

Radiotherapy in Early Rectal Cancer

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ONCOLOGICAL OUTCOMES OF STAGE II-III RECTAL CANCER

Patient outcomes remain poor despite routine adoption of TME

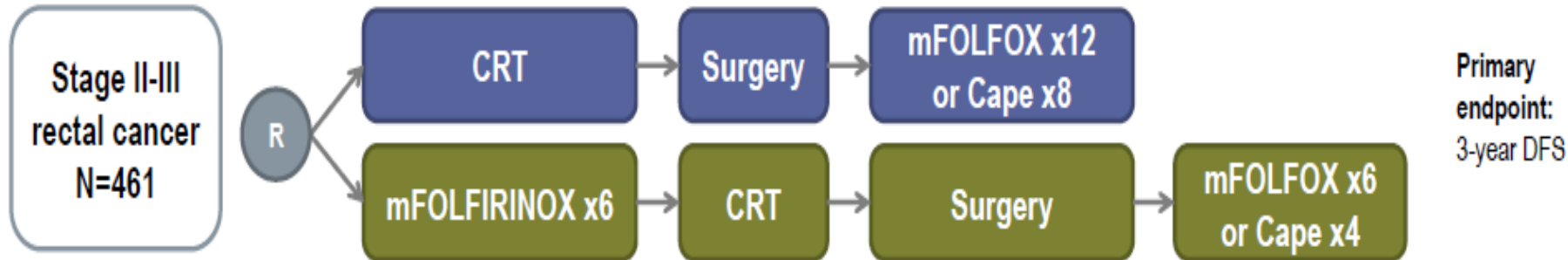
Oncologic outcomes following TME surgery alone*

TNM stage	10-year local recurrence	10-year overall survival
I	3%	72%
II	8%	55%
III	19%	37%

*Data from the control group of the Dutch TME trial.
van Gijn W, et al. Lancet Oncol 2011;12(6):575-82.

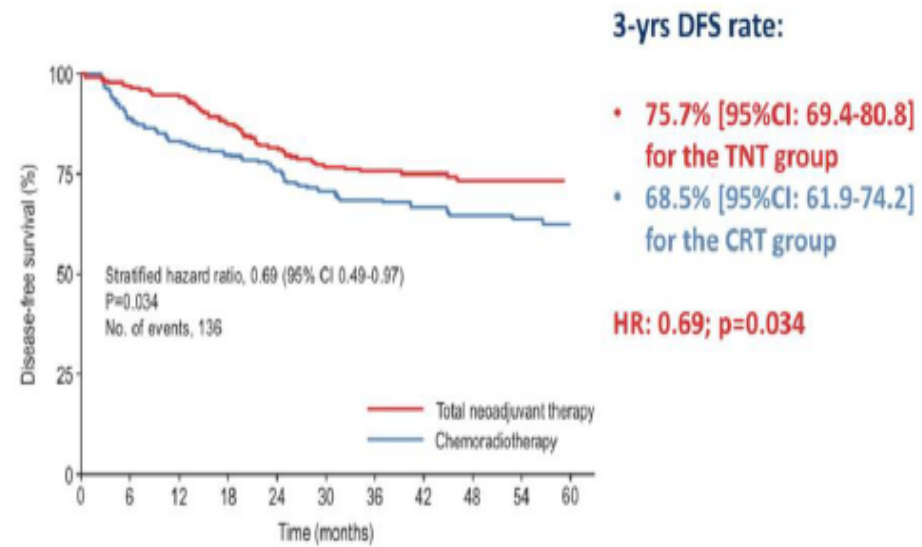
THE PRODIGE 23 TRIAL

3 months of induction mFOLFIRINOX followed by chemoradiotherapy is superior than chemoradiotherapy alone



Treatment	pCR	P-value
Standard	12.1%	<0.001
Experimental	27.8%	

Reduced risk of post-operative complications with TNT
No difference in QoL



	0	6	12	18	24	30	36	42	48	54	60
Total neoadjuvant therapy	231	217	210	194	176	150	126	104	80	62	51
Chemoradiotherapy	230	201	188	177	167	146	117	91	65	55	40

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Early rectal cancer

The benefit of Chemo-Radiotherapy



Less invasive surgery



Less morbidity

Organ preservation

Early Rectal Cancer

Radical TME surgery carries considerable morbidity :

- **Stoma rates**
- **Faecal incontinence**
- **Urinary and sexual dysfunction**

Impair quality of life

Early Rectal Cancer

Local excision techniques:

- **Less morbidity**
- **Minimal chance of functional impairment**

Better of quality of life

Local excision for Rectal Cancer

Low- risk T1N0 rectal cancers

- Well, moderate differentiation,
- No lymphatic or vascular invasion,
- Resection margins > 1 mm,
- Diameter of carcinoma < 3 cm
- No tumour budding
- Superficial submucosal invasion (Sm1)

Local excision for Rectal Cancer

Indications

- **Low- risk T1N0 rectal cancers.**
- **High-risk T1N0, T2N0 rectal cancer (only in elderly frail , stoma averse)**

