Advances and Innovations in Endoscopic Oncology and Multidisciplinary Gastrointestinal Cancer Care

Minimally Invasive Cancer Management: Make the Case Gastroenterologist or Surgeon (Surgeon)

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Disclosures

- I do not have any relevant financial relationships.

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

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.

Starting at the beginning…
Rectal polyps & The Role of the Surgeon

Transanal Endoscopic Surgery

- TES was developed as an alternative to radical proctectomy given the lower morbidity and mortality associated with the procedure.
- TES does not evaluate the mesorectal lymph nodes, appropriate patient selection is paramount.
- Therefore, TES is contraindicated for T2 lesions and should be offered only for T1 tumors with associated low-risk features as described.

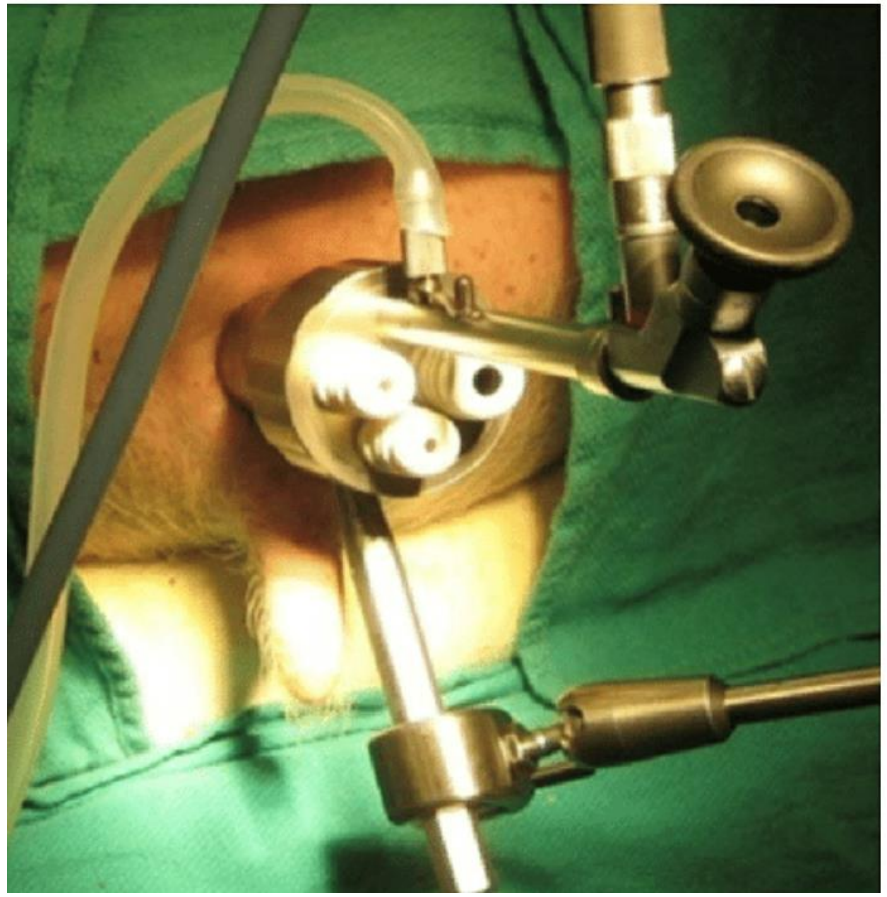
A Surgeon Approach to Early Stages of Rectal Cancer (Malignant polyps)

