City of Hope

Annual

Advances and Innovations in Endoscopic Oncology and Multidisciplinary Gastrointestinal Cancer Care

Next Gen Endoscopic Resection in Rectal and Esophageal Cancer

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Disclosures

- I do not have any relevant financial relationships with any ineligible companies.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

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- 2 Endoscopic Resection in Local Advanced Esophageal Cancer
- 3 Experience in our center

Advanced Rectal Cancer

Current Management for Rectal Cancer

Gold Standard	• Total Mesorectal Excision (TME)
Drawback	• Anal Dysfunction • Permanent Ostomy
Patient Demands	• Good Long-term Prognosis • Preserve Organ Function

Non-preservation of Anal Function = Permanent Ostomy

23% of patients underwent Miles surgery, resulting in a permanent ostomy

Preservation of Anal Function ≠ Functioning Well

Patients who undergo **low anterior resection** may experience long-term and severe Low Anterior Resection Syndrome (LARS), affecting 20.5% to 47.6% of individuals.

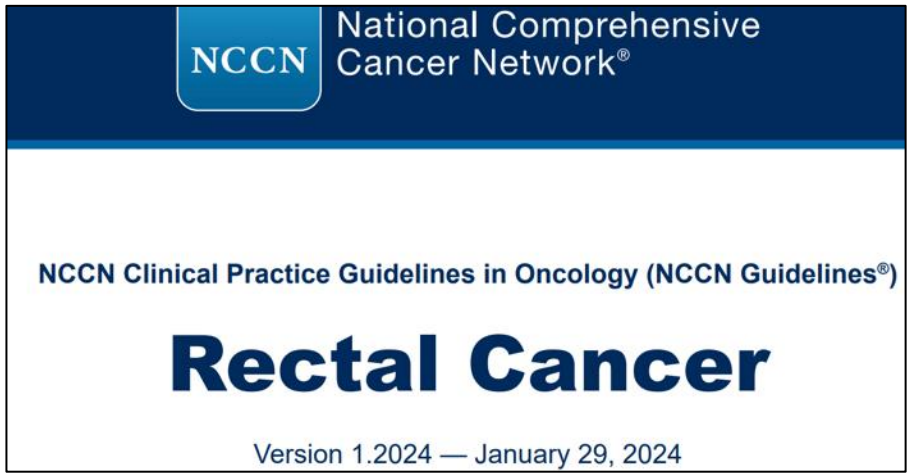
70.6% in those who undergo ultra-low anterior resection.

Nat Rev Gastroenterol Hepatol. 2024
Support Care Cancer. 2021
JAMA. 2015

Current Management for Rectal Cancer



"For treatment decision-making, ***both long-term oncologic outcomes and impact on quality-of-life*** *indices should be considered"*



*"……****restoration of organ integrity*** *should be achieved without compromise of oncologic resection and consideration of anticipated patient* ***functional outcome and quality of life****"*

Current Management for Rectal Cancer

Standard treatment: **Locally Advanced Rectal Cancer(cT3-4 or N+)**

Total Neoadjuvant Therapy (TNT) + **TME** ± **Adjuvant Chemotherapy**

Post-neoadjuvant Chemoradiotherapy:

- 60% of patients experience tumor downstaging
- 10 to 40% of patients achieve cCR
- 15 to 27% of patients achieve pCR

The 5-year DFS for pCR patients is 83.3%

Objectives

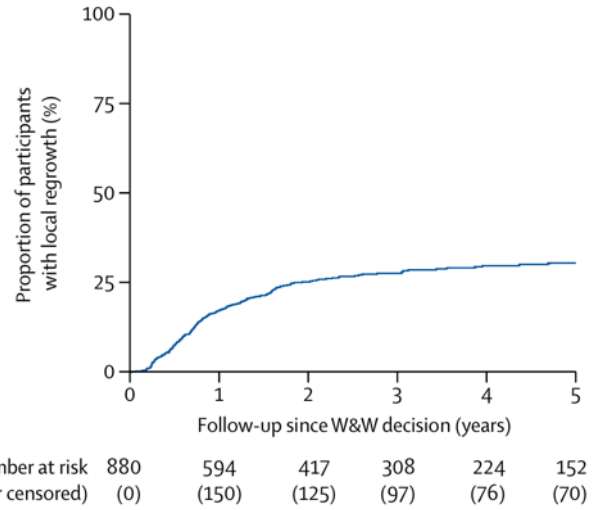
- **Reduce unnecessary surgery**
- **Improve quality of life**
- **No compromising therapeutic efficacy**

Watch & Wait for Rectal Cancer

Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study

*Maxime J M van der Valk, Denise E Hilling, Esther Bastiaannet, Elma Meershoek-Klein Kranenbarg, Geerard L Beets, Nuno L Figueiredo, Angelita Habr-Gama, Rodrigo O Perez, Andrew G Renehan, Cornelis J H van de Velde, and the IWWD Consortium**

Local Regrowth



2-year local recurrence rate is 25.2%

- 97% are within the intestinal wall.
- 88% are within the first 2 years.

Cumulative distant metastasis rate of 8%

- 75% of metastases occur within the first 3 years

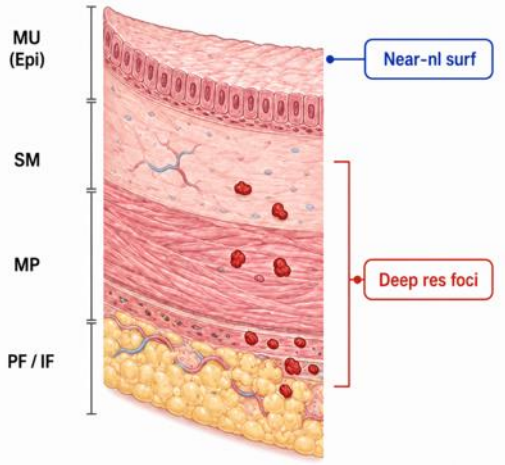
5-year survival rate

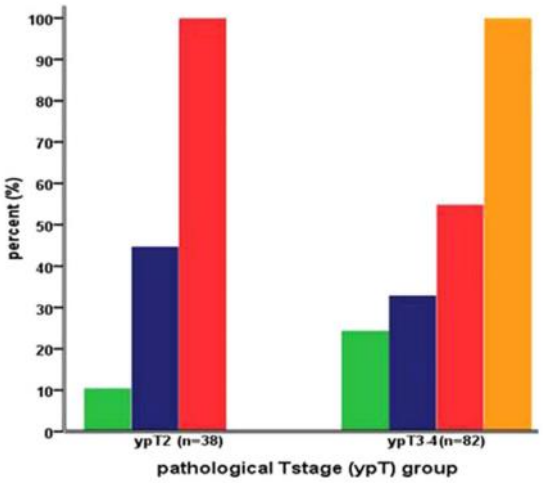
- OS 85%
- DFS 94%

Majority of tumor regrowth occurs within the intestinal wall → Addition of local resection may reduce the risk of recurrence

Lancet. 2018.

Regression Patterns of Rectal Adenocarcinoma





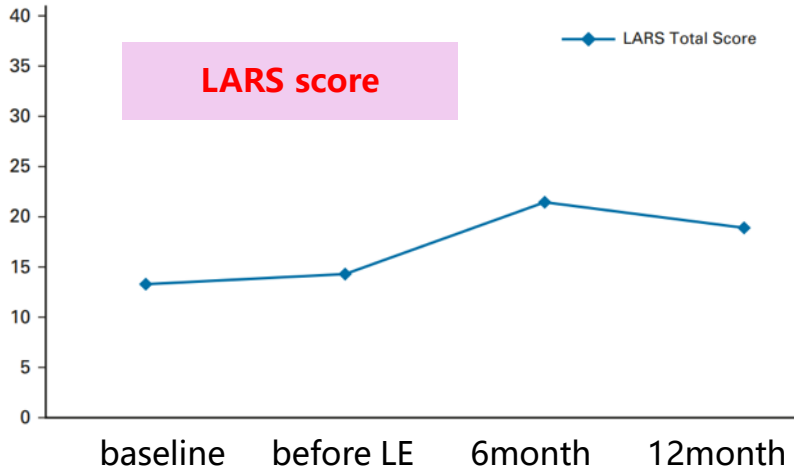
- Residual tumor is more often in SM, MP and lF than on the mucosal surface.
- In ypT2-4: Mucosa 20%; SM 36.7%; MP 69.2%.
- Sensitivity of post-NAT primary-site biopsyfor residual tumor: 12.9%

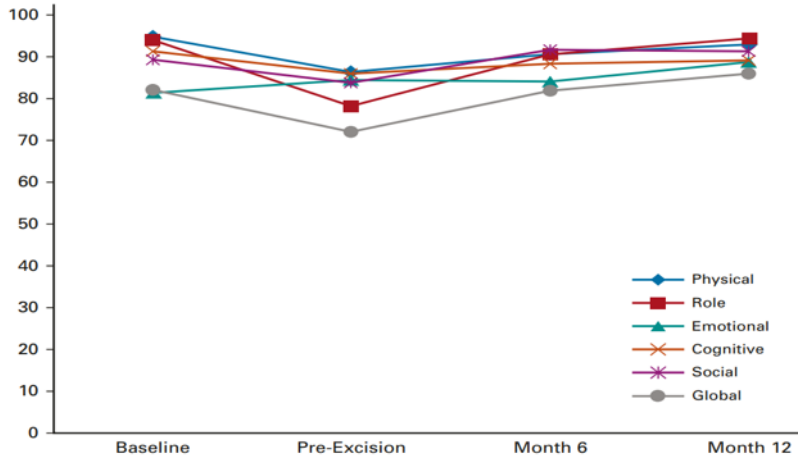
cCR ≠ No Residual Tumor Cells

The organ preservation rate is high with nCRT+TEM

Neoadjuvant Chemotherapy, Excision, and Observation for Early Rectal Cancer: The Phase II NEO Trial (CCTG CO.28) Primary End Point Results

cT1-3abN0M0 Rectal cancer → **nCRT** mFOLFOX6/CAPOX → 2-6weeks → **ypT0/1 N0/X: local resection Patients with unsuccessful downstaging: surgery or observation**



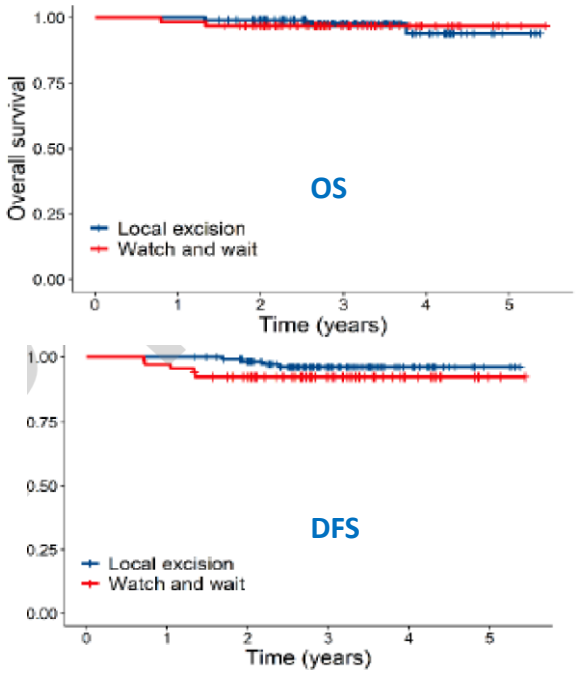


- **The overall organ preservation rate is 79%.**
- The 1-year and 2-year local recurrence-free survival rates are 98% and 90%, respectively. *J Clin Oncol. 2023*

Patients with mCR should undergo local resection

Evaluation After nCRT	Strategy	Outcomes (n)				
		Organ Preservation	TME	Local Recurrence	Pelvic Recurrence	Metastasis
cCR n=107	W&W n=65	53	12	18	2	5
	LE n=42	34	8	/	3	2
mCR n=158	W&W n=1	1	0	0	0	0
	LE n=70	56	14	/	5	2

mCR: (major clinical response)



Results:

- Most patients with cCR have a pCR, making them suitable for a Watch & Wait approach.
- **The local recurrence rate for patients with mCR is approximately 50%,** so the Watch & Wait strategy should be considered cautiously.