Existing data support the use of TES for local excision of rectal carcinoid tumors <2 cm, rectal adenomatous polyps, and low-risk T1N0 rectal cancers. Local excision of T2N0 rectal cancers should only be performed in patients who are poor candidates for transabdominal surgery or as

Local recurrence after local excision

- **Low-risk T1N0** → **5%**
- **High-risk T1N0** → **12%**
- **T2N0** → **28%**

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 - T2N0 → 28%
- TME**
- Chemo-radiotherapy**
-
- The diagram lists three cancer stages with their respective local recurrence rates after local excision. A bracket on the right groups the 12% and 28% rates under the label 'Chemo-radiotherapy'. The 5% rate is not grouped. The label 'TME' is positioned above the 12% and 28% rates.
- | Stage | Local Recurrence Rate | Treatment Option |
|----------------|-----------------------|--------------------|
| Low-risk T1N0 | 5% | Local excision |
| High-risk T1N0 | 12% | Chemo-radiotherapy |
| T2N0 | 28% | Chemo-radiotherapy |

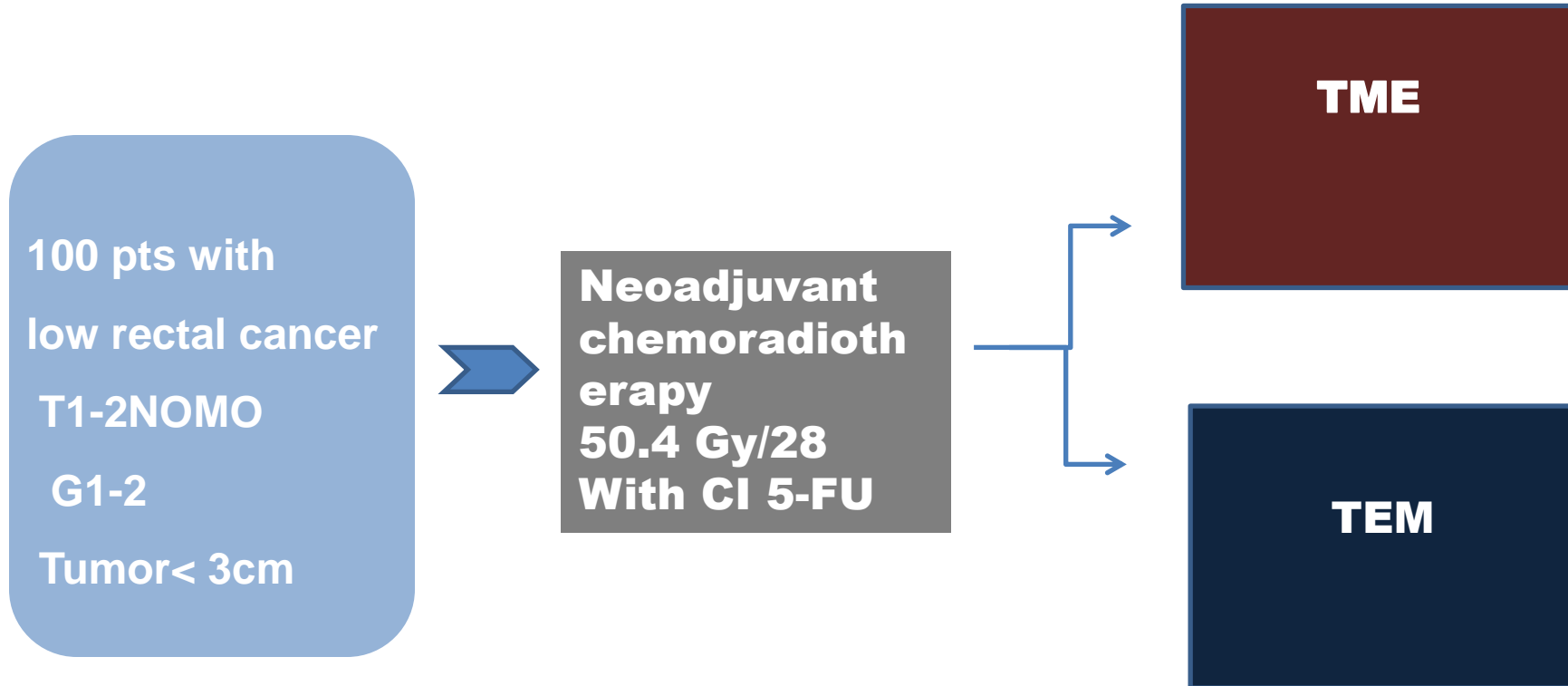
Chemo-Radiotherapy in Early Rectal cancer

➤ **Neoadjuvant**

➤ **Adjuvant**

➤ **Definitive**

**Randomized clinical trial of local resection
versus total mesorectal excision for T2 rectal
cancer after neoadjuvant therapy (URBINO Trial)**



Randomized clinical trial of local resection *versus* total mesorectal excision for T2 rectal cancer after neoadjuvant therapy (URBINO Trial)