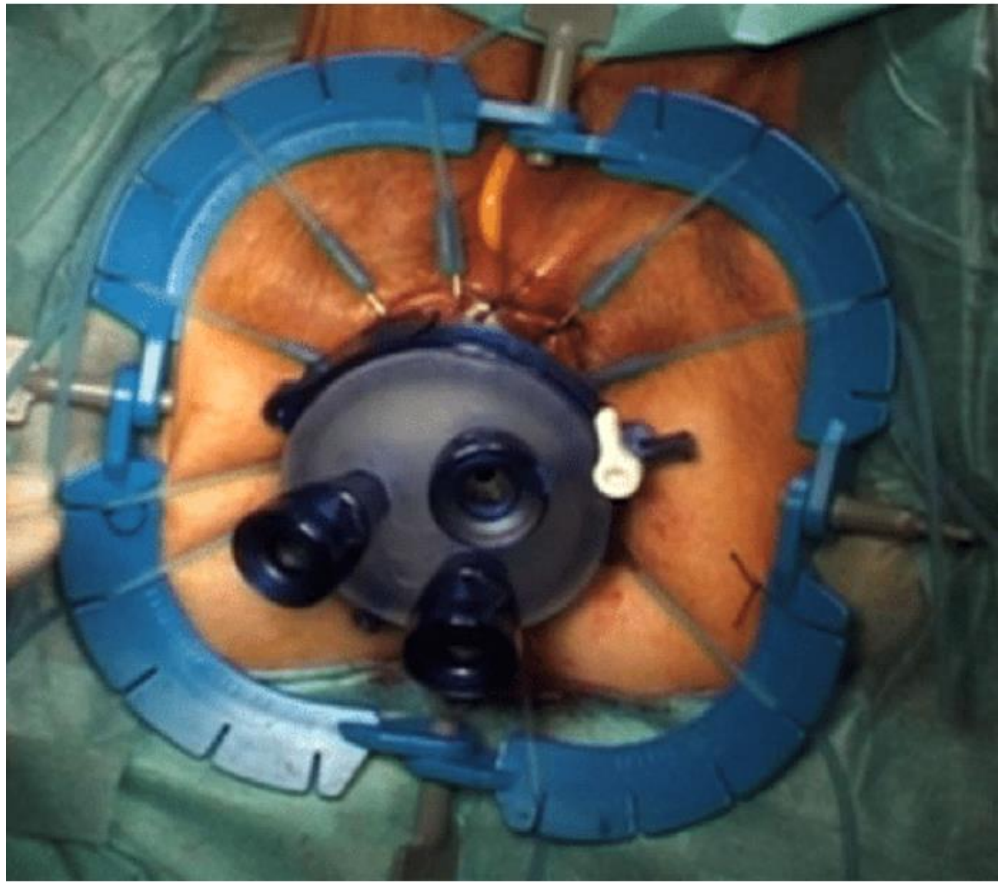
- Local Excision Techniques

- TEM, TEO & TAMIS & Transanal Excision

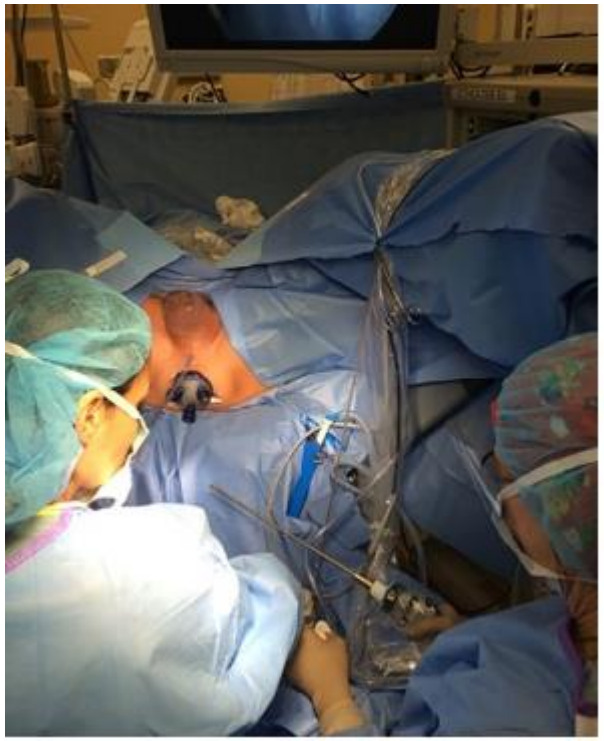
Rahman etal Evaluation and Management of malignant Colorectal Polyps. Surgical Clinics N Am 2023.

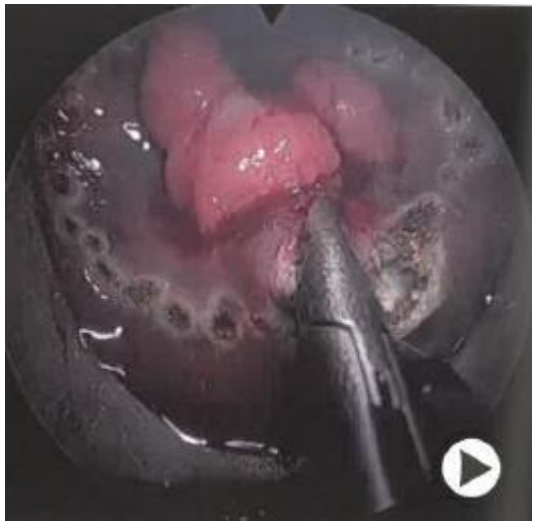
Local excision Techniques

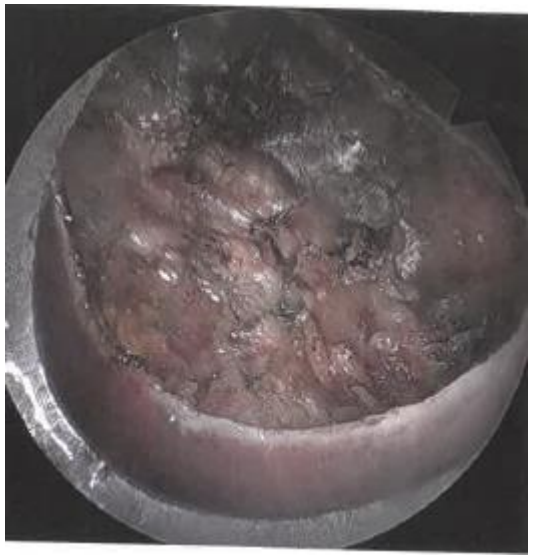


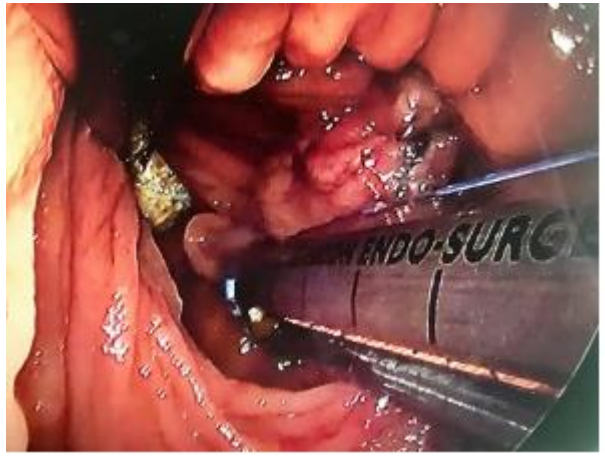


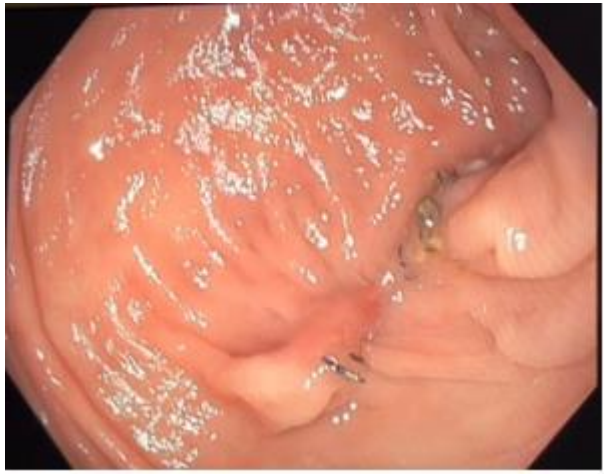
Local excision Techniques











Rectal polyps
Significance of Depth of Invasion

Table 1
Paris classification and associated risk of submucosal invasion

Lesion Morphology	Paris Classification	Submucosal Invasion Rate
Protruding lesions	0-Ip: pedunculated	<20 mm: 1.7%[10]
	0-Is: sessile	>20 mm: 30%[10]
	0-Isp: subpedunculated	
Flat elevated lesions	0-IIa: Flat mucosal elevation	4.1%[11]
	0-IIa + c: Flat elevation, central depression	31.8%[11]
	0-IIa + Is: flat elevation, raised broad based nodule	
Flat lesions	0-IIb: flat mucosal change	11.1%[11]
	0-IIc: mucosal depression	<5 mm: 7%[10]
		>20 mm: 87%[10]
	0-III: central excavation	

Rahman etal Evaluation and Management of malignant Colorectal Polyps. Surgical Clinics N Am 2023

Table 4
High- and low-risk features of malignant polyps

High-Risk Features	Low-Risk Features
Haggitt 4	Haggitt <3
Sm 2 or 3	Sm1
>1 mm submucosal invasion	<1 mm submucosal invasion
Presence of lymphovascular invasion	Absence of lymphovascular invasion
High grade, poorly differentiated	Low grade, well or moderately differentiated
Tumor extending to <1 mm of resected margin	Tumor margin >1 mm
Tumor budding	Absence of tumor budding
Cribriform or micropapillary variants	Complete polyp removal
Mucinous or signet ring cell adenocarcinoma	
Removed piecemeal	

Rahman etal Evaluation and Management of malignant Colorectal Polyps. Surgical Clinics N Am 2023.

