Radiotherapy in Early Rectal Cancer

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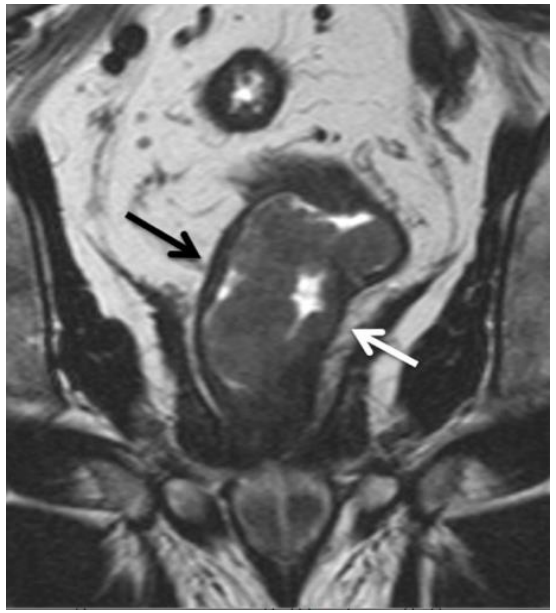
Case#

45 year- old male patient

Presented with distal early rectal cancer

MRI reveled T2 rectal tumor with no suspicious LN



How would you treat this patient ?

The standard of care for early rectal cancer is 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%

Early Rectal Cancer

Radical TME surgery carries considerable morbidity :

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

Impair quality of life

Early distal rectal cancer

- **Permanent stoma !!!**

Early Rectal Cancer

Local excision techniques:

- Less morbidity
- Minimal chance of functional impairment

Better 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
- Superfiaial submucosal invasion (Sm1)

Local recurrence after local excision

- Low-risk T1N0 : 5%
- High-risk T1N0 :12%-19%
- T2N0 : 22%-29%

Local recurrence after local excision

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TME

Chemoradiotherapy

Early rectal cancer

The benefit of Chemo-Radiotherapy

Less invasive surgery

Less morbidity

Organ preservation

Chemo-Radiotherapy in Early Rectal cancer

- Neoadjuvant
- Adjuvant
- Definitive

Chemo-Radiotherapy in Early Rectal cancer

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