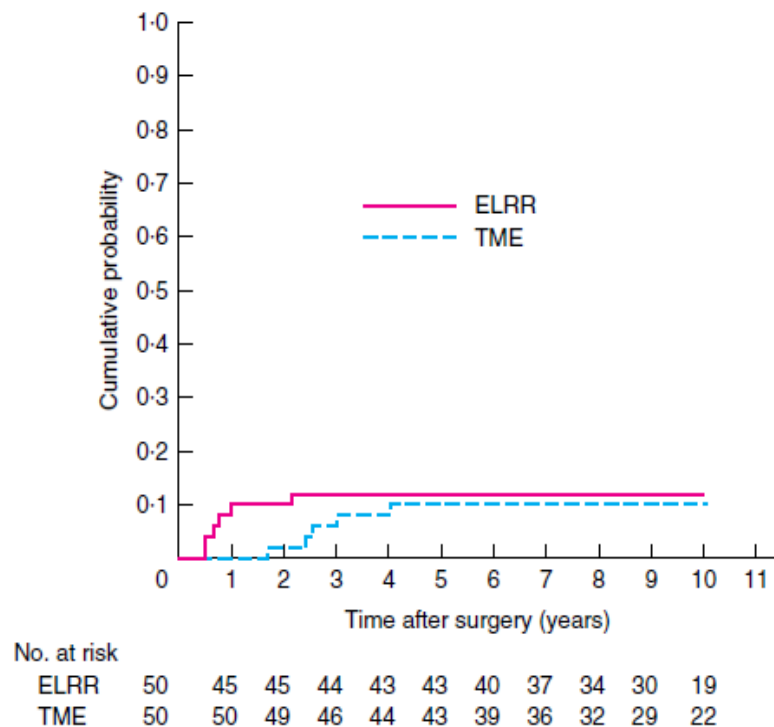


Fig. 2 Cumulative probability of developing recurrence or metastases according to type of operation. ELRR, endoluminal locoregional resection; TME, total mesorectal excision. $P = 0.686$ (log rank test)

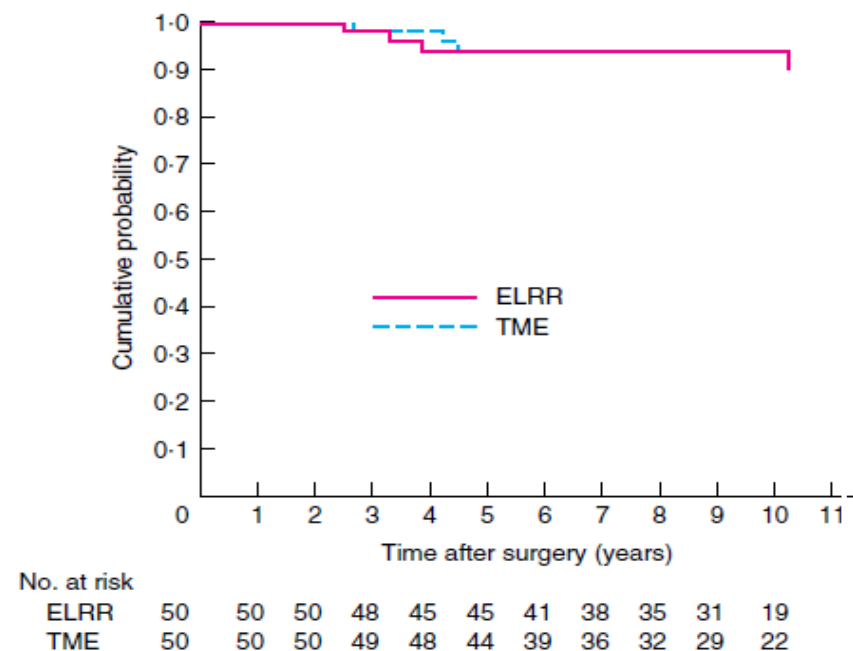
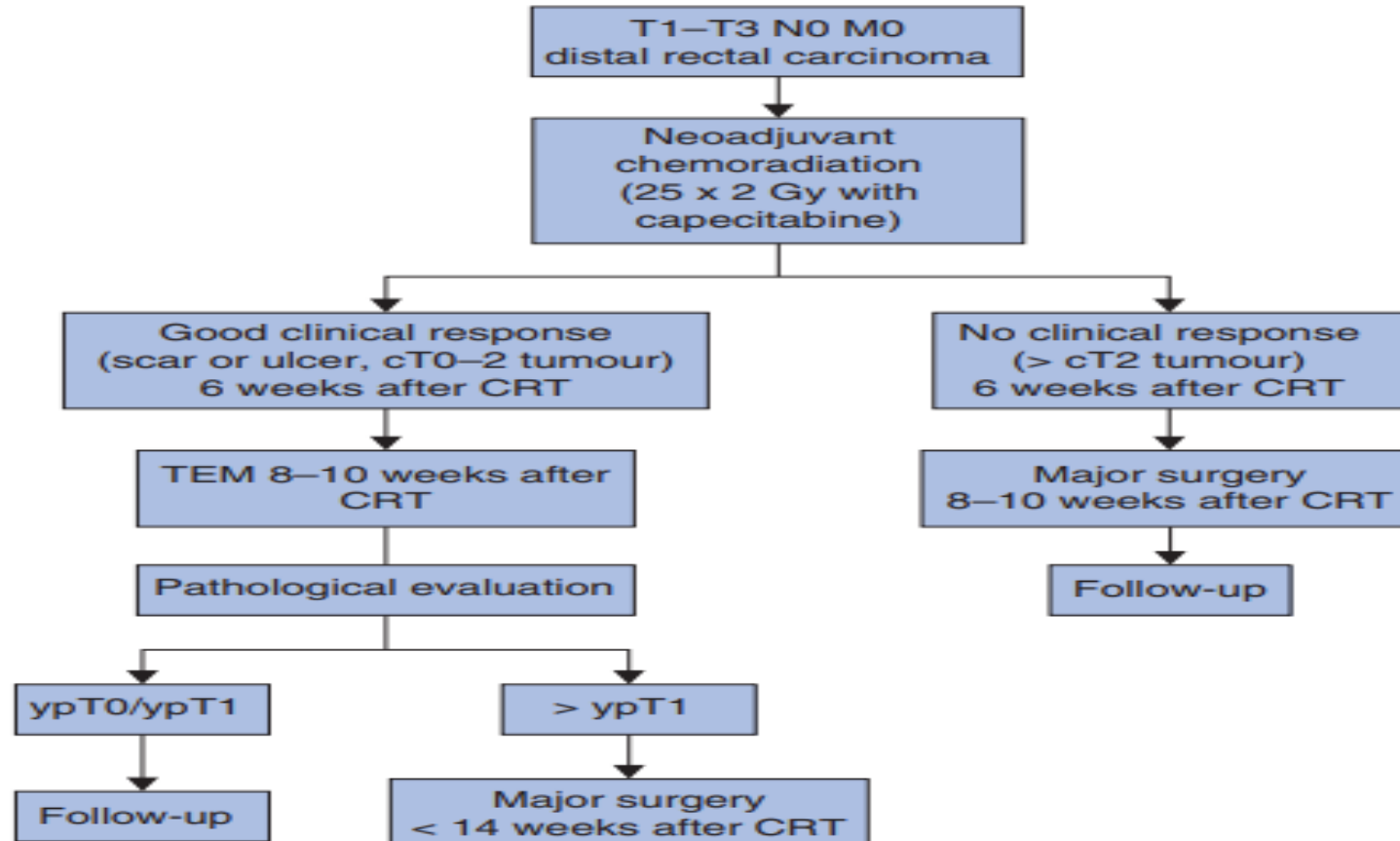