EMR vs TES

- The TREND study was a 1:1 randomized control trial that evaluated EMR versus TES for rectal adenomas greater than 3 cm in size. Of the 176 patients included in the analysis, at 3 months, the adenoma remnant rate was higher in the EMR group compared with the TES group (19 vs 5%, P=.008). However, at 24 months, the adenoma recurrence rate in the EMR group and TES group was not statistically significant (15% vs 11%, P= .23)

- Recent trial found that the negative resection margin was high for both EMR and TES (94.3% vs 100%); however, the fragmentation rate was higher in the EMR group compared with TES (22.6% vs 0%, P=. 001)

Barendse RM, Musters GD, De Graaf EJR, et al. Randomised controlled trial of transanal endoscopic microsurgery versus endoscopic mucosal resection forlarge rectal adenomas (TREND Study). Gut 2018;67(5):837–46.

Shen JM, Zhao JY, Ye T, et al. Transanal minimally invasive surgery vs endoscopic mucosal resection for rectal benign tumors and rectal carcinoids: a retrospective analysis. World J Clin Cases 2020;8(19):4311–9.

ESD vs TES

- Study with 204 pts no difference between ESD and TES when evaluating en bloc resection rate (90 vs 100%, P 5 .08), local recurrence at 6 months (2.9 vs 5.8%), or an R0 resection (83 vs 91%, P=.6). There was, however, a higher rate of infection/abscess in the TEM group compared with ESD (20% vs 0%).

- 2020 meta-analysis involving 326 patients compared ESD versus TES and found no-difference between the two procedures when evaluating local recurrence, en block resection rates, or R0 resection rates.

Kim M, Bareket R, Eleftheriadis NP, et al. Endoscopic submucosal dissection (ESD) offers a safer and more cost-effective alternative to transanal endoscopic microsurgery (TEM): an international collaborative study. J Clin Gastroenterol 2022;486–9.

Sagae VMT, Ribeiro IB, de Moura DTH, et al. Endoscopic submucosal dissection versus transanal endoscopic surgery for the treatment of early rectal tumor: asystematic review and meta-analysis. Surg Endosc 2020;34(3):1025–34.

What happens with Rectal Cancer after TNT

What is the role of TES in Advanced Rectal Cancer After TNT

pCR 28.4%
Distant Met 20%

pCR 14.3%
Distant Met 26.8%

Same OS
Same operative complications

***RAPIDO TRIAL Lancet Oncol* 2021; 22:29-42**

Consolidation TNT with Triplet Chemo

PRODIGE Trial

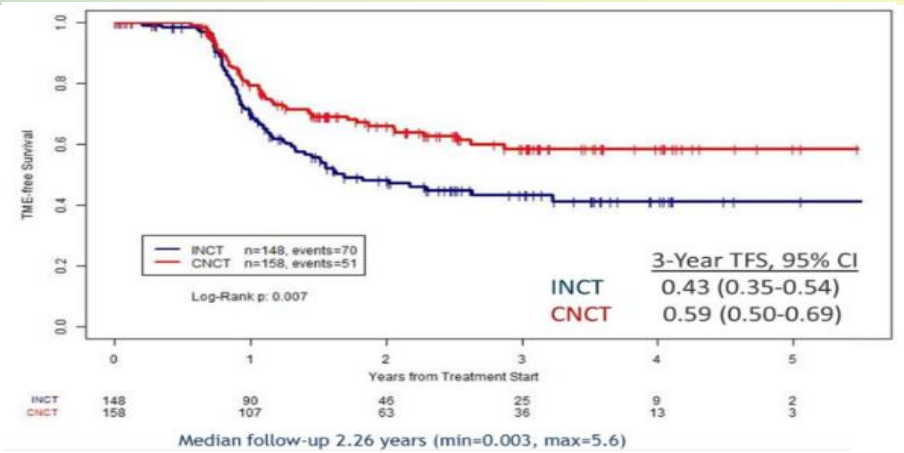
pCR 28%
3 yr DFS 76%

pCR 13%
3 yr DFS 69%

Same operative characteristics

Lancet Oncol 2021; 22:702-15

Organ Preservation



Induction

Chemotherapy → Chemoradiation → Observation

43%

Consolidation

Chemoradiation → Chemotherapy → Observation

59%

Same DFS (77/78%)

J Clin Oncol 2022;40:2546-2556

OPRA: Long Term Results

Lessons Learned

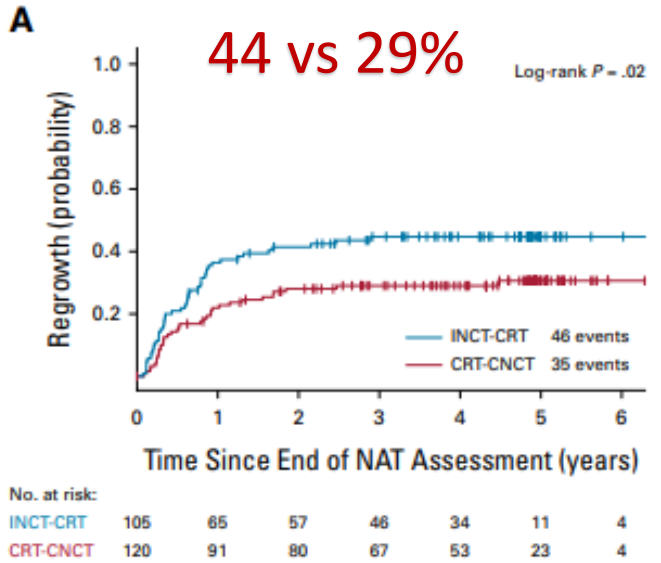
74% offered W&W

36% regrowth
94% within 2 years
99% within 3 years

R0 resection rates the same between immediate and salvage TME
13% developed mets even with sustained CR