Int J Surg. 2024

nCRT + TEM vs. Surgery

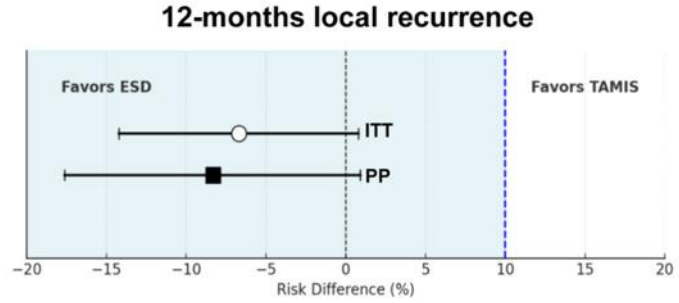
Research	Publication time	stage	Treatment strategy	Sample size	Local recurrence	metastasis	DFS	OS
ReSARCh	2024	II-III	nCRT+TEM	90	（3 year） 8.9%	4.4%	90%	97.6%
TAU-TEM	2023	cT2-3	nCRT+TEM	86		-		
			TME	87				
CCTG CO.28	2023	cT1-3	nCRT+TEM	58	(2 year) 3.4%	0	90%	100%
PKUCH-R01	2022	cT2-3	nCRT+ TEM after regrowth	64	(2 year) 18.4%	6.3%	(3 year) 92.2%	/
TREC	2021	cT1-2	nCRT+TEM	27	(3 year) 11%	11%	85%	88%
			TME	28	0	7%	76%	93%
GRECCAR2	2020	cT2-3	cCR/ncCR apply TEM	74	(5 year) 7%	18%	70%	84%
			cCR/ncCR apply TME	71	7%	19%	72%	82%
CARTS	2019	cT1-3	cCR/ncCR apply TEM	55	(5 year) 7.7%	/	81.6%	82.8%
ACOSOG Z6041	2015	cT2	nCRT+TEM	79	(3 year) 4%	/	88.2%	94.8%

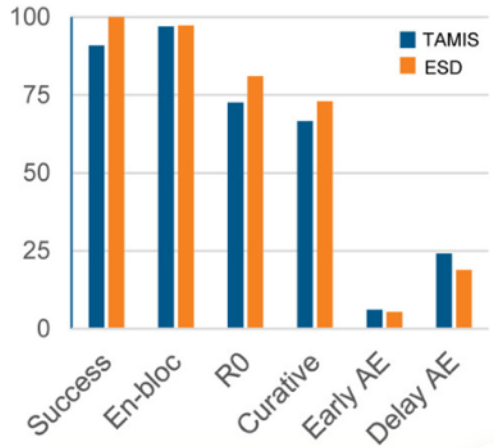
The Long-term Efficacy of nCRT + TES is Comparable to Surgical Intervention

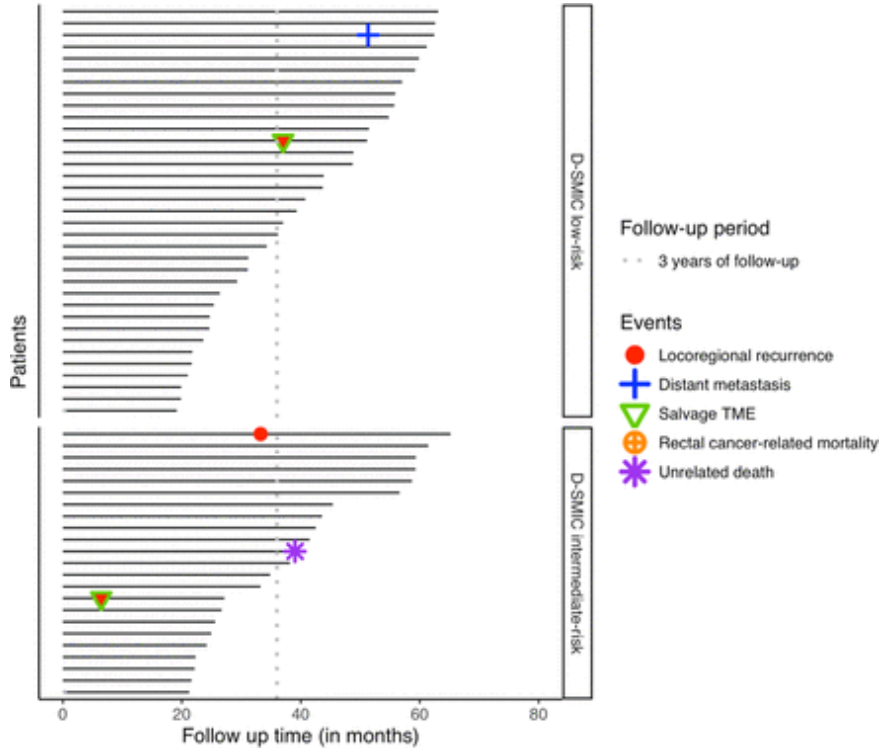
Int J Surg. 2024;Ann Oncol. 2023;J Clin Oncol. 2023;Ann Surg. 2022

Lancet Gastroenterol Hepatol. 2020;Lancet Gastroenterol Hepatol. 2021;JAMA Surg. 2019; Lancet Oncol. 2015

Salvage ESD vs. TEM







Endoscopic Resection and TEM Have Comparable Postoperative Complication Rates

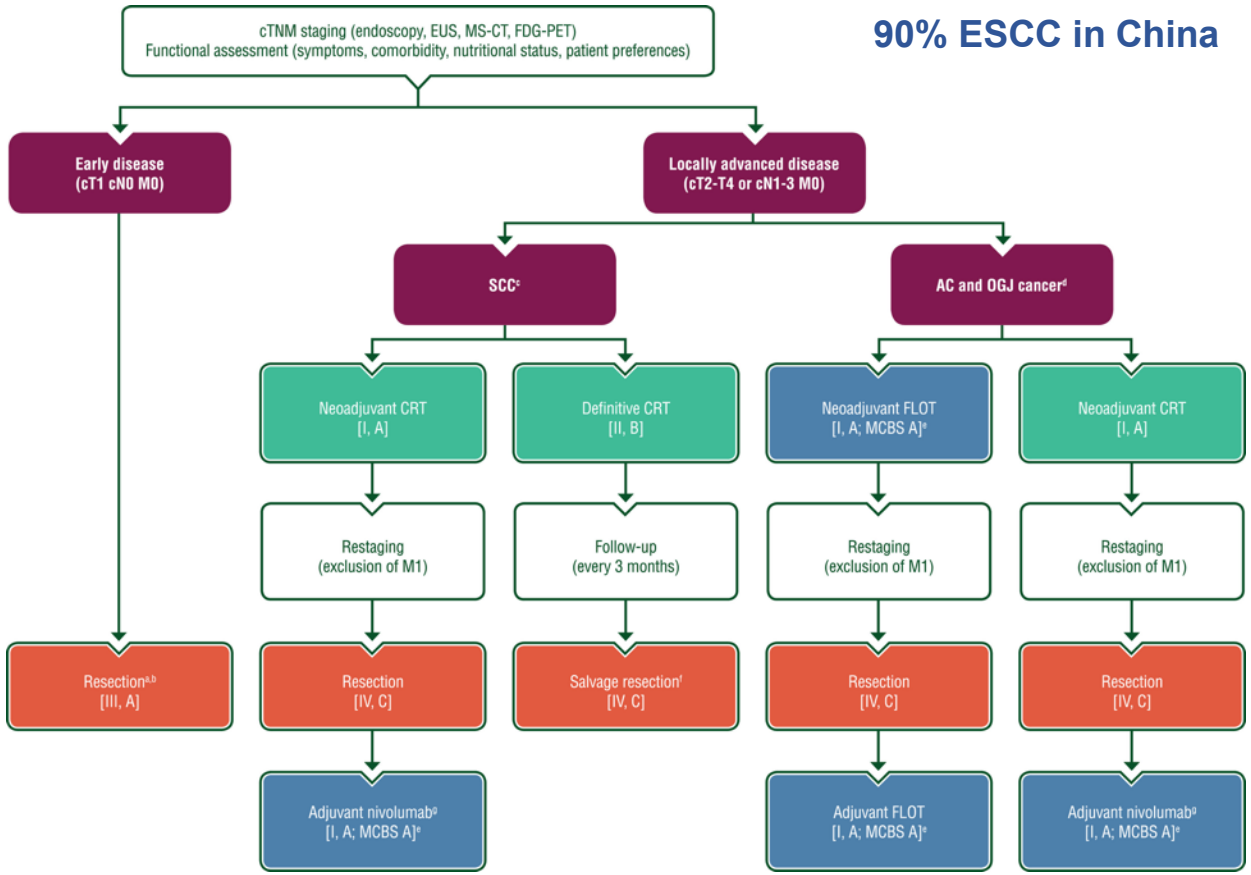
TEM Has a Higher Recurrence Rate Than Endoscopic Resection

GUT. 2025

3 year recurrence rate for low risk group 7%, intermediate risk group 13%

Advanced Esophageal Cancer

Treatment Algorithm for Esophageal Cancer



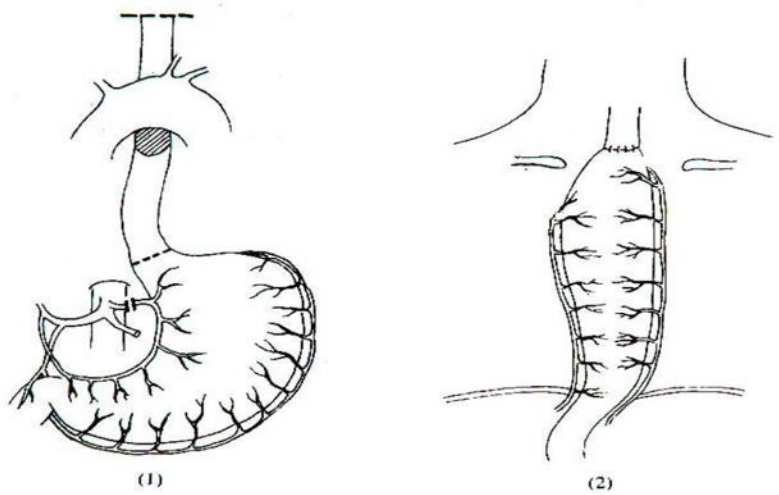
90% ESCC in China

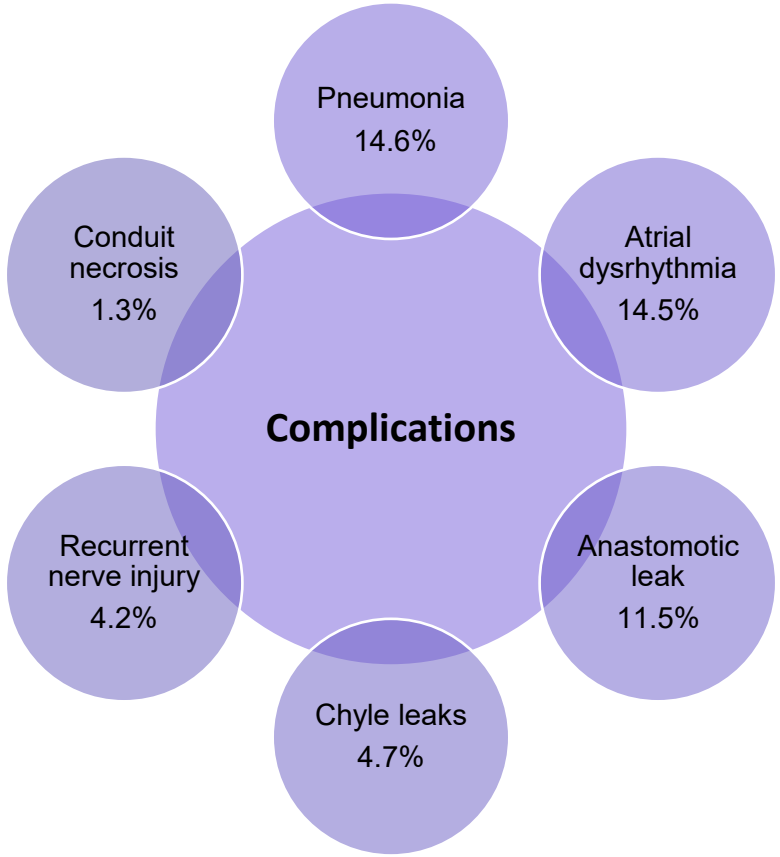
Endoscopic en bloc resection is the treatment of choice for most T1 tumors

ESMO Clinical Practice Guideline. 2022.
ASGE Guideline. 2023.