Fig. 3 Cumulative probability of cancer-related survival according to type of operation. ELRR, endoluminal locoregional resection; TME, total mesorectal excision. $P = 0.687$ (log rank test)

Chemoradiation therapy for rectal cancer in the distal rectum followed by organ-sparing transanal endoscopic microsurgery (CARTS study)



Chemoradiation therapy for rectal cancer in the distal rectum followed by organ-sparing transanal endoscopic microsurgery (CARTS study)

- **Tumor downstaging → 55% of pts**
- **Rectal preservation → 64% of pts**
- **5-year DFS → 81.6 %**
- **5-year OS → 82.8 %**

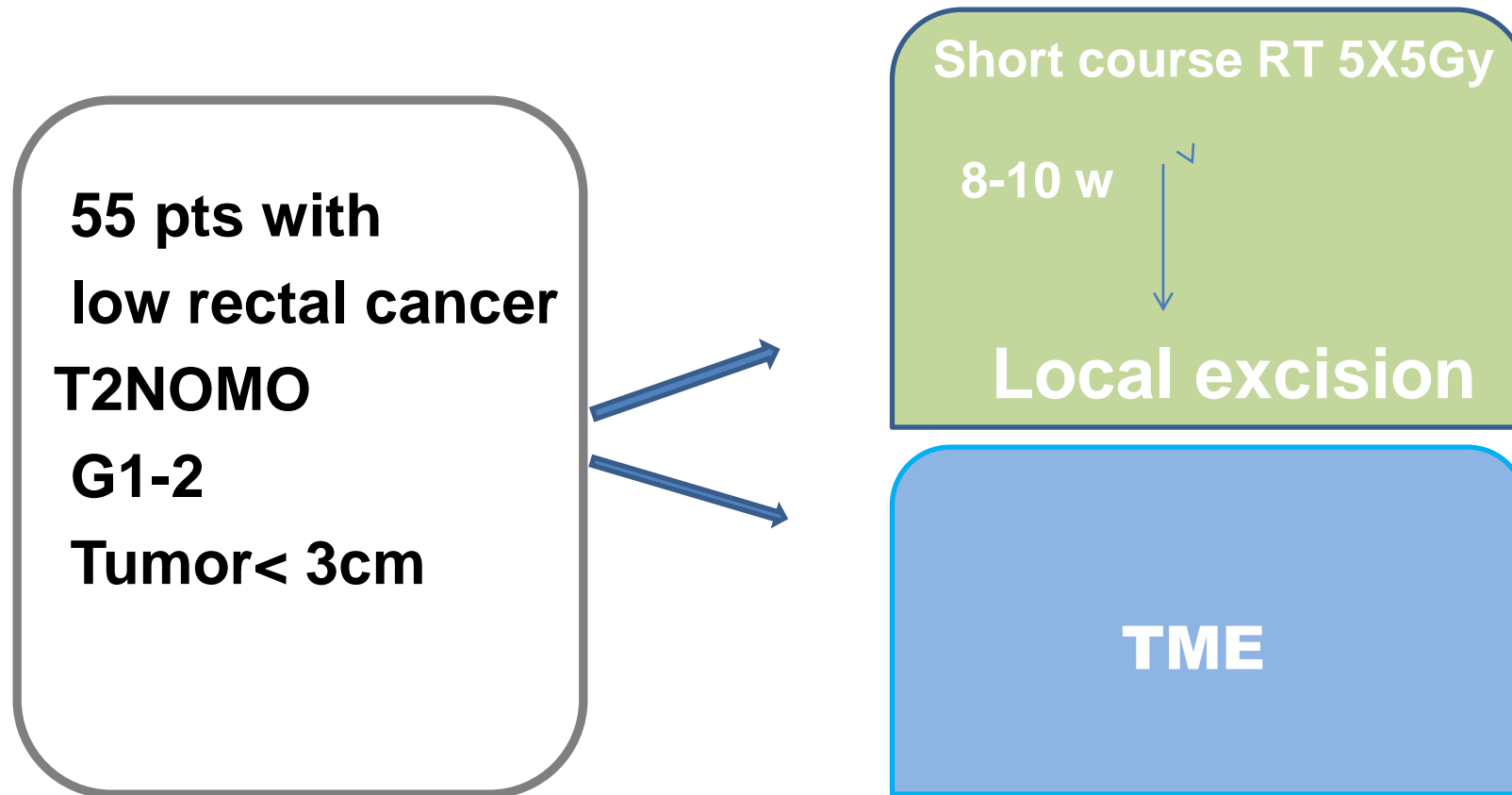
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Conclusion

- **In early-stage rectal cancer (cT1-3N0M0), CRT with TEM enables organ preservation surgery in approximately two-thirds of patients with good long-term oncological outcome and HRQL**

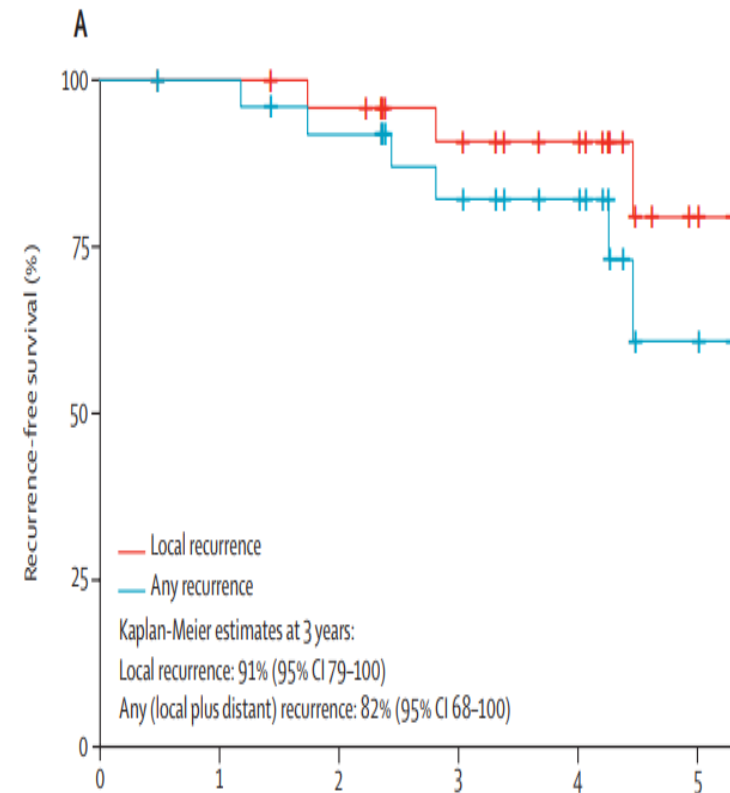
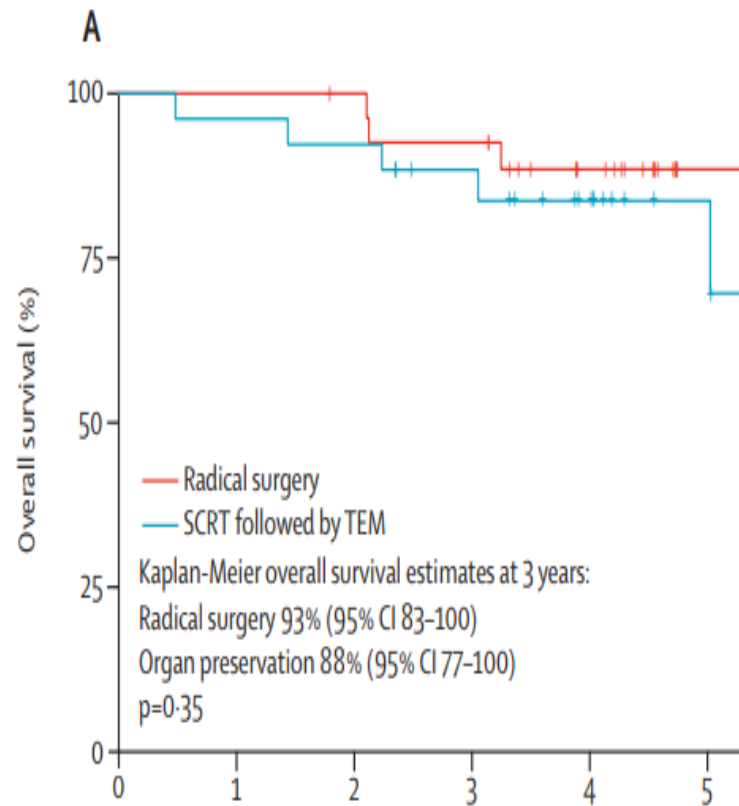
**Organ preservation in early rectal
cancer using short course RT**