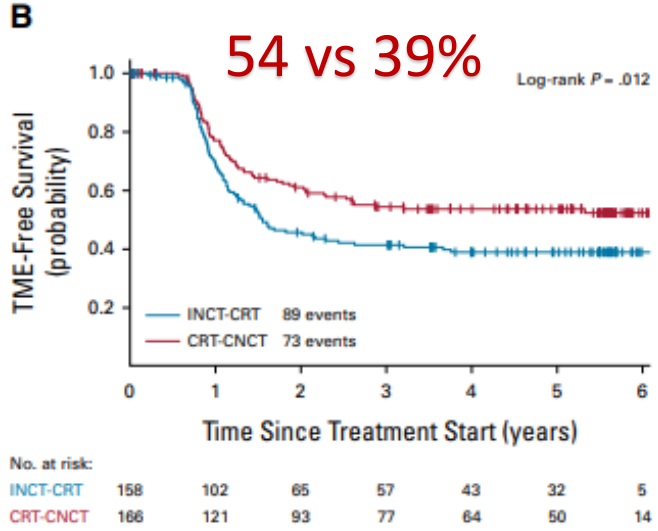
Regrowth

44 vs 29%

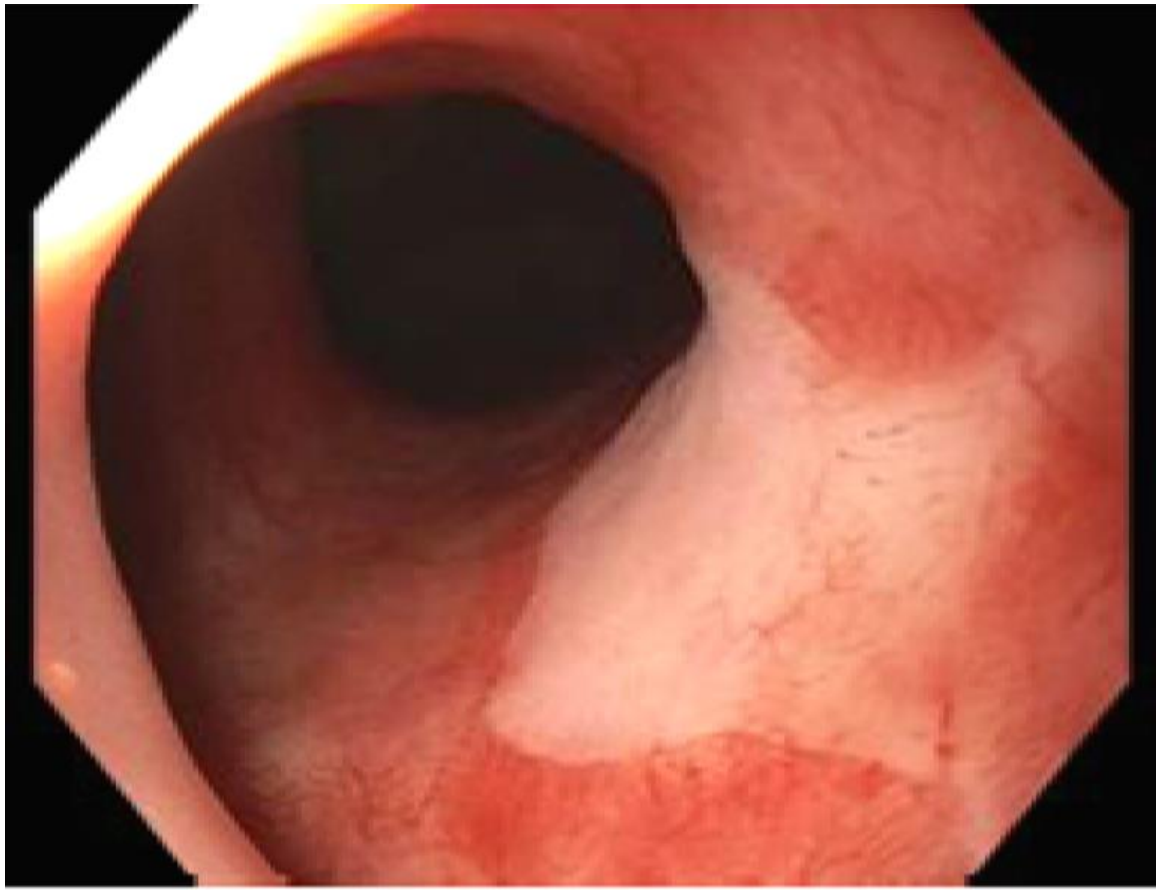


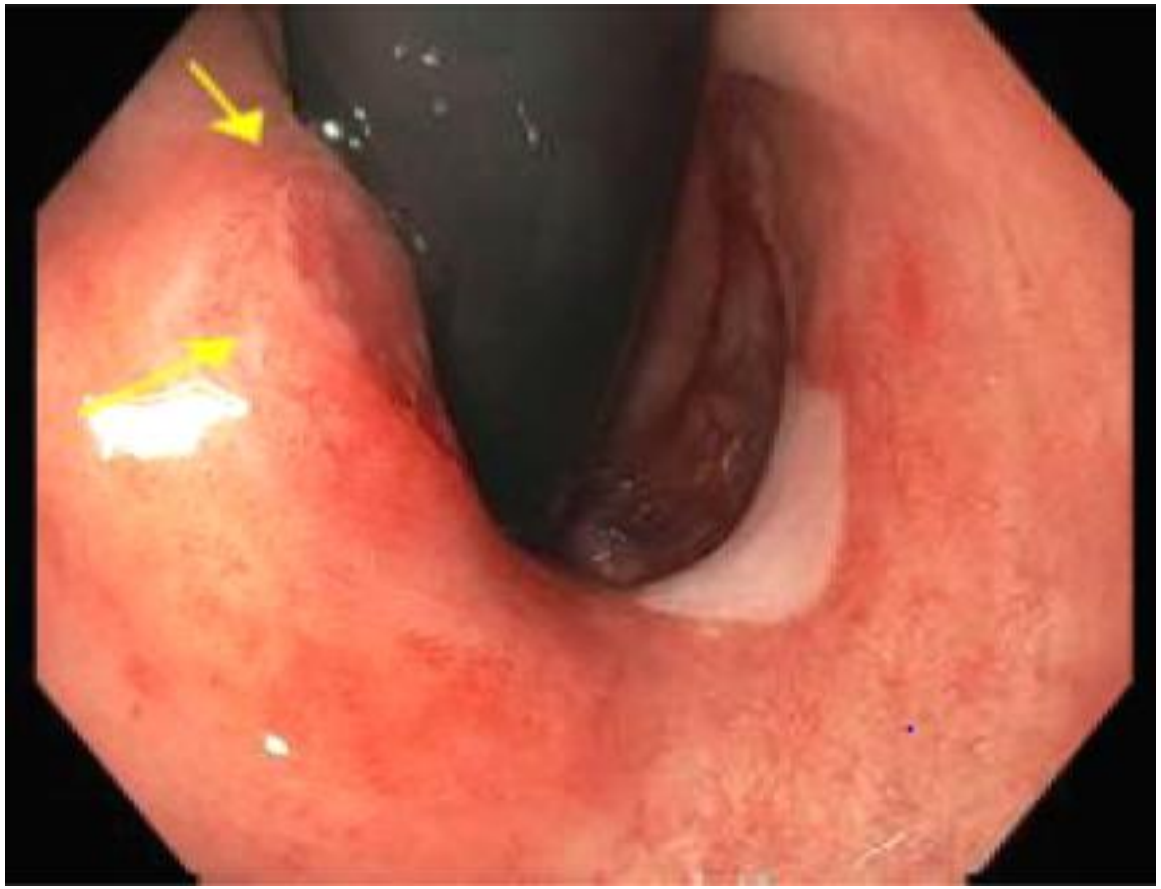
Organ Preservation

54 vs 39%



J Clin Oncol 2022;40:2546-2556





Current standard

JAMA Oncology | Original Investigation

Chemoradiotherapy Plus Induction or Consolidation Chemotherapy as Total Neoadjuvant Therapy for Patients With Locally Advanced Rectal Cancer

Long-term Results of the CAO/ARO/AIO-12 Randomized Clinical Trial

Salvage Surgery

Systematic Reviews

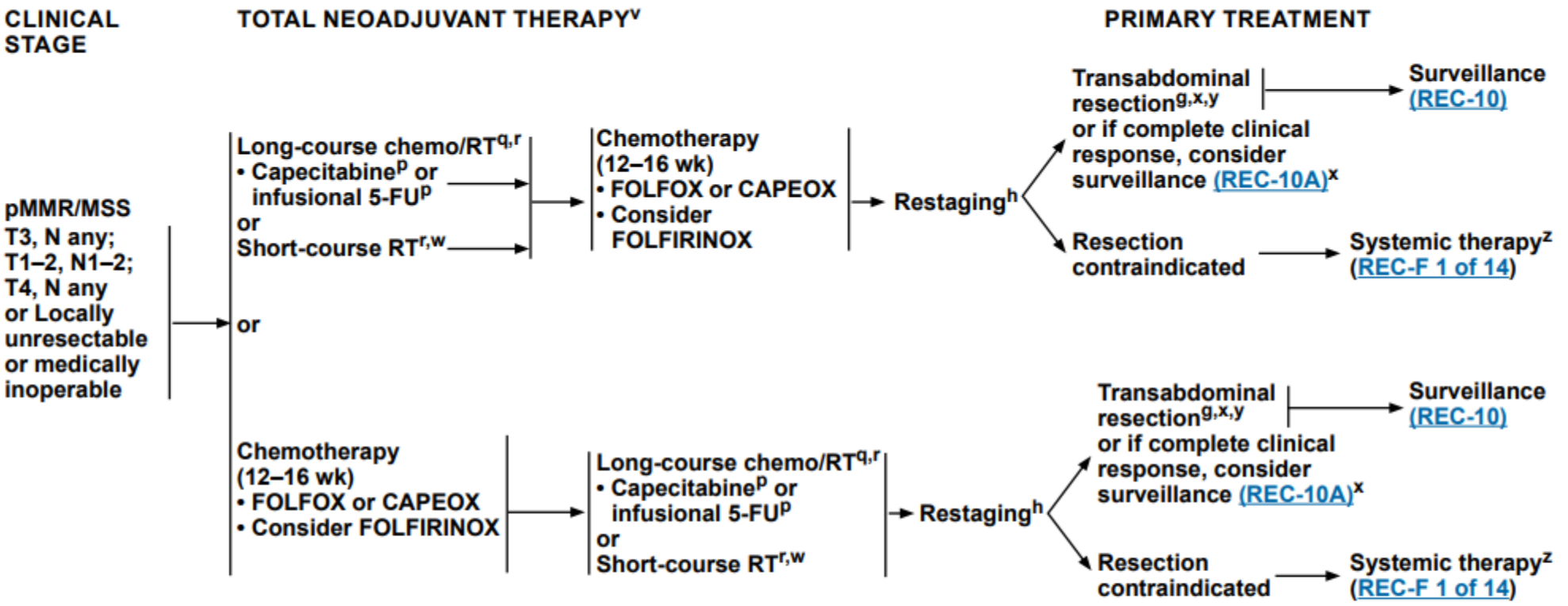
15 studies
Regrowth rate 21.3%
Salvage surgery possible in 92.3%

17 studies
Regrowth rate 22.1%, 96% within 3 yrs
Salvage surgery possible in 88%
Distant failure in 8%, 60% without regrowth

Ann Surg Oncol 2017;24:1904
Ann Surg 2018:268:955

NCCN Guidelines Version 1.2023
pMMR/MSS Rectal Cancer

NCCN Guidelines Index
Table of Contents
Discussion



[g] Principles of Surgery (REC-C).
[h] Principles of Imaging (REC-A).
[p] Bolus 5-FU/leucovorin/RT is an option for patients not able to tolerate capecitabine or infusional 5-FU.
[q] Principles of Perioperative Therapy (REC-D).
[r] Principles of Radiation Therapy (REC-E).
[v] In select cases (eg, a patient who is not a candidate for intensive therapy) neoadjuvant therapy with chemo/RT or RT alone may be considered prior to surgery.
[w] Evaluation for short-course RT should be in a multidisciplinary setting, with a discussion of the need for downstaging and the possibility of long-term toxicity.
[x] In those patients who achieve a complete clinical response with no evidence of residual disease on digital rectal examination (DRE), rectal MRI, and direct endoscopic evaluation, a "watch and wait," nonoperative (chemotherapy and/or RT) management approach may be considered in centers with experienced multidisciplinary teams. The degree to which risk of local and/or distant failure may be increased relative to standard surgical resection has not yet been adequately characterized. Decisions for nonoperative management should involve a careful discussion with the patient of their risk tolerance.
[y] For select patients who may be candidates for intraoperative RT (IORT), see Principles of Radiation Therapy (REC-E).
[z] FOLFIRINOX is not recommended in this setting.