Surgery for locally advanced resectable ESCC

Surgery is the backbone of curative-intent treatment for locally advanced resectable esophageal cancer





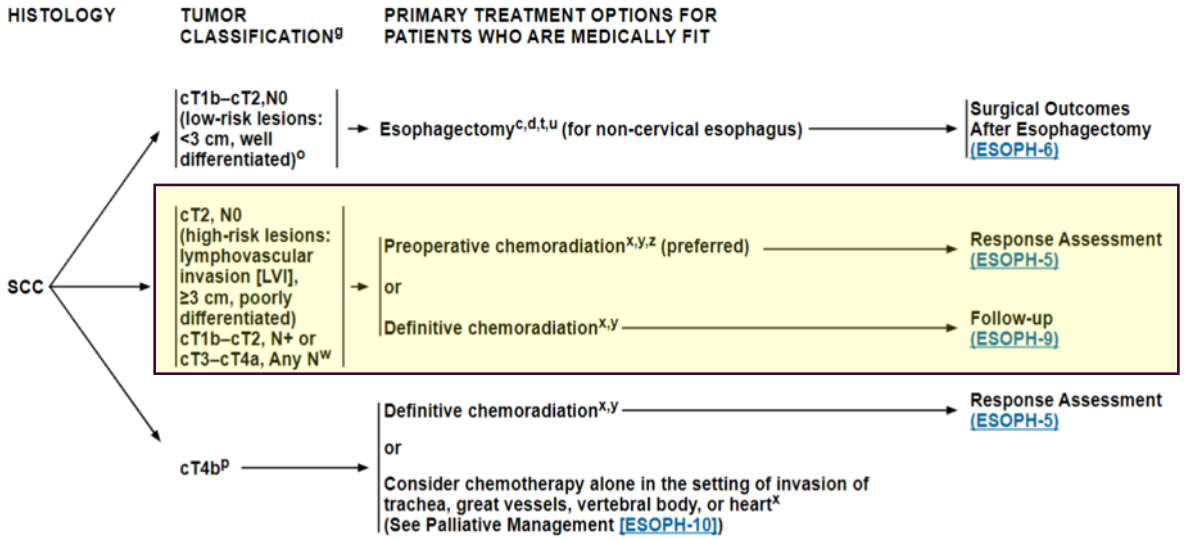
Overall incidence of complications was 59%

(Clavien-Dindo ≥ 3 31.2%), 90-day mortality 4.5%

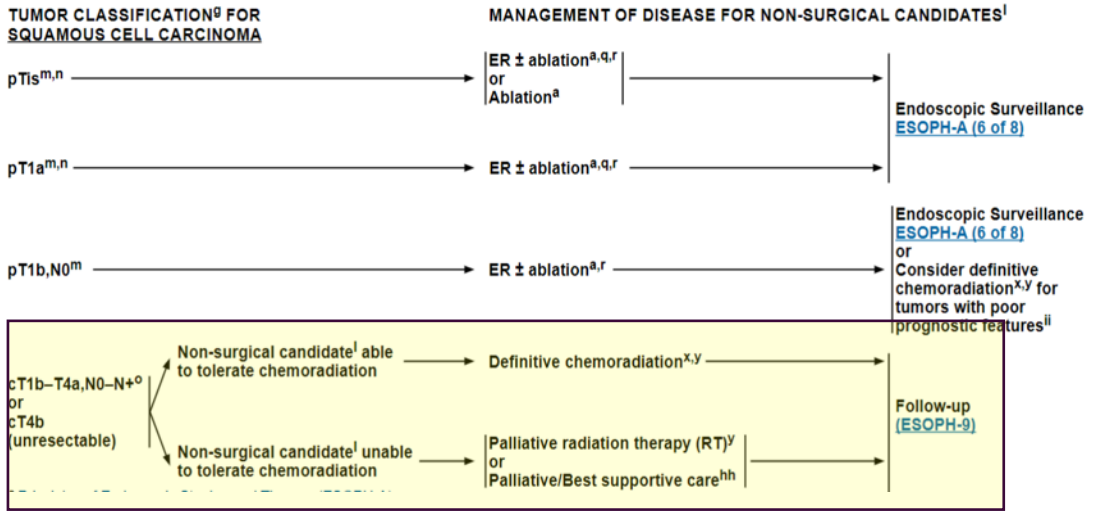
ESMO Clinical Practice Guideline. 2022.
Ann Surg. 2022.

Current Guideline

Medical fit for surgery



Non-surgical candidates



Patients who are medically unable to tolerate major surgery or patients who are medically fit who decline surgery.

2025 NCCN Guideline

Pre-operative Treatment for ESCC

Neoadjuvant Chemotherapy (nCT)

Neoadjuvant Chemoradiotherapy (nCRT)

R0 Resection Rate ↑

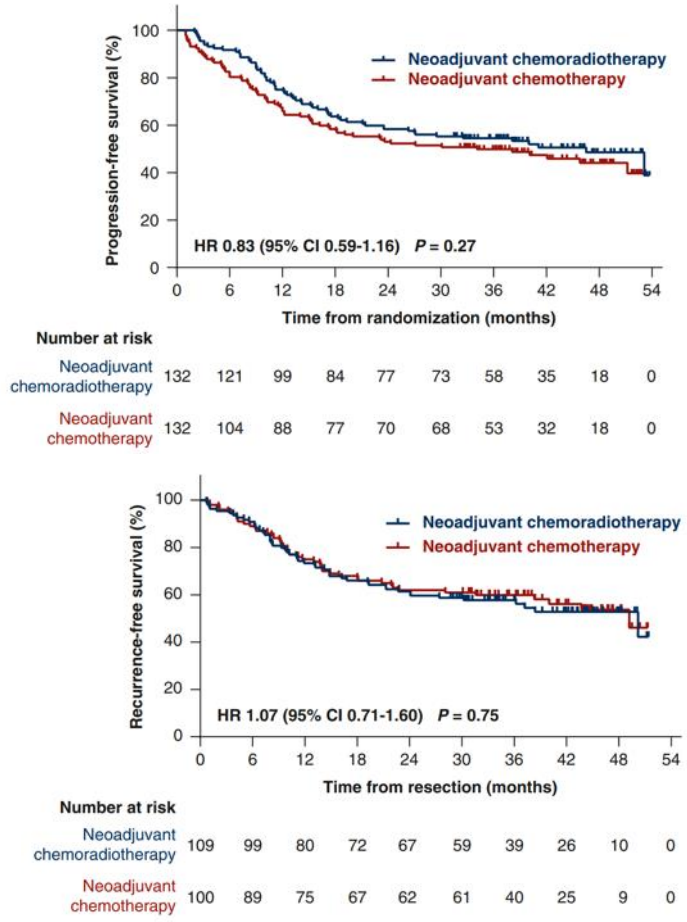
nCT: 96.2%

nCRT: 97.3%

Survival Rate ↑

1-years OS Rate 82.6-87.1%

5-year OS Rate >60%

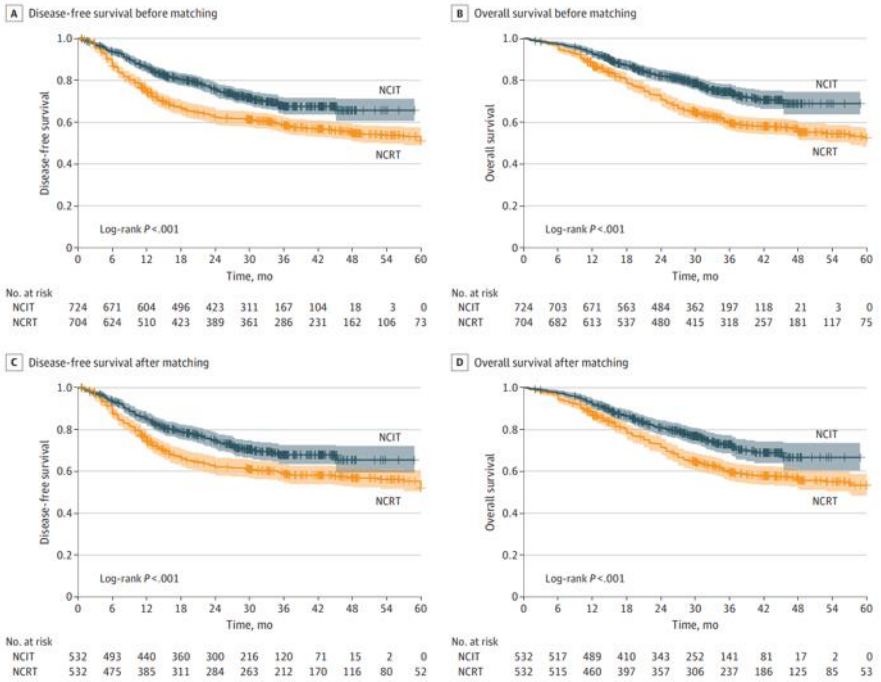


Ann Oncol. 2023.
Ann Surg. 2022.

Addition of Immunotherapy Improve Outcomes

Eight high-volume centers in China

nCIT vs nCRT



- A prospective study enrolled 1,428 patients with cT1-T4a ESCC.
- The pCR rate was 25.9% after nCRT and 22.9% after nCIT

	NCIT	NCRT	HR
OS	81.3%	71.3%	1.57 (1.26-1.96)
DFS	73.9%	61.4%	1.37 (1.11-1.69)

nCIT significantly improves OS and DFS in locally advanced ESCC

JAMA Surgery. 2025

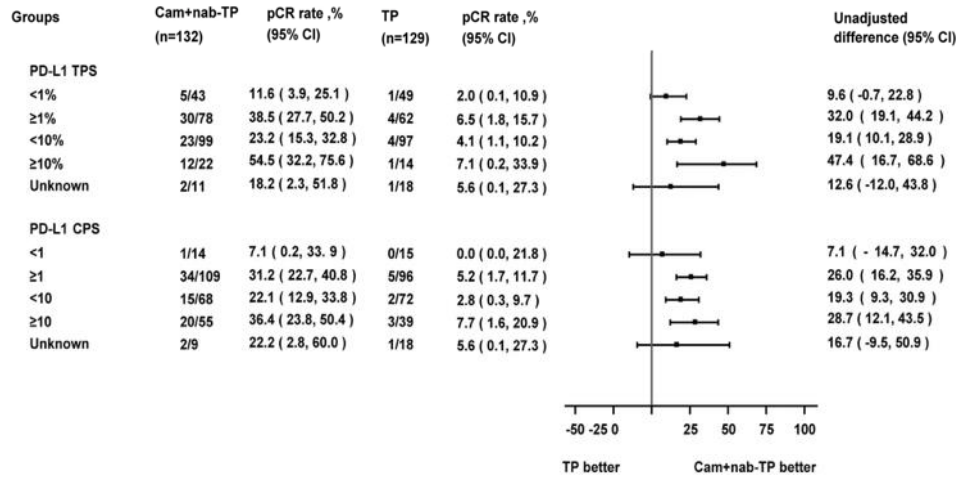
Neoadjuvant Immunotherapy Improves pCR Rates

391 resectable locally ESCC

nCIT vs nCT

Variables	Cam+nab-TP (*n*=132)	TP (*n*=129)
pCR		
Rate, % (95%CI)[a]	28.0 (20.6, 36.5)	4.7 (1.7, 9.8)
Difference (vs TP group), % (95%CI)[b]	23.5 (15.1, 32.0)	
OR (vs TP group) (95%CI)[b]	8.11 (3.28, 20.06)	
P value (vs TP group)[c]	<0.0001	
MPR		
Rate, % (95%CI)[a]	59.1 (50.2, 67.6)	20.9 (14.3, 29.0)
Difference (vs TP group), % (95%CI)[b]	38.3 (27.4, 49.3)	
OR (vs. TP group) (95%CI)[b]	5.51 (3.18, 9.56)	

Pre-treatment PD-L1 and pCR



Neoadjuvant chemoimmunotherapy achieves higher pCR rates

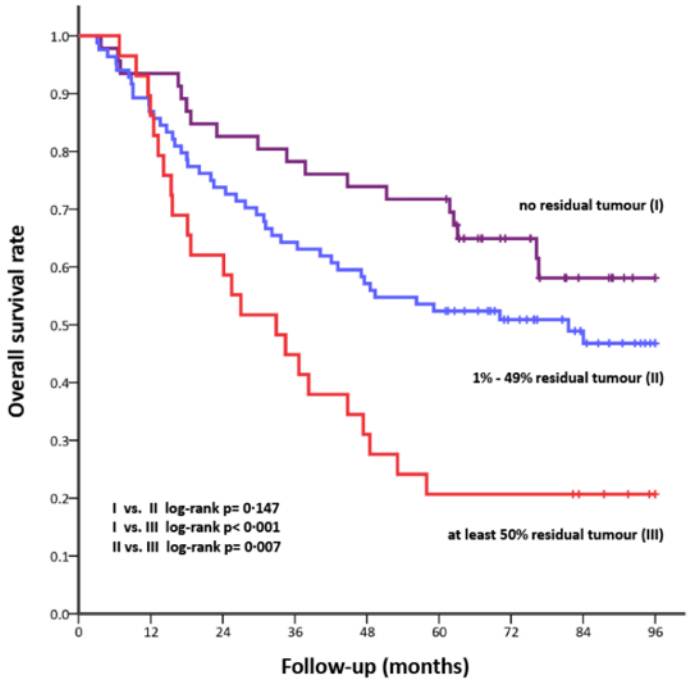
Patients with TPS/CPS ≥10 are more likely to achieve pCR

Nature Medicine. 2025

pCR is Beneficial for Long-term Outcomes

CROSS Trial (Netherlands)

Ten-Year Outcome



- **29% pathologically complete response**
- Long-term outcomes of pCR patients was significantly better than that of non-pCR

	pCR	non-PCR	HR
OS	92.6	69.2	2.70 (1.48-4.92)
DFS	85.0	59.4	2.75 (1.59-4.78)

Organ preservation for cCR patients?

- Standard resection after nCRT?
- or Active surveillance after cCR ?

?