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

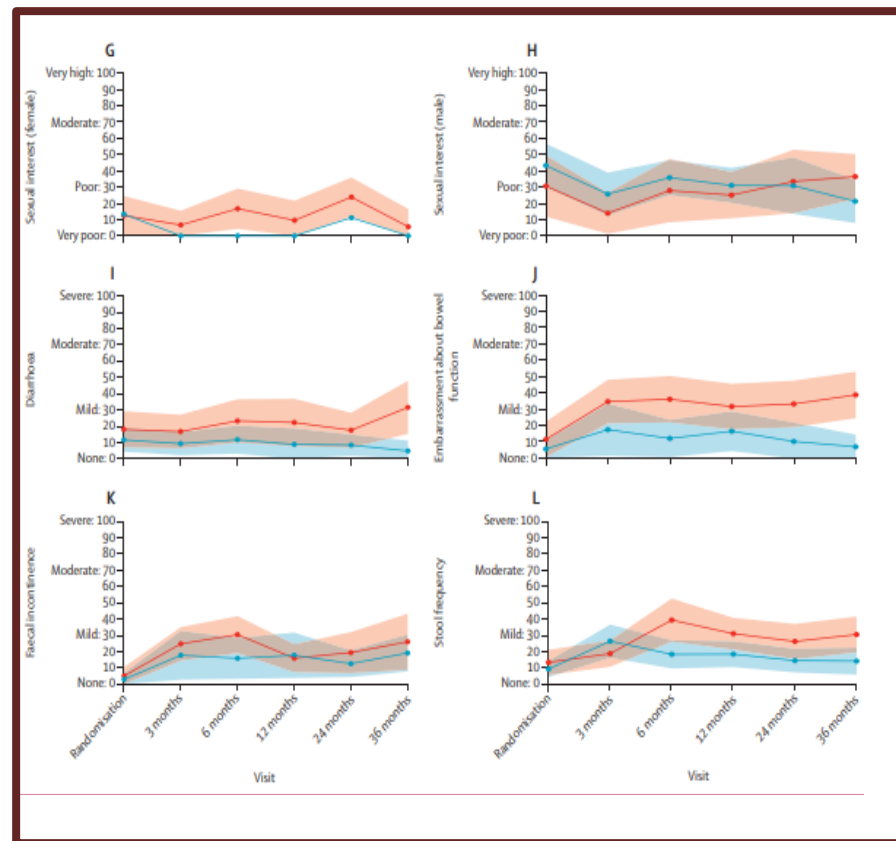
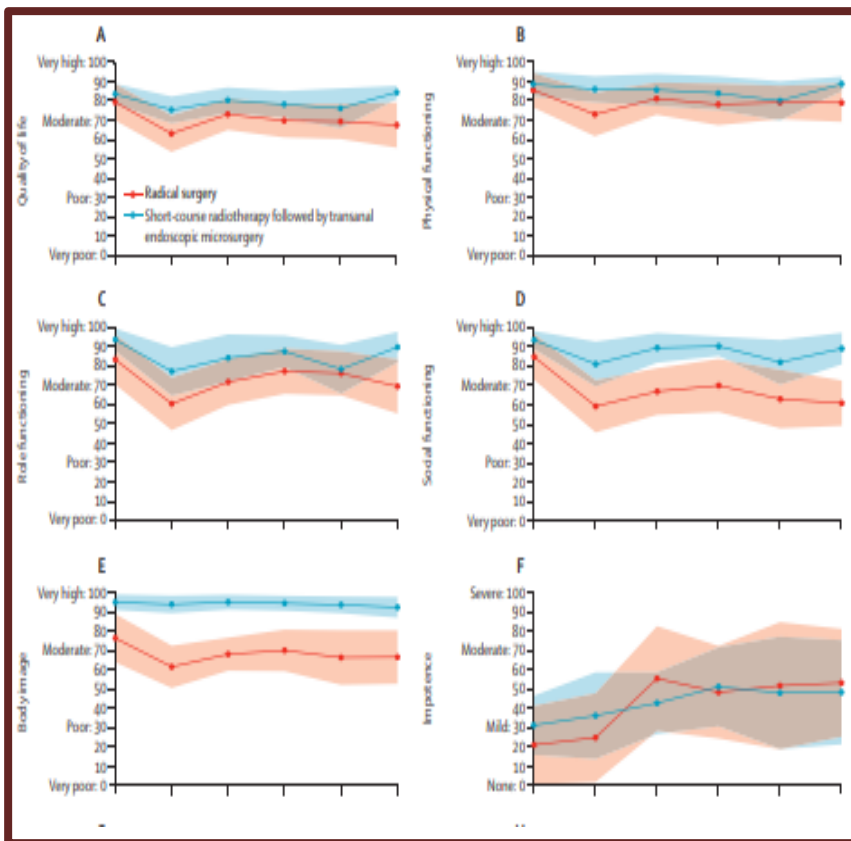