Avoiding Overtreatment: 'Watch and Wait'

Surveillance

DW-MRI q6 mo x3 yr then q 1 yr
Flex sig q4 mo x3 yr then q 6mo

CEA q3 mo x2 yr/q6mo x 2 yr
CT Annually

Organ Preservation and Local Excision?

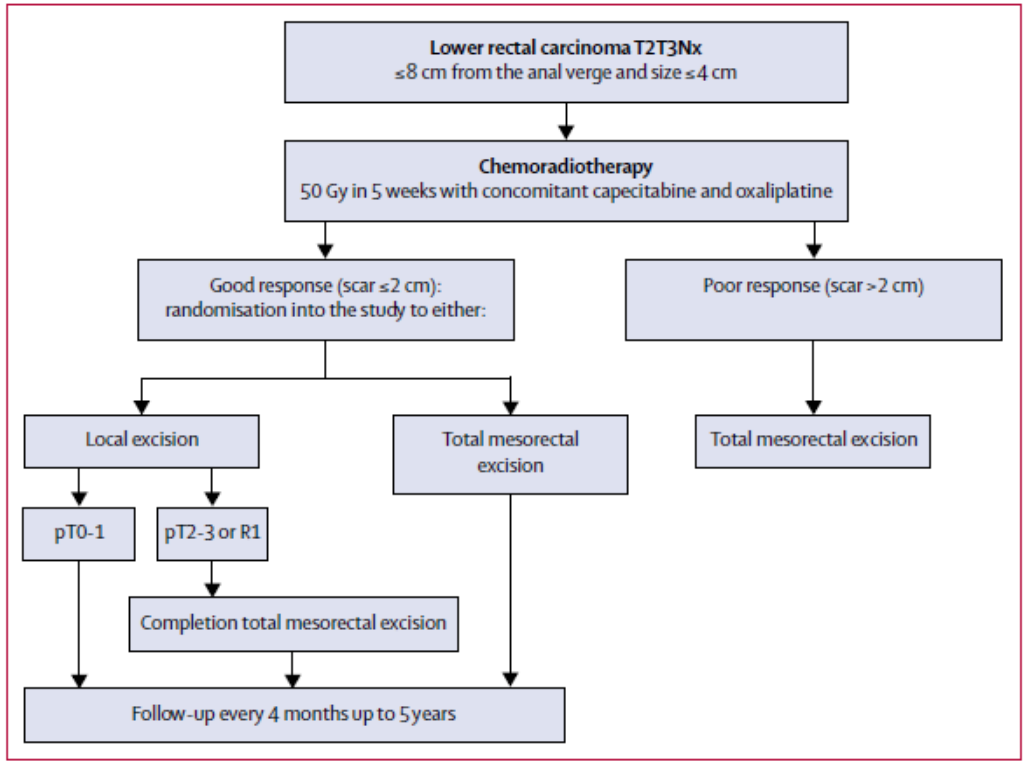


***Figure 1*: Study design**
T=tumour stage. N=nodal stage. p=pathological stage.

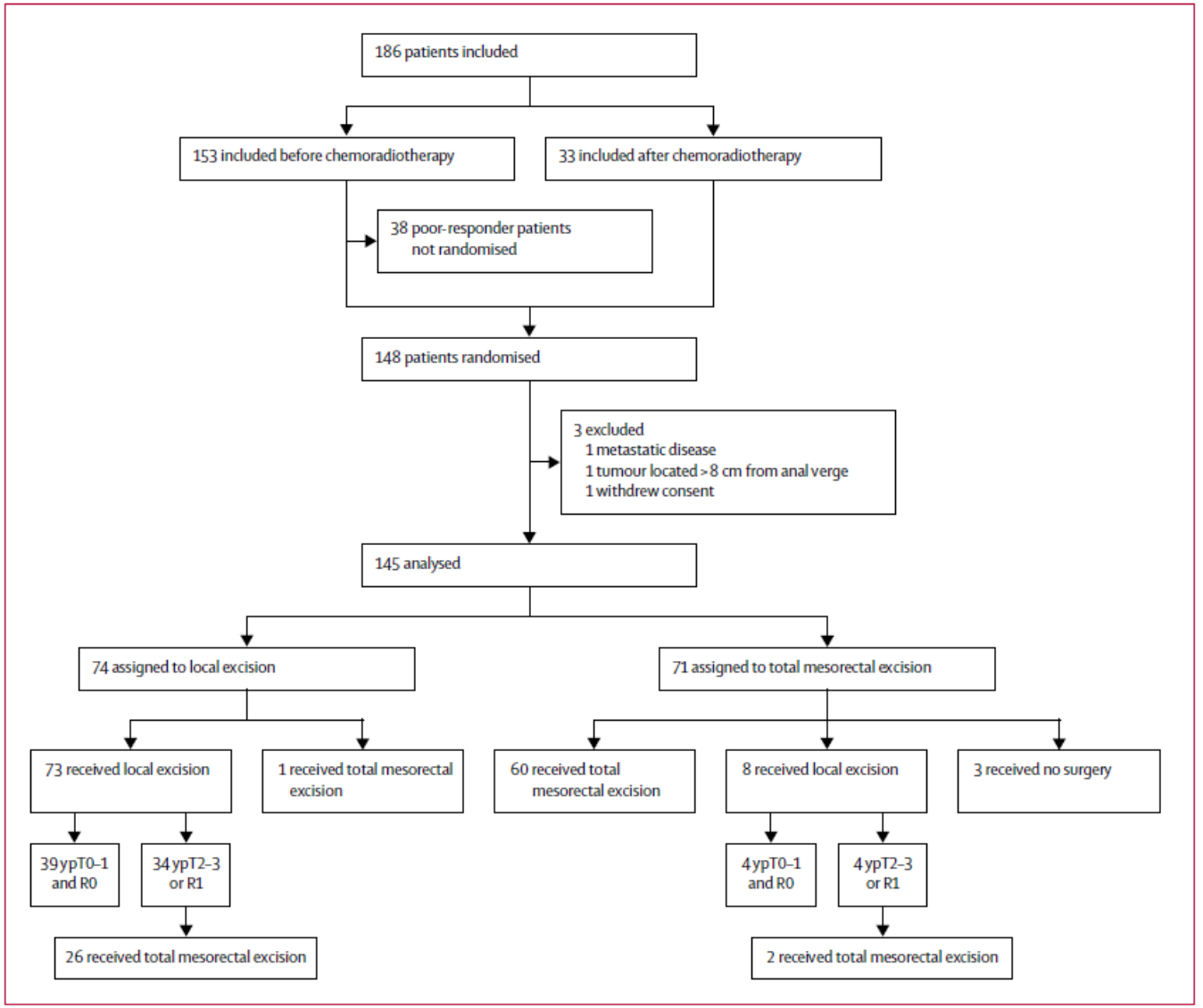


***Figure 2*: Trial profile**

Rullier E, Rouanet P, Tuech J-J, et al. Organ preservation for rectal cancer (GRECCAR 2): a prospective, randomised, open-label, multicentre, phase 3 trial. *Lancet* 2017; 390: 469–79.