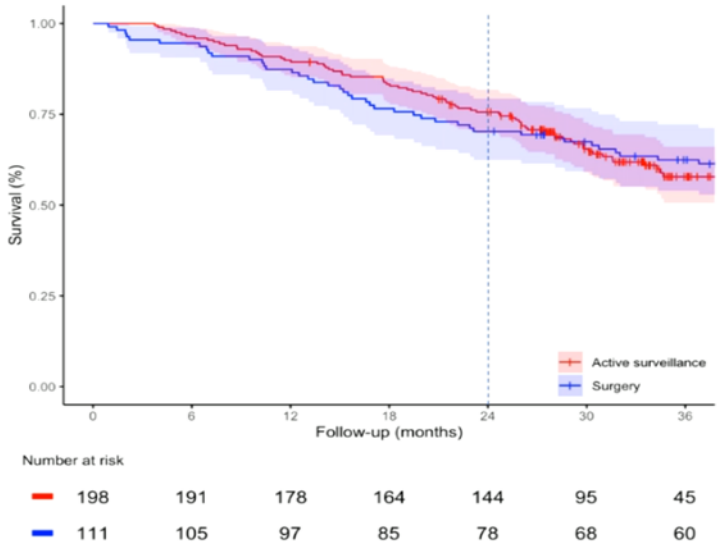
NEJM. 2012.
Lancet Oncol. 2015.
J Clin Oncol. 2021.

AS had Noninferior Short-term Outcomes

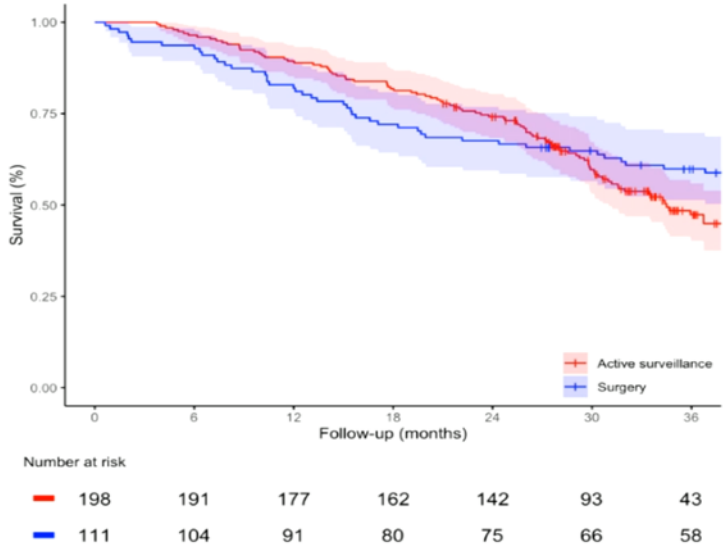
Prospective multicentre randomised, non-inferiority phase III clinical study (SANO)

Median follow-up: 38 months (32-48)

OS



PFS



The feasibility of AS strategy in patients achieving cCR after neoadjuvant therapy

Lancet Oncology, 2025

Disease Progression During Active Surveillance

SANO Trial

	AS	Surgery	OR
Metastases <30 mo	76/176 (43%)	30/87 (34%)	1.45 (0.85-2.48)

Conclusion

- Surgery for patients with locoregional regrowth could be operated safely
- 35% patients spared unbeneficial surgery

	AS (n=83)	Surgery (n=101)
Any Complication	68 (82%)	85 (84%)
Anastomotic Leakage	18 (22%)	27 (27%)
Pulmonary Infection	20 (24%)	29 (29%)
90-day Mortality	3 (4%)	5 (5%)

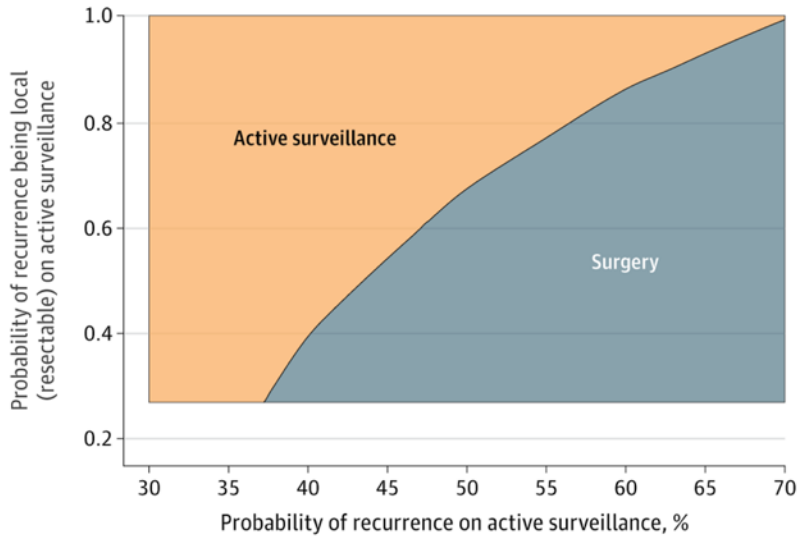
48% （96 patients） developed locoregional regrowth

17% （33 patients） developed distant metastases

Lancet Oncology, 2025

Active surveillance may not remain superior over long term

Decision-analytical model based on SANO data



Model-derived thresholds favoring surveillance

<43% overall recurrence probability

>94% probability that recurrence remains local and resectable

High surgical burden substantial expected loss of quality of life

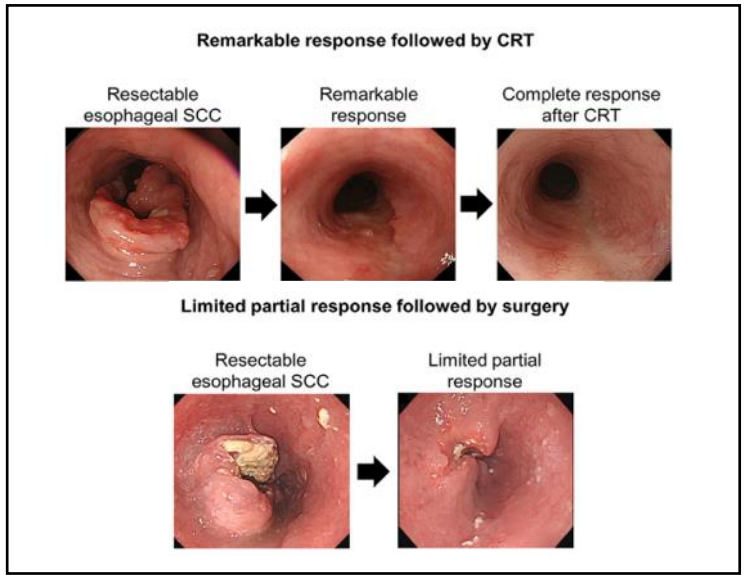
The benefit of organ preservation depends on recurrence risk, salvageability, and the time horizon—not cCR alone.

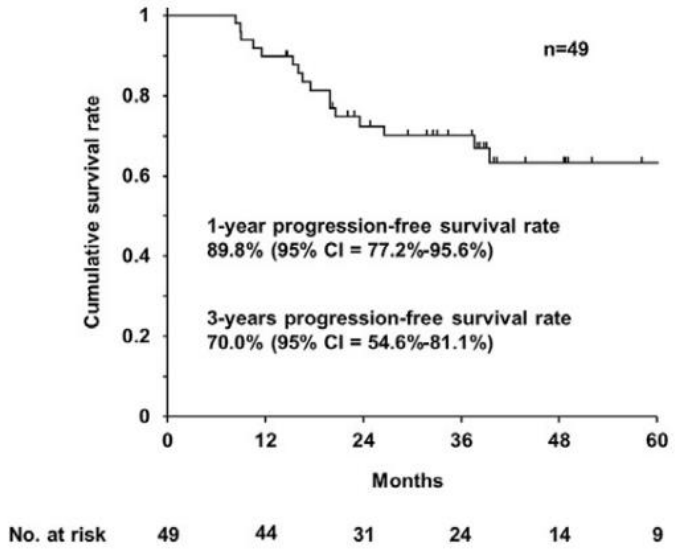
JAMA Surg. 2026

Disease Progression in Patients Achieving cCR

Japanese Multicenter Prospective, Multicenter Randomized Phase 2 Trial

Organ Preservation After Downstaging for Locally Resectable ESCC (IB-III Stage)





cCR patients during the 36-month follow-up period

30% (16 cases) showed local progression or distant metastasis

How to preserve organs in patients achieving cCR?

Int J Radiat Oncol Biol Phys. 2024

ESMO 2026 · LBA78 · 5-YEAR RESULTS

Active surveillance vs surgery in oesophageal cancer

SAN0 STUDY

Patients with a clinical complete response after neoadjuvant chemoradiotherapy

5-year overall survival

50% vs 54%

Surveillance vs surgery

Not statistically significant

Distant metastases at 5 years

46% vs 29%

Surveillance vs surgery

P less than 0.01

What else did the trial show?

309 patients

198 assigned to active surveillance; 111 to standard surgery.

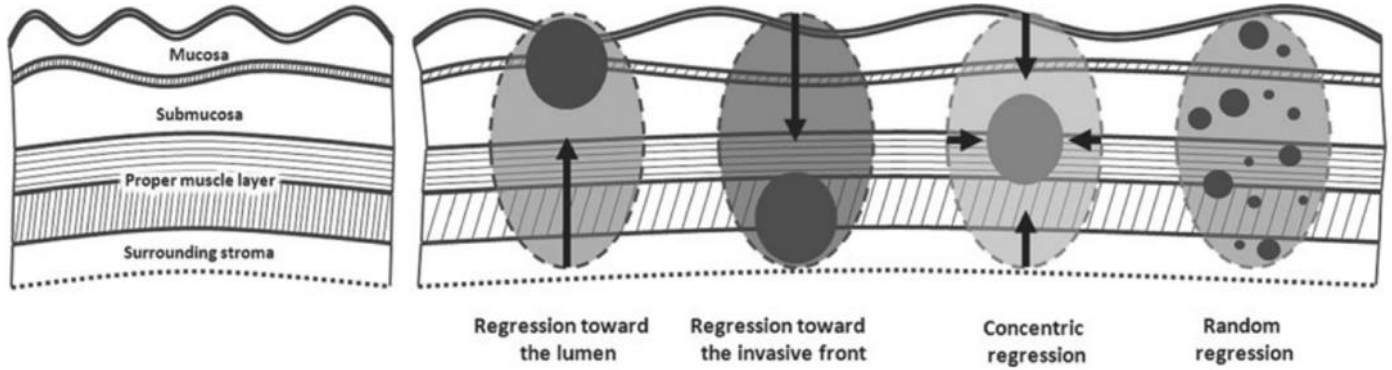
43% potentially spared oesophagectomy

85 of 198 patients met the study's definition of avoiding non-beneficial surgery.

Tumor Regression Patterns for ESCC

102 esophageal cancer patients after neoadjuvant therapy :

- 71 (70%) were in pathological partial regression (≥ TRG2), with
- 89% of residual tumor cells located in the mucosal or submucosal layer
- 5 cases had residual tumor cells in the muscularis propria
- 3 cases had residual cells in the single lymph node



Tumor regression patterns after neoadjuvant therapy

Ann Surg. 2013

Organ Preservation For Advanced ESCC

MDT Discussion

- Clinical Staging (cT1b-3 N0 M0)
- Lesion Biopsy

Neoadjuvant Therapy

- Assessment of tumor regression
- Lesion Biopsy

Endoscopic Resection

- Post-operative follow-up
- Maintenance treatment

Improve Local Tumor Control

Reduction of Organ Destruction

Improved Quality of Life

ER as an important supplement to surgery

For patients who are unable (or refuse) to undergo surgical treatment

Cervical Tumors



Multiple comorbidities



Severe spinal deformity



High surgical difficulty High risk of postoperative complications

Experience in our center

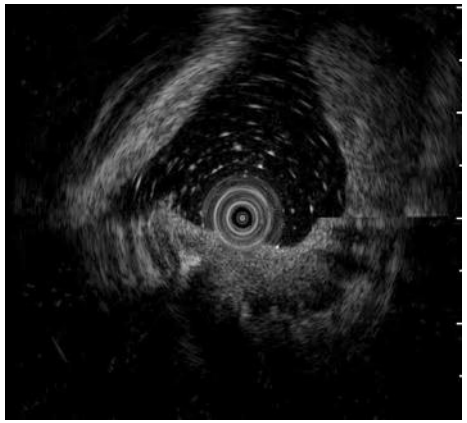
Advanced Rectal Adenocarcinoma

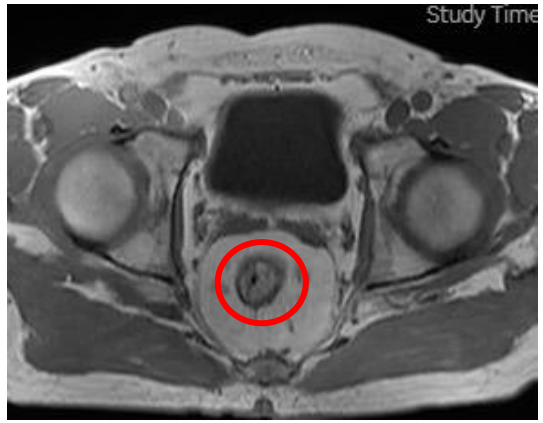
Case Rectal cancer nCRT+EFTR

Male, 57 years old

Colonoscopy: A roughly 4.0 cm neoplasm is observed in the rectum, 3 cm from the anal verge.