TREC study

Organ preservation was achieved in 70% randomised patients



Quality of life



Toxicities

Short-course radiotherapy and transanal endoscopic microsurgery is associated with lower acute and late side effects than total mesorectal excision , with minimal impact on patients' QOL

**Adjuvant chemor-radiotherapy after local
excision**

A systematic review of local excision followed by adjuvant therapy in early rectal cancer: are pT1 tumours the limit?

J. E. Cutting, S. E. Hallam, M. G. Thomas and D. E. Messenger

University Hospitals Bristol National Health Service Foundation Trust, Bristol, UK

Received 7 March 2018; accepted 2 July 2018; Accepted Article online 10 July 2018

Abstract

Aim Total mesorectal excision remains the cornerstone of treatment for rectal cancer. Significant morbidity means local excision may be more appropriate in selected patients. Adjuvant therapy reduces local recurrence and improves survival; however, there is a paucity of data on its impact following local excision, which this systematic review aims to address.

Methods A systematic search of the MEDLINE, Embase and Cochrane databases using validated terms for rectal cancer, adjuvant therapy and local excision was performed. Included studies focused on local excision with adjuvant therapy for adenocarcinoma of the rectum. Primary outcome measures were local recurrence, survival and morbidity. Studies providing neoadjuvant therapy or local excision alone were excluded.

Results Twenty-two studies described 804 patients. Indications for local excision included favourable histology, patient choice and comorbidities. T1, T2 and T3 tumours accounted for 35.1%, 58.0% and 6.9% of cases,

respectively. The most frequent local excision technique was transanal excision (77.7%). Adjuvant therapy included long-course chemoradiation or radiotherapy. Median follow-up was 51 months (range 1–165). The pooled local recurrence was 5.8% (95% CI 3.0–9.5) for pT1, 13.8% (95% CI 10.1–17.9) for pT2 and 33.7% (95% CI 19.2–50.1) for pT3 tumours. The overall median disease-free survival was 88% (range 50%–100%) with a pooled overall morbidity of 15.1% (95% CI 11.0–18.7).

Conclusions This area remains highly relevant to modern clinical practice. The data suggest that local excision followed by adjuvant therapy can achieve acceptable long-term outcomes in high-risk pT1 tumours, but not in T2 tumours and above in whom radical surgery should be offered.

Keywords Colorectal Cancer, local excision, adjuvant therapy

A systematic review of local excision followed by adjuvant therapy in early rectal cancer: are pT1 tumours the limit?

- Adjuvant therapy with long-course chemoradiation or radiotherapy.

• **Local recurrence was**

- **pT1** → **5.8%**
- **pT2** → **13.8%**
- **pT3** → **33.7%**
- **Disease-free survival** → **88%**

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Take home message

- Total mesorectal excision is the standard of care for early-stage rectal cancer. However, radical surgery has considerable morbidity
- Local excision techniques provide less morbidity and a minimal chance of transient functional impairment, which may lead to better outcomes in terms of quality of life

Take home message

- Low-risk pT1, local excision as a definitive treatment is generally accepted
- High-risk T1, T2 rectal cancer TME is the standard of care till now , alternatively (neo) adjuvant chemoradiotherapy offer a reduction in the risk of local recurrence if added to local excision

*Thank
you*

- In low-risk pT1 tumours, local excision as a definitive treatment is generally accepted
- In high –risk T1 , or T2 rectal cancer
- TME is the standard of care till now , alternatively
- (neo) adjuvant chemoradiotherapy might offer a reduction in the risk of local recurrence if added to local excision

- Local excision alone is indicated in case of low-risk tumours (T1N0)

in high-risk tumours and additional completion surgery is recommended. Alternatively, (neo)adjuvant chemoradiotherapy might offer a reduction in the risk of local recurrence for pT1-2 rectal cancer patients, but data are still scarce. Nevertheless, in patients who undergo a local excision definitive treatment can be tailored, which may lead to a higher percentage of patients in which the rectum can be preserved.

