamcinolone acetonide; PSL, prednisolone; PGA, polyglycolic acid; N/A, not available. The dose was shown in one session. Yamaguchi and Isomoto belong to the same institution.