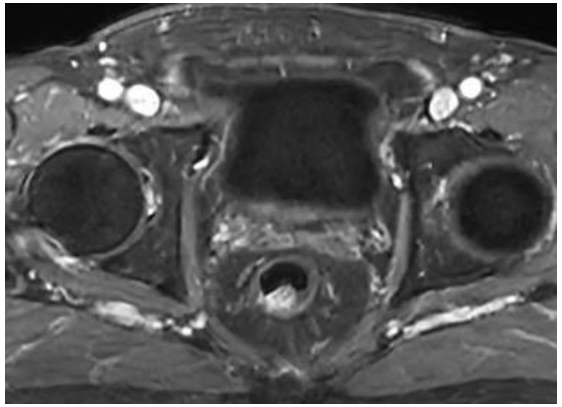




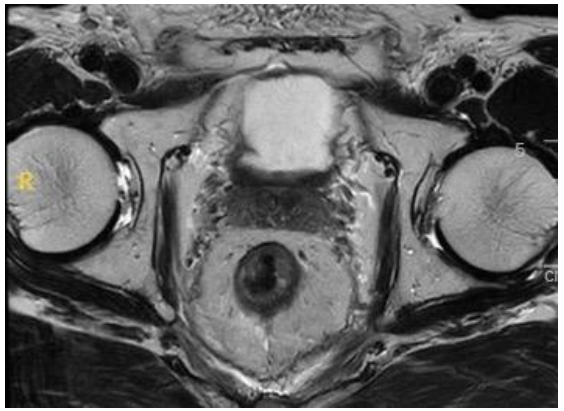


Case Rectal cancer nCRT+EFTR

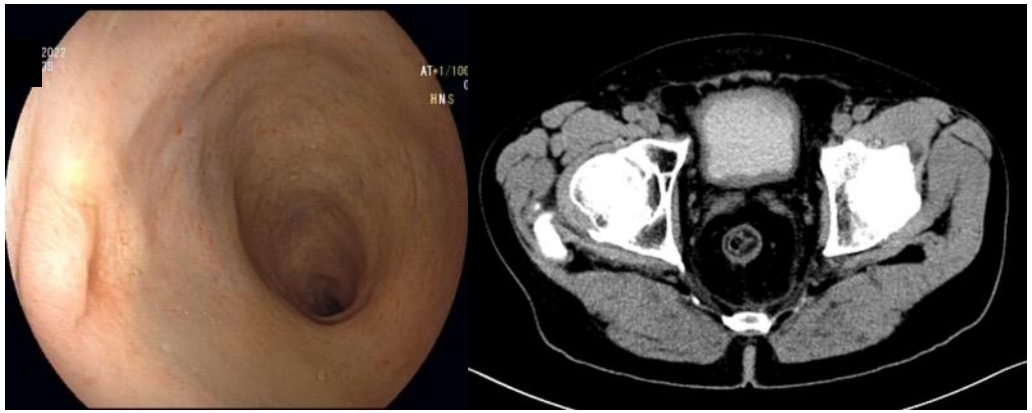
3 months after nCRT



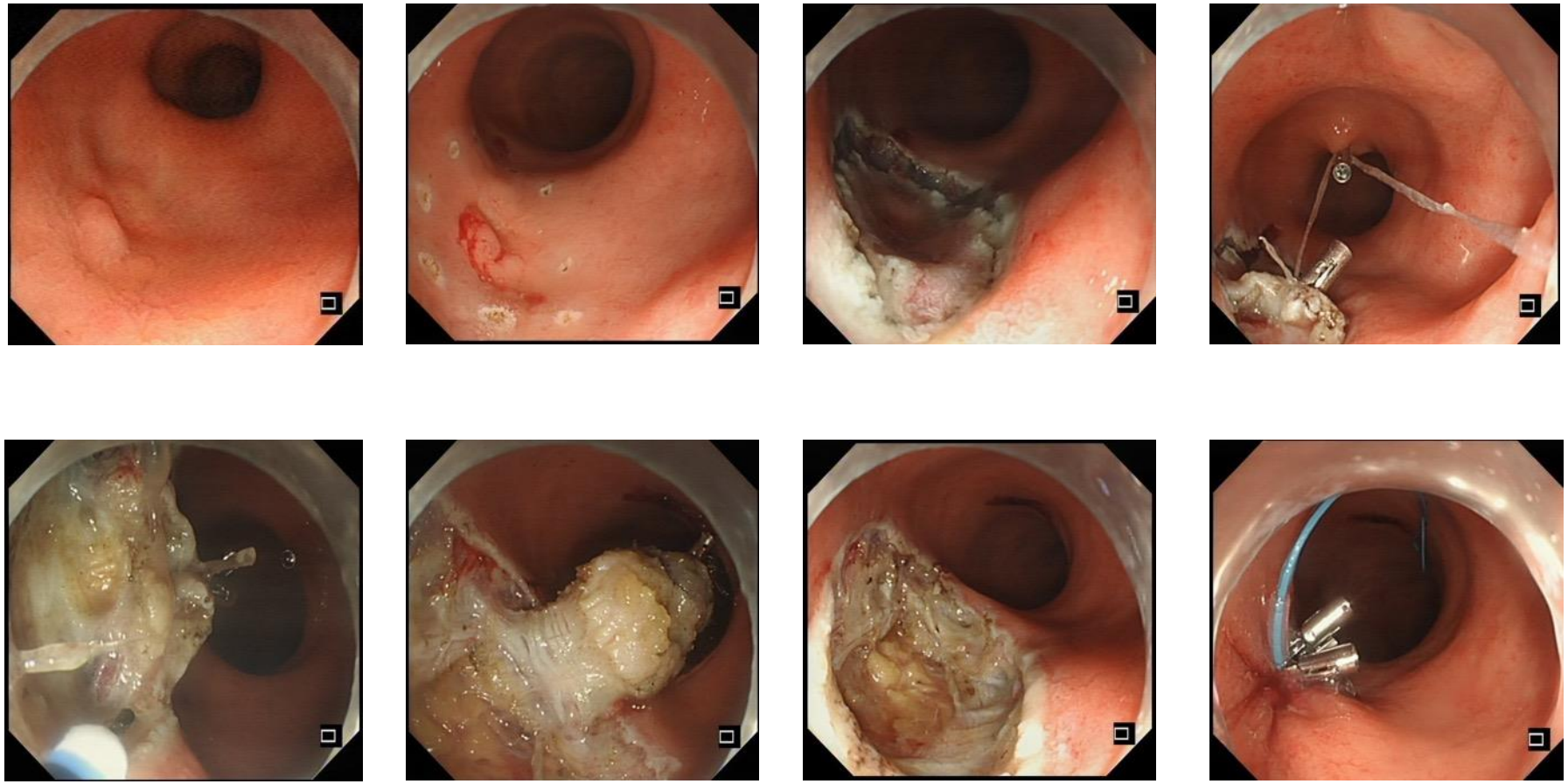
5 months after nCRT



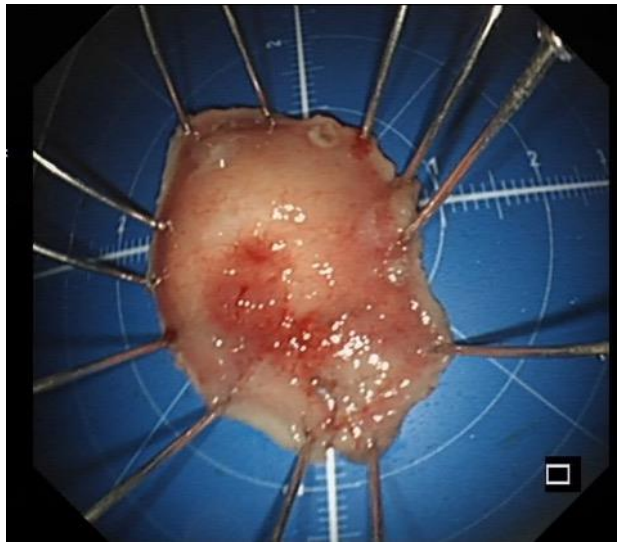
8 months after nCRT



Case EFTR procedure following nCRT



Case Pathological Evaluation





Pathology： **(Rectum) Adenocarcinoma, with differentiation between Grade II and Grade III, measuring approximately 1.2 x 0.7 cm, infiltrating into the submucosal layer (SM2, depth >1000um) (ypT1).**

Case Follow up

1 year after EFTR:







Experience in our center

Refining watch-and-wait in low rectal cancer after neoadjuvant chemoradiotherapy: pilot study of endoscopic full-thickness resection

Zhipeng Qi,[1] Mingyan Cai ,[1] Ayimukedisi Yalikong,[1] Haixing Wang,[2] Xian Zhang,[3] De-xiang Zhu,[4] Yunshi Zhong [1]

Table 1 Demographic characteristics (n=28)

Variable	Value, n (%)
Gender	
Male	18 (64.29)
Female	10 (35.71)
Age, median (IQR), years	65 (58–70.25)
Minimum	41
Maximum	84
Lesion	
Diameter, median (IQR), cm	4(3–5)
Distance from anal verge, median (IQR), cm	3.25(2–5)
Clinical staging before therapy (all M0)	
cT2 (9 cN0 1 cN1)	10
cT3 N0 (14 MRF+14; 2 EMVI+)	18

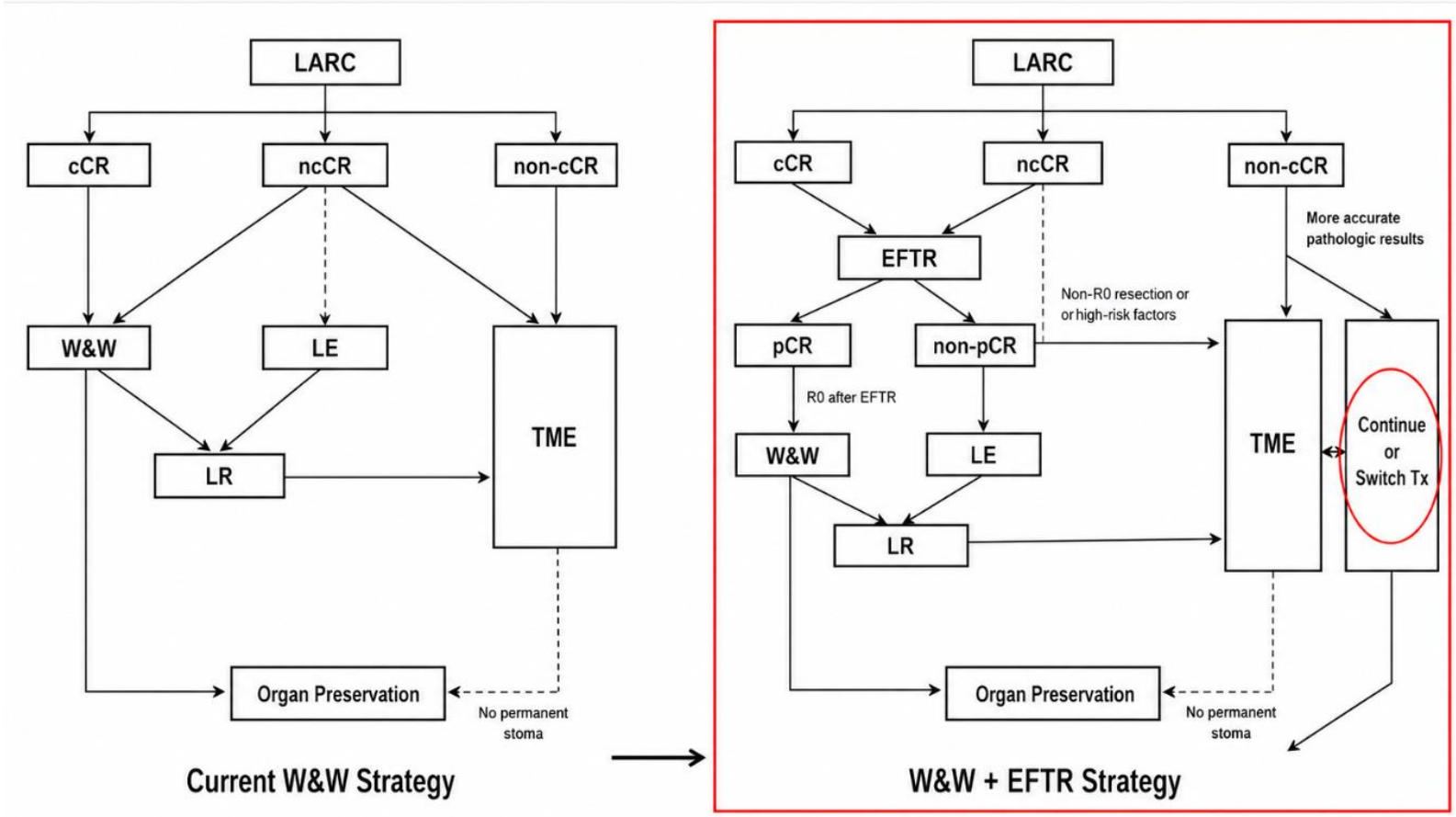
EMVI, extramural vascular invasion; MRF, mesorectal fascia.