- Despite the evidence presented above, it remains inconclusive whether neoadjuvant therapy followed by TES is equivalent to radical surgery (TME) in treating cT1-3N0 rectal cancer. More trials are ongoing to compare the now three potential approaches to treating this cohort of patients: standard TME without neoadjuvant therapy, neoadjuvant therapy followed by TES, and neoadjuvant therapy followed by watchful waiting (for those who achieve a complete response to neoadjuvant therapy, which may further reduce morbidity).
- For now, patients with \geq T2N0 rectal cancer should continue to be counseled to undergo abdominal surgery with TME for optimal oncologic outcomes. Local excision should only be used in patients who are frail or otherwise unfit for abdominal surgery or in the settings of clinical trials.

organpreservation practices were well established for frail,elderly, comorbid, and stoma-averse individuals with early-stage rectal cancer but underdeveloped in the wider patient population considered suitable for total mesorectalexcision

- Radical resection of rectal cancer carries considerable morbidity, such as low anterior resection syndrome, sexual and urinary dysfunction, and stoma formation, which can affect quality of life. To reduce this impact, organ-preserving strategies have been developed

- Recent systematic reviews do not support adoption of an organ preservation approach for treatment of early-stage rectal cancer in fit patients because of insufficient high quality evidence

ONCOLOGIC OUTCOMES

Compared with transabdominal resection with total mesorectal excision (TME), local excision offers reduced perioperative morbidity and improved functional outcomes but yields no nodal information. Thus, only patients with minimal risk of harboring occult metastasis should

Existing data support the use of TES for local excision of rectal carcinoid tumors <2 cm, rectal adenomatous polyps, and low-risk T1N0 rectal cancers. Local excision of T2N0 rectal cancers should only be performed in patients who are poor candidates for transabdominal surgery or as

Patients should be informed that local excisional procedures, including TES, offer no nodal information and could potentially leave micrometastasis in the mesorectum or residual disease in the excision bed. To avoid local recurrence or distant metastasis, patients may require additional surgery (typically salvage TME) after local excision when the surgical specimen shows high-risk pathologic features, such as positive margins, tumor grade \geq T2, perineural or lymphovascular invasion, and poor differentiation.

T2N0 rectal cancer — Because the recurrence rate is higher and survival lower after local as compared with transabdominal excision of T2N0 rectal cancers, transabdominal surgery (TME) is the standard of care for these cancers. Local excision should only be performed in such patients they are not candidates for abdominal surgery because of medical reasons or if the procedure is being performed as a part of a clinical trial.

- In low-risk pT1 tumours, local excision as a definitive treatment is generally accepted. In pT1 tumours with histopathological risk features, additional treatment is recommended to sufficiently treat potential lymph node metastases and to reduce the risk of local recurrence [11]. High-risk pT1 tumours can be defined by at least one of the following histopathological characteristics: poor differentiation, lymphatic or vascular invasion, resection margins ≤ 1 mm, diameter of carcinoma, tumour budding, and deep submucosal invasion (i.e. sm 2–3, Haggitt 4 or >1000 μm) (Table 1) [11,15–17]. Although conflicting evidence is available regarding deep submucosal invasion as a sole risk factor for lymph node metastases, Kikuchi level sm 3 may still be considered a risk factor, since few studies separate sm 2 from sm 3 lesions

- [11]. Histopathological risk factors Poor differentiation
Lymphatic or small vessel invasion Venous or large vessel
invasion Resection margin ≤ 1 mm Diameter of carcinoma > 3
cm Tumour budding Deep submucosal invasion (i.e. sm 3,
Haggitt 4 or $> 1000 \mu\text{m}$)

- total mesorectal excision is the standard of care for early-stage rectal cancer. However, radical surgery has considerable morbidity
- organ preservation approach for the treatment of early-stage rectal cancer to reduce the morbidity associated with radical surgery without compromising oncological outcome

- The flaws of the current imaging techniques in clinical staging of early rectal cancer, create the opportunity for local excision as a diagnostic and potentially curative tool. Local excision of lesions up to 3–5 cm could be treated with upfront radical local excision. In this strategy, local excision can be used to definitively diagnose the tumour stage, and by the evaluation of histopathological risk factors the necessity of additional treatment options can be weighed. This approach offers the potential of organ preservation for the majority of patients, since only a small proportion will need completion surgery.

- recurrence of patients with high-risk pT1 and pT2 tumours, and revealed rates of 13.6% and 28.9%, respectively.

- The standard approach for high-risk pT1 and pT2 rectal cancers that have been locally excised, is completion TME surgery. This approach is the treatment option associated with the lowest local recurrence rates. A meta-analysis included fourteen studies that evaluated local recurrence rates for completion TME after local excision of pT1-2 rectal cancer and showed a local recurrence rate of 4.1% for high-risk pT1 tumours and 4.3% for pT2 tumours

Disadvantage of neoadjuvant chemort

- This implies that neoadjuvant chemoradiotherapy led to overtreatment of patients with non-responding or partially responding tumours, and likely resulted in increased morbidity. More importantly, as clinical staging by imaging has been shown to lack accuracy, this treatment strategy also incorporates patients with low-risk tumours, who could have been treated with local excision only^{7,8}.

Advantages of neoadjuvant

- has been shown to downsize tumours and even lead to complete remission in over 50 per cent of patients