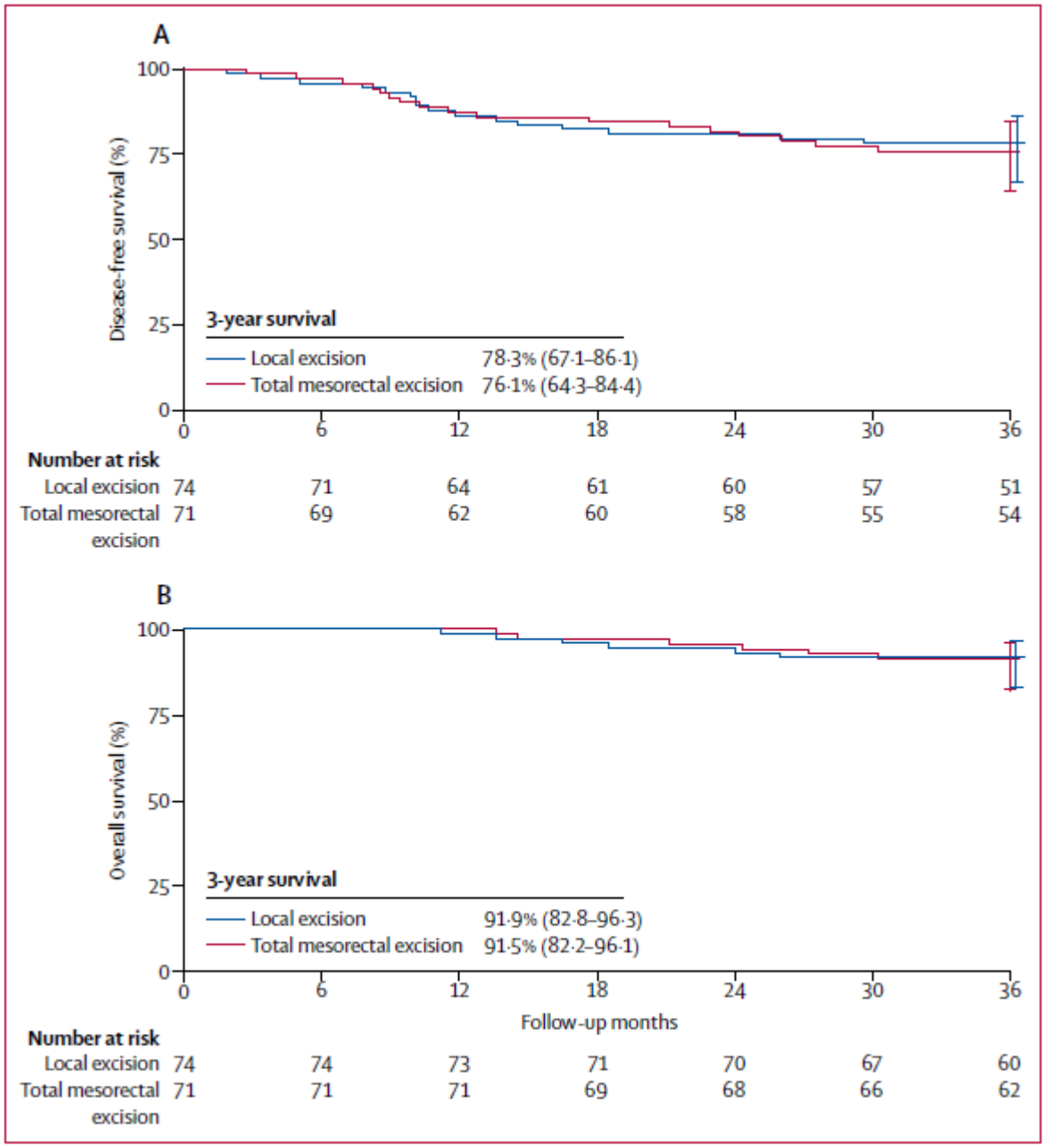


Figure 3: **Survival after local excision versus total mesorectal excision**

Rullier E, Rouanet P, Tuech J-J, et al. Organ preservation for rectal cancer (GRECCAR 2): a prospective, randomised, open-label, multicentre, phase 3 trial. *Lancet* 2017; 390: 469–79.

Option for organ preservation for early stages of rectal cancer

Organ Preservation for Early Rectal Cancer

CONTEXT

Key Objective

Can 3 months of modified folinic acid–fluorouracil-oxaliplatin 6 (mFOLFOX6)/capecitabine-oxaliplatin (CAPOX) followed by transanal excision surgery be used to treat magnetic resonance imaging-stage cT1-3bN0 rectal cancer?

Knowledge Generated

Induction mFOLFOX6/CAPOX followed by transanal excision surgery was well tolerated and resulted in downstaging to ypT0/T1 cN0 tumors in 57% of 58 enrolled patients with well to moderately differentiated adenocarcinoma and preserved mismatch repair. Overall, 79% of patients pursued an organ-sparing strategy, with two patients experiencing a locoregional relapse during the 15.4-month follow-up period. Quality of life and rectal function scores demonstrated almost no change compared with baseline.

Relevance

Early results suggest that this novel treatment strategy leads to downstaging to ypT0/T1 cN0 in the majority of selected patients with early rectal cancer. The approach offers a much-desired organ-sparing option and warrants further investigation.

TABLE 3. Clinical Stage, psOPR, and Pathologic Outcomes of Patients Treated With TES or TME Surgery

	TES ypT Status, N0/X					TME ypT Status				TME ypN Status	
cT Stage	T0	T1	T2	T3	psOPR, No. (%)	T0	T1	T2	T3	N0	N1
T1 (n = 8)	3	2	1	1	5/8 (63)	1	0	0	0	1	0
T2 (n = 37)	10	10	16	0	20/37 (54)	4	0	0	2	5	1
T3 (n = 13)	7	2[a]	3	1	8/13 (62)	3	0	0	0	2	1
Totals (N = 58)	20	14	20	2	33/58 (57)	8	0	0	2	8	2
	TES = 56				90% CI, 45 to 68	TME = 10					

Kennecke HF etal Neoadjuvant Chemotherapy, Excision and Observation for Early Rectal cancer ; JCO 2022 41 (2)

Organ Preservation for Early Rectal Cancer

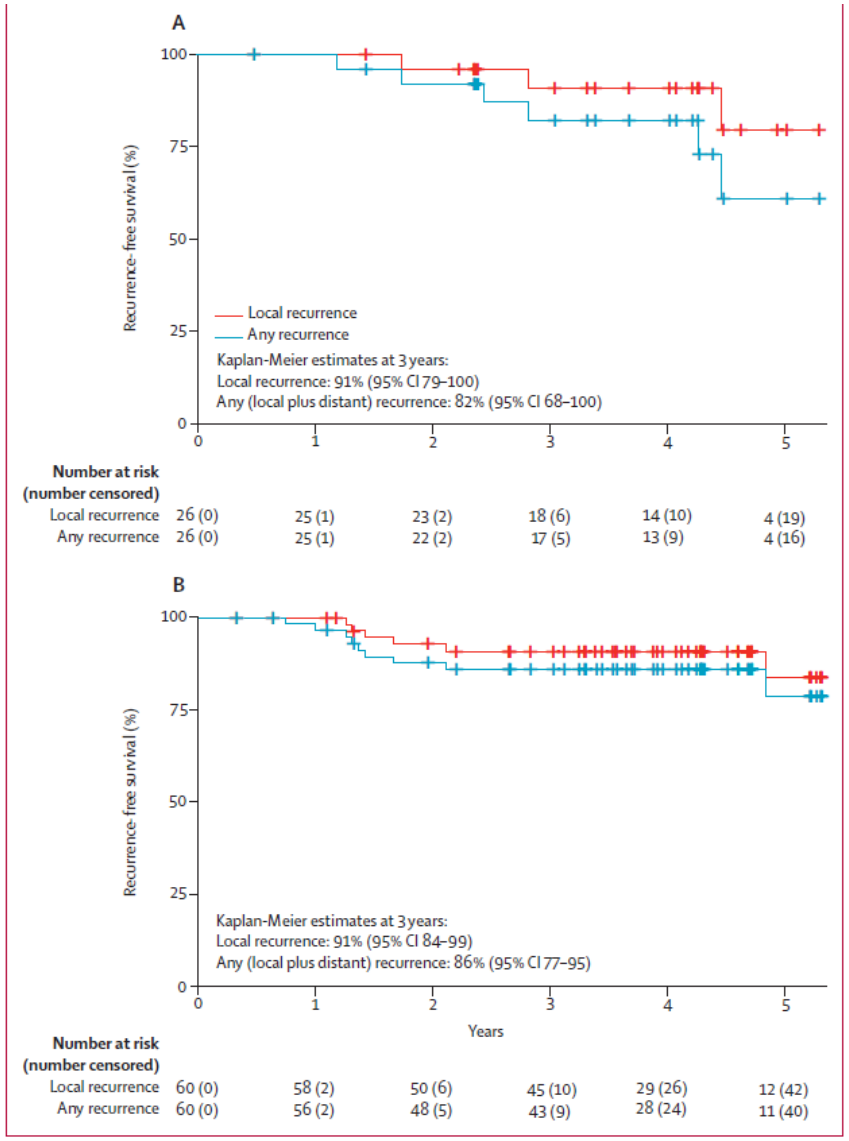


Figure 3: Cumulative risk of any local recurrence compared to risk of any recurrence (local or distant) with organ preservation therapy in intention-to-treat population

Added value of this study

The TREC study demonstrates the feasibility of randomly assigning patients with early-stage rectal cancer to a multimodality organ preservation strategy (incorporating short-course radiotherapy and transanal endoscopic microsurgery) versus radical surgery without radiotherapy. The comparison of organ preservation with radical surgery showed some benefits of organ preservation with respect to fewer serious surgical complications, low acute patient-reported toxicity, and little impact on QOL and function at 3 months. Sustained benefits for up to 3 years in overall QOL, social function, body image, and decreased embarrassment about bowel function were also observed with organ preservation. **The risk of unsalvageable local recurrence was low in TREC.**

Radical surgery versus organ preservation via short-course radiotherapy followed by transanal endoscopic microsurgery for early-stage rectal cancer (TREC): a randomised, open-label feasibility study, Lancet 2021

Transanal Endoscopic Surgery vs Radical Resection for Early-Stage Rectal Cancer

meta-analysis of 13 studies 5 randomized and 8 cohort studies showed that the treatment effect and safety of both TEM and radical surgery

NO DIFFERENCE:

- distant metastasis (RR, 0.59 (0.34, 1.02), $P > 0.05$)
- overall recurrence (RR, 1.49(0.96, 2.31), $P > 0.05$), disease-specific-survival (RR, 0.74 (0.09, 1.57), $P > 0.05$),\
- dehiscence of the suture line or anastomosis leakage (RR, 0.57 (0.30, 1.06), $P > 0.05$),
- postoperative bleeding (RR, 0.47 (0.22, 0.99), $P > 0.05$),
- pneumonia (RR, 0.37, (0.10, 1.40), $P > 0.05$) were not significantly different.

DIFFERENCE:

- perioperative mortality (RR, 0.26 (0.07, 0.93, $P < 0.05$)),
- local recurrence (RR, 2.51 (1.53, 4.21), $P < 0.05$),
- **Overall survival_ (RR, 0.88 (0.74, 1.00), $P < 0.05$),**
- **disease-free-survival (RR, 1.08 (0.97, 1.19), $P < 0.05$),** temporary stoma(RR, 0.05 (0.01, 0.20), $P < 0.05$),
- permanent stoma (RR, 0.16 (0.08, 0.33), $P < 0.05$), postoperative complications(RR, 0.35 (0.21, 0.59), $P < 0.05$), rectal pain (RR, 1.47 (1.11, 1.95), $P < 0.05$)

International Journal of Colorectal Disease (2023) 38:49
https://doi.org/10.1007/s00384-023-04341-9

Thank you

Questions?