Table 2 Treatment, histopathology and postoperative details (n=28) of patients undergoing EFTR

Variable	All (n=28)	cCR (n=6)	ncCR (n=22)
Interval between radiotherapy and EFTR, median (IQR), weeks	12 (8–14.5)	13.5 (12.25–15.5)	11.5 (8–13.75)
Pathological T staging			
ypT0*	17 (60.71%)	6	11
ypT1	5 (17.86%)	0	5
ypT2	6 (21.43%)	0	6
Lesion diameter after treatment, median (IQR), cm	3 (2.5–3.5)	2.75 (1.75–3.625)	3.25 (2.5–4)
En bloc and R0 resection	28	6	22
Salvage surgery	1 (3.57%)	0	1
Postresection adjuvant chemotherapy	5	0	5
LARS score			
0–20 (no LARS)	27 (96.43%)	6	20
30–40 (major LARS)	1 (3.57%)	0	1
Adverse event			
Postoperative bleeding	2 (7.14%)	0	2
Urogenital injury	0	0	0
Follow-up time, median (IQR), months	25 (18–28)	25 (18–26)	25 (11–27)
Local regrowth or distant metastasis reported	0	0	0

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Potential algorithm for role of EFTR in Rectal Cancer



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Experience in our center

Advanced Esophageal Squamous Cell Carcinoma

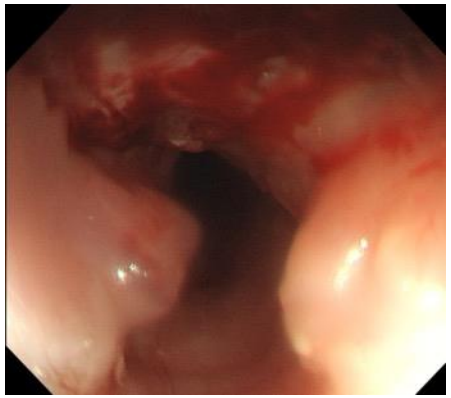
Case 1：Cervical ESCC Patient

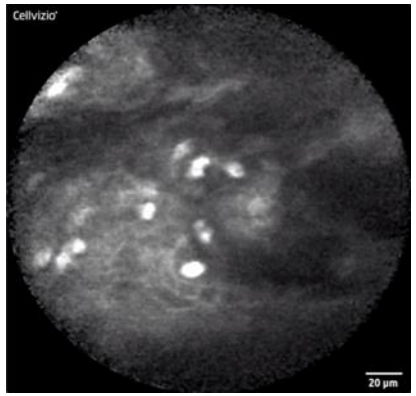
Male, 76 years old

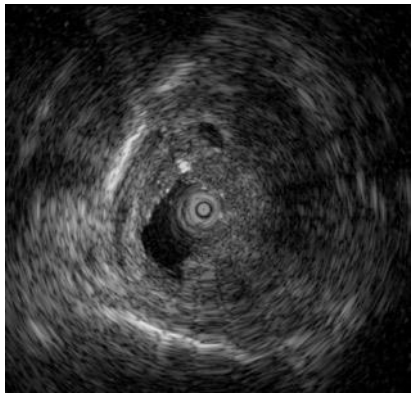
CC： Intermittent choking on food for more than 3 months.

Gastroscopy: Esophageal mass was seen 16-24 cm from the incisors, occupying the lumen of the esophagus for 3/4 weeks.

Pathology: Low differentiated squamous carcinoma.



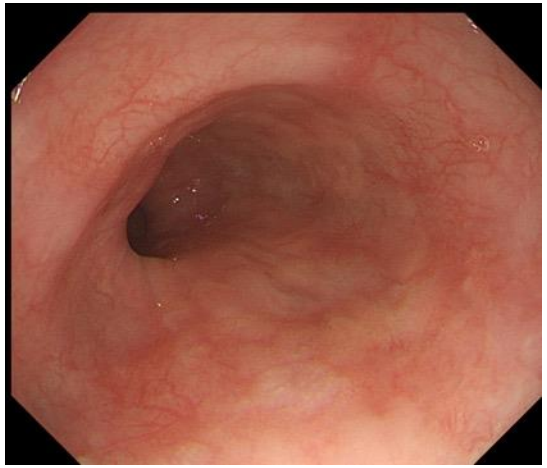




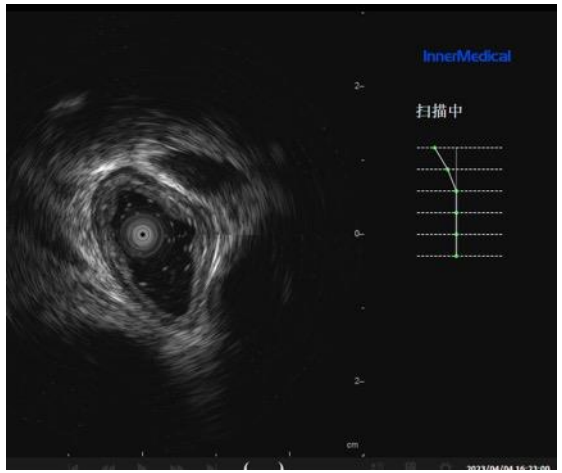


Case 1：Cervical ESCC Patient

4 months after conversion therapy

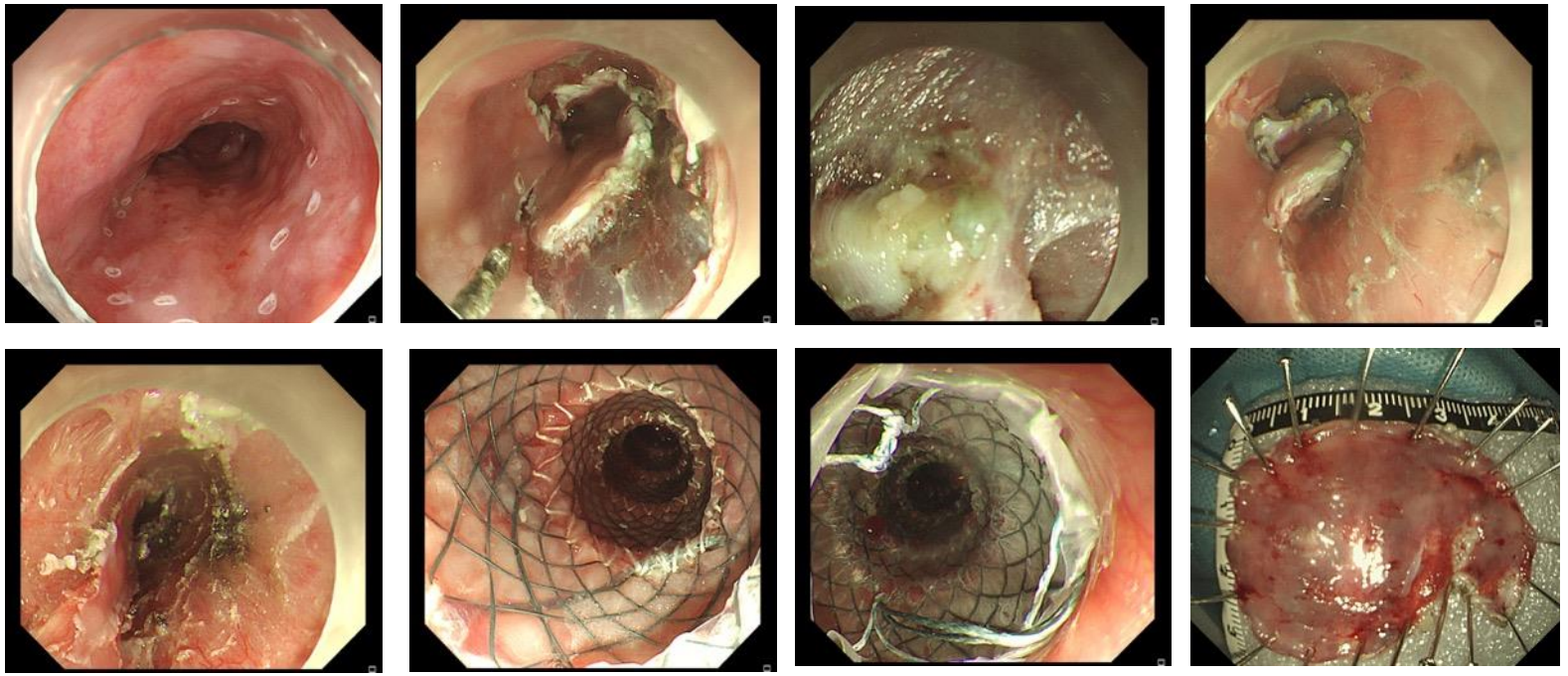




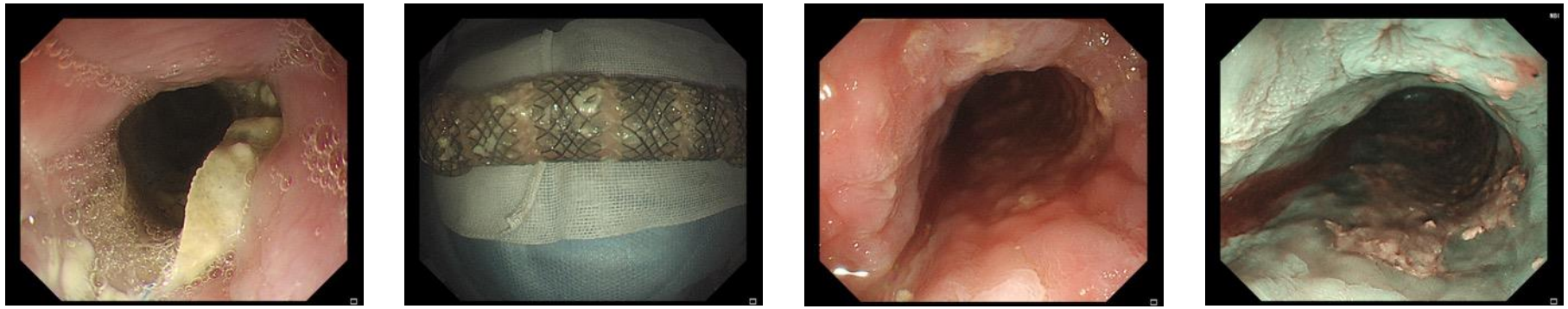


Case 1：Cervical ESCC Patient

ESD after conversion therapy



Case 1：Cervical ESCC Patient



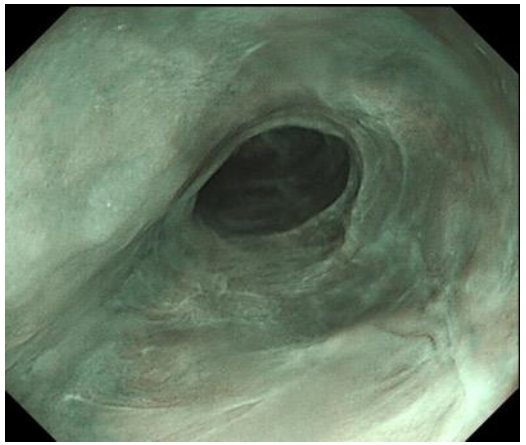
Postoperative Pathology:

Squamous cell high-grade intraepithelial neoplasia with carcinoma, squamous cell carcinoma moderately-highly differentiated, partially microinvasive squamous carcinoma, infiltration of the mucosal lamina propria (M2), horizontal margins and basal margins were negative.

Case 1：Cervical ESCC Patient

Gastroscopy at 12 months postoperatively:





Postoperative patients were treated with immunotherapy

and followed up regularly for 44 months, with no recurrence

CASE 2：ESCC Patient with Comorbidities

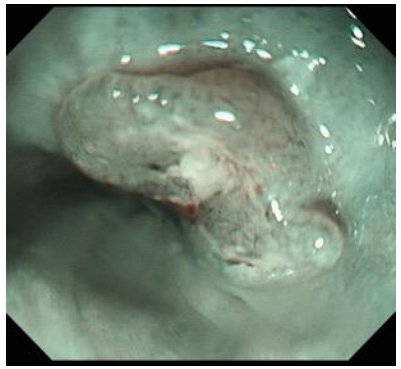
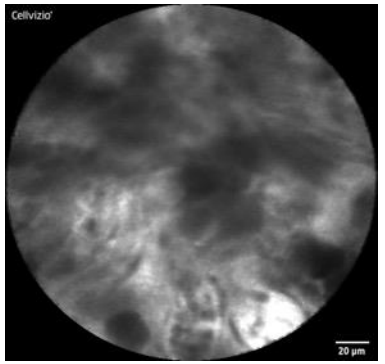
Male, 78 years old

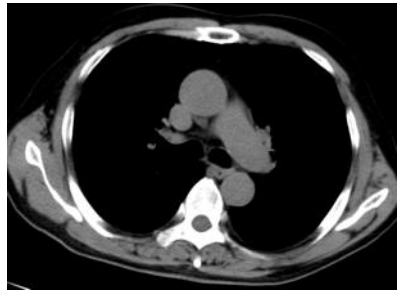
CC： Intermittent dysphagia for 1 month.

Past medical history: COPD, pulmonary hypertension, coronary artery disease, and prior coronary stent placement（**Surgery was risky**）

Gastroscopy: Esophageal mass was seen 31-34 cm from the incisors,

Pathology: Well differentiated squamous carcinoma.



CASE 2：ESCC Patient with Comorbidities

1 month



3 months

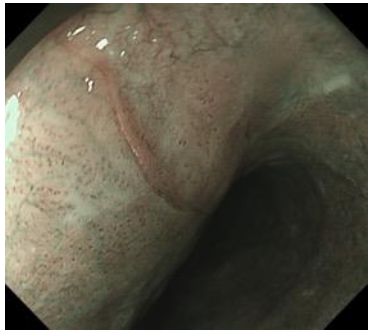


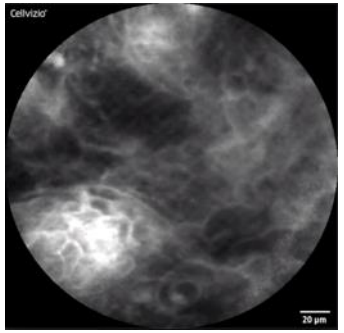
4 months

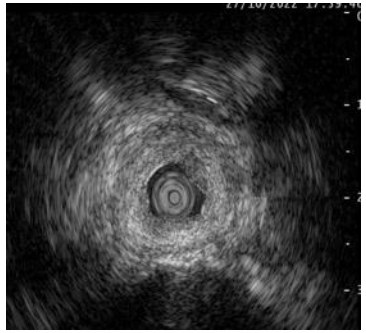


Significant tumor shrinkage



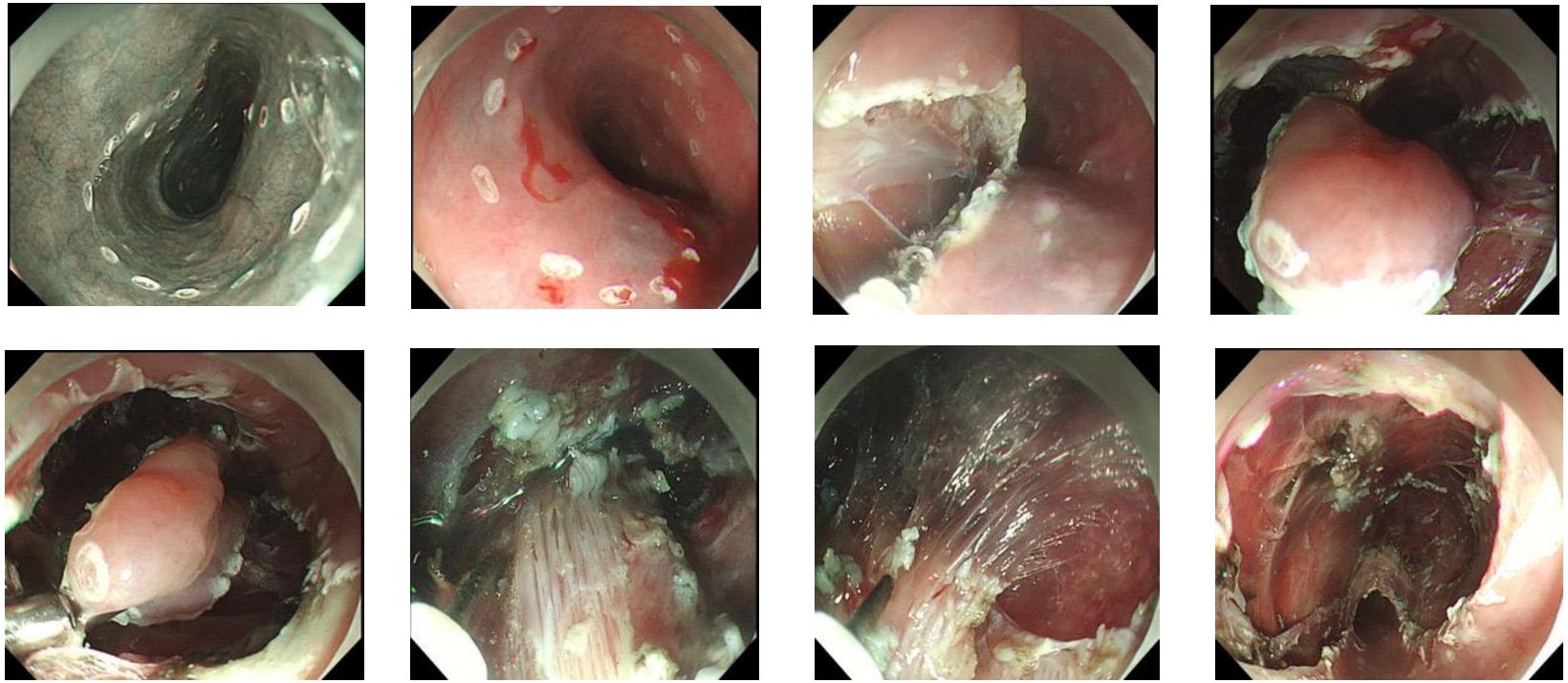






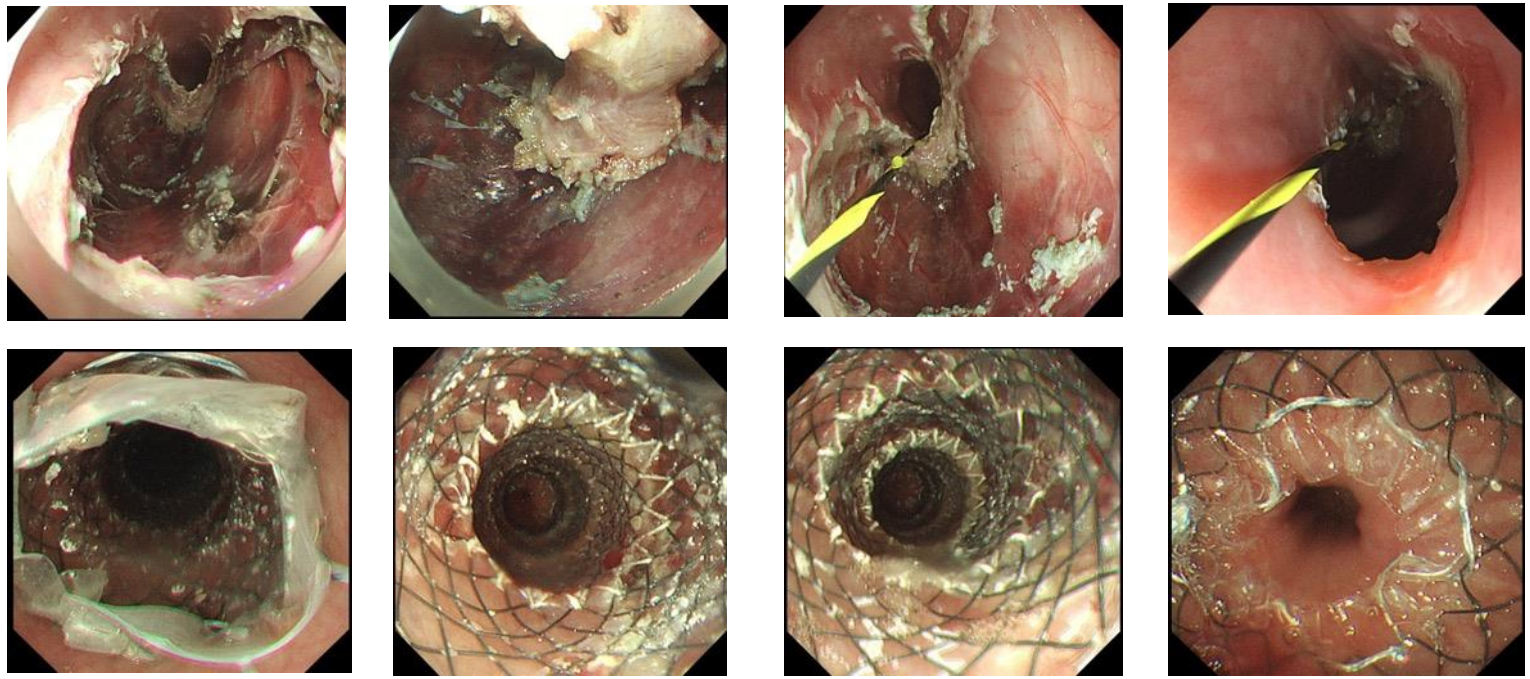
CASE 2：ESCC Patient with Comorbidities

EFTR after conversion therapy

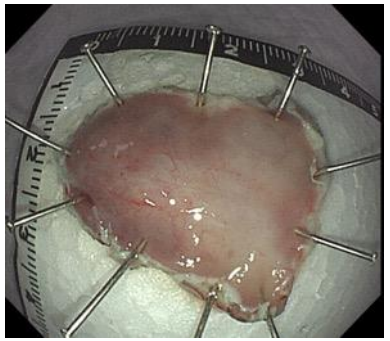
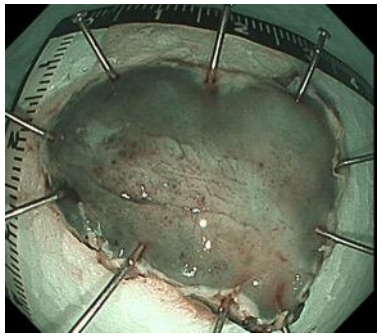
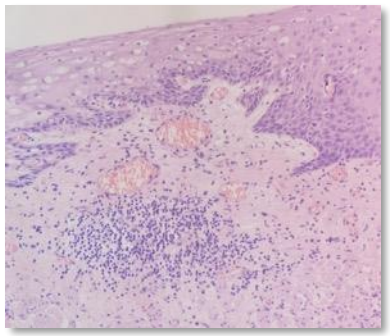
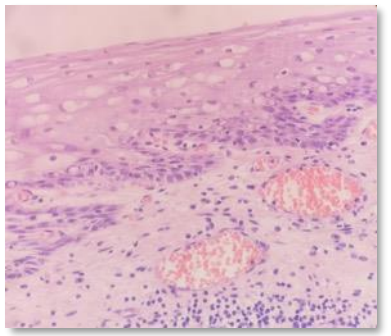


CASE 2：ESCC Patient with Comorbidities

Stent placement after conversion therapy



CASE 2：ESCC Patient with Comorbidities

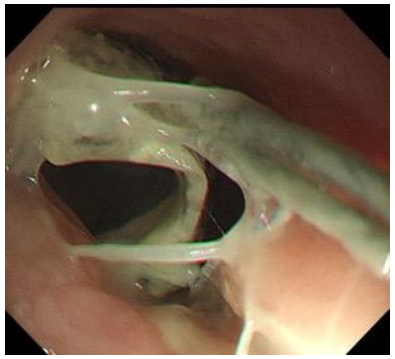
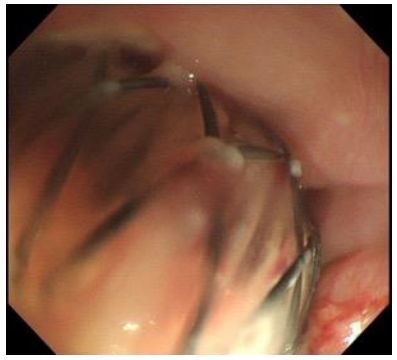





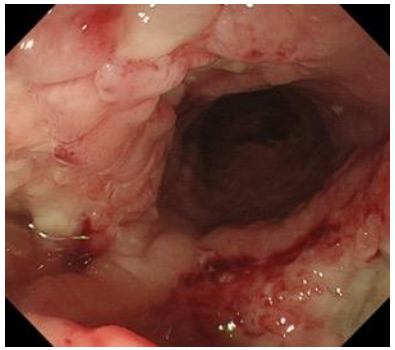
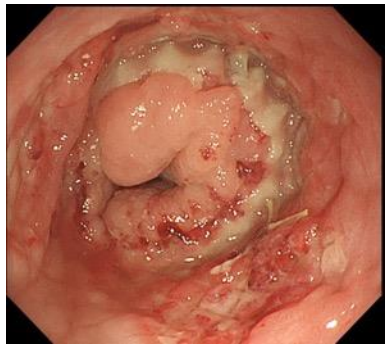
Postoperative Pathology

High-grade squamous intraepithelial. Tumor regression grade (TRG) 0.

CASE 2：ESCC Patient with Comorbidities

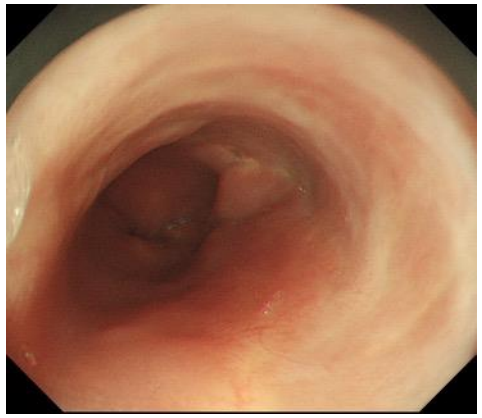
Esophageal stent removed 3 weeks after EFTR

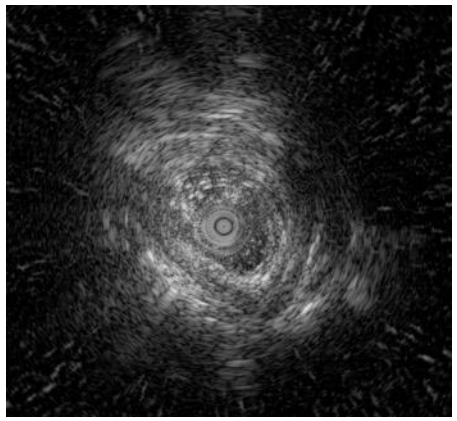




CASE 2：ESCC Patient with Comorbidities

Gastroscopy at 12 months postoperatively:







Postoperative patients were treated with immunotherapy and followed up regularly for 43 months, with no recurrence

Endoscopic resection after downstaging of oesophageal carcinoma by neoadjuvant chemoimmunotherapy: – a new multimodal concept?

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► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/gutjnl-2024-333337).

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MESSAGE

Oesophageal surgery is the current standard for advanced oesophageal cancer within multimodal protocols involving perioperative chemoimmunotherapy and/or radiotherapy. However, oesophagectomy is afflicted with significant morbidity and mortality so that organ-preserving strategies would be worthwhile to develop. We report a case of advanced oesophageal squamous cell cancer (cT2) treated by neoadjuvant therapy and presumably downstaged to a superficial lesion. Semicircumferential endoscopic full-thickness resection (EFTR) was performed, followed by implantation of a metallic stent. Histology showed residual intramucosal high-grade dysplasia. Three months postoperation, the wound healed well, with no occurrence of oesophageal stenosis. The patient received immunotherapy until 24 months post-EFTR and has been followed for 26 months without the recurrence of the disease. Further studies have to show the oncological success, but also oncological risks associated with such an innovative approach.

PATIENT HISTORY

A 68-year-old male patient with a history of chronic obstructive pulmonary disease, pulmonary hypertension, coronary artery disease and prior coronary stent placement presented with a 1-month history of intermittent dysphagia. Endoscopy revealed oesophageal mucosal elevation and ulcers at 31–34 cm from the incisors (figure 1A). Preoperative imaging using CT and endoscopic ultrasound indicated the cT2 stage, without evidence of lymph node involvement or distant metastases (figure 1B). Pathological analysis confirmed the diagnosis of well-differentiated squamous cell carcinoma (figure 2A). The tumour stroma was enriched with programmed cell death protein-1 (PD-1) positive immune cells (figure 2B). After the full discussion with the multidisciplinary team (MDT), the patient was unsuitable for surgery. The conversion therapy and endoscopic resection were attempted.

DESCRIPTION OF TREATMENT PROCEDURE

The patient underwent four cycles of neoadjuvant chemotherapy, comprising cisplatin at an area under the curve of 5 administered on Day 1 every

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Experience in our center

Core design

Retrospective, single-center pilot cohort · June 2022–February 2025

Selected non-surgical cT1b–2N0–2M0 ESCC (n = 40) → Neoadjuvant therapy → **Endoscopic resection ESD or EFTR** → Pathology + outcomes Median follow-up: 23 mo

1 Clinical response assessment

Endoscopy + systematic biopsy EUS + contrast-enhanced CT

cCR	ncCR	iCR
19 (47.5%)	15 (37.5%)	6 (15.0%)

Biopsy negative for invasive carcinoma: 34/40 (85.0%)

Most patients appeared to have a complete or near-complete clinical response.

2 ER for specimen-based restaging

ESD	EFTR
28 (70.0%)	12 (30.0%)

En bloc	R0 resection
100%	92.5%

Safety: stricture 35.0%
30-day mortality 2.5%

ER was technically feasible, but post-procedural morbidity remained clinically relevant.

3 Pathology exposes discordance

Local pCR / ypT0	Residual disease
17 (42.5%)	23 (57.5%)

Residual tumor remained in patients classified as cCR, while local pCR also occurred in ncCR and iCR.

Whole-specimen pathology provided ypT stage, TRG, margins, and adverse features.

Conventional assessment did not reliably identify local pathological eradication.

4 Pathology refines outcome stratification

Disease progression: 12/40 (30.0%)

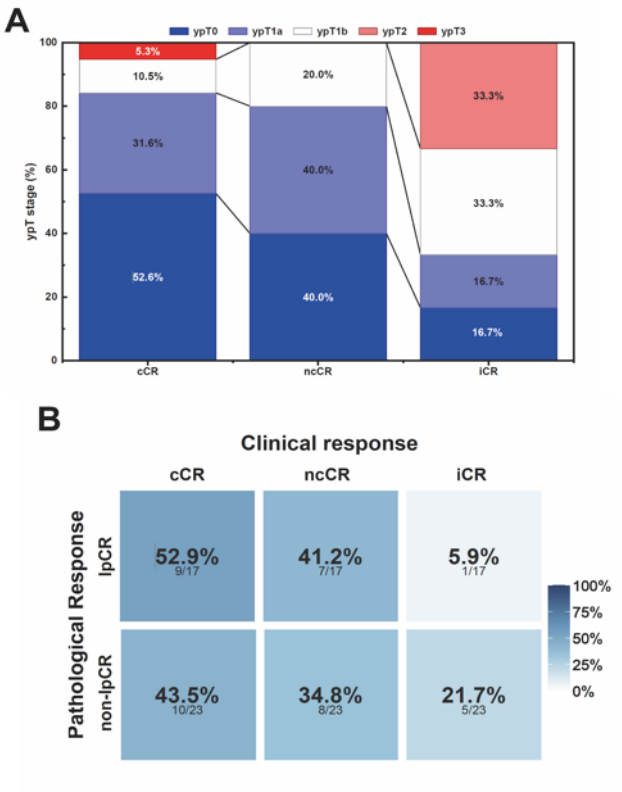
Local pCR	Without local pCR
2/17 (11.8%)	10/23 (43.5%)

PFS by local pCR: P = 0.014
PFS by clinical response: P = 0.429

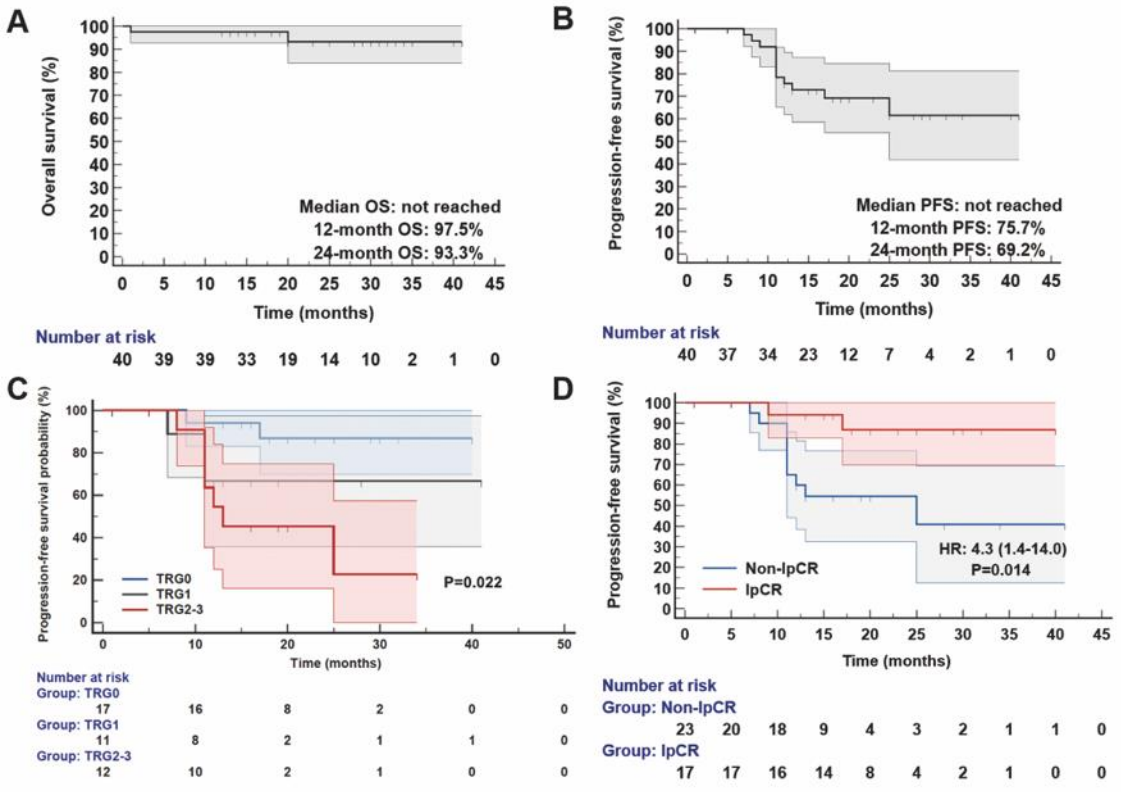
ER-derived local pCR, rather than clinical response alone, separated PFS.

Experience in our center

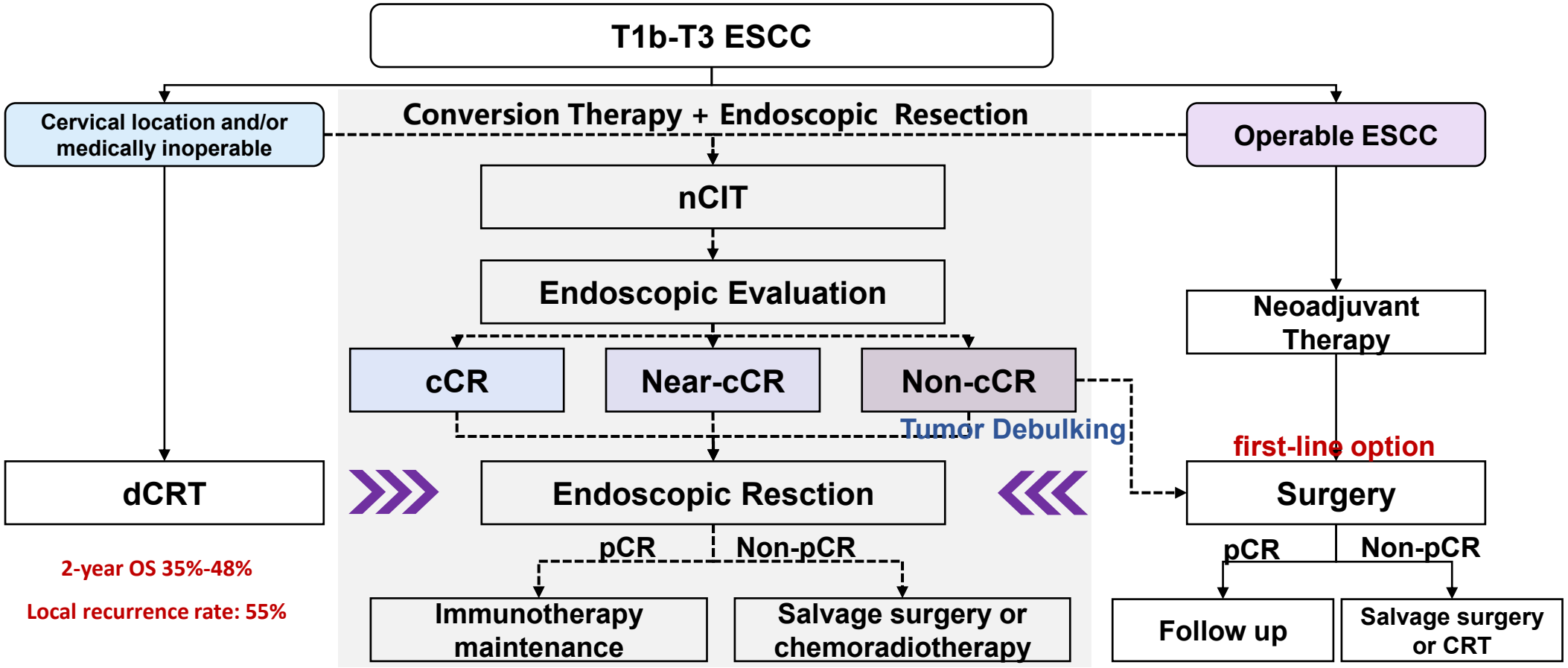
Discordance between clinical response and pathological response



Patients achieving TRG0 (lpCR) had no residual tumor and exhibited an improved PFS



Potential algorithm for role of ER in ESCC



Summary

- After conversion therapy, if the lesion significantly regresses after clinical evaluation, endoscopic resection of residual lesions can be attempted to preserve esophageal function.
- Endoscopic resection after conversion therapy can be used as a supplementary treatment for advanced esophageal cancer that unsuitable (or refuse) surgical intervention.
- Blood biomarkers are needed to be explored to ensure the oncological safety of organ preserving endoscopic resection technique.

Thank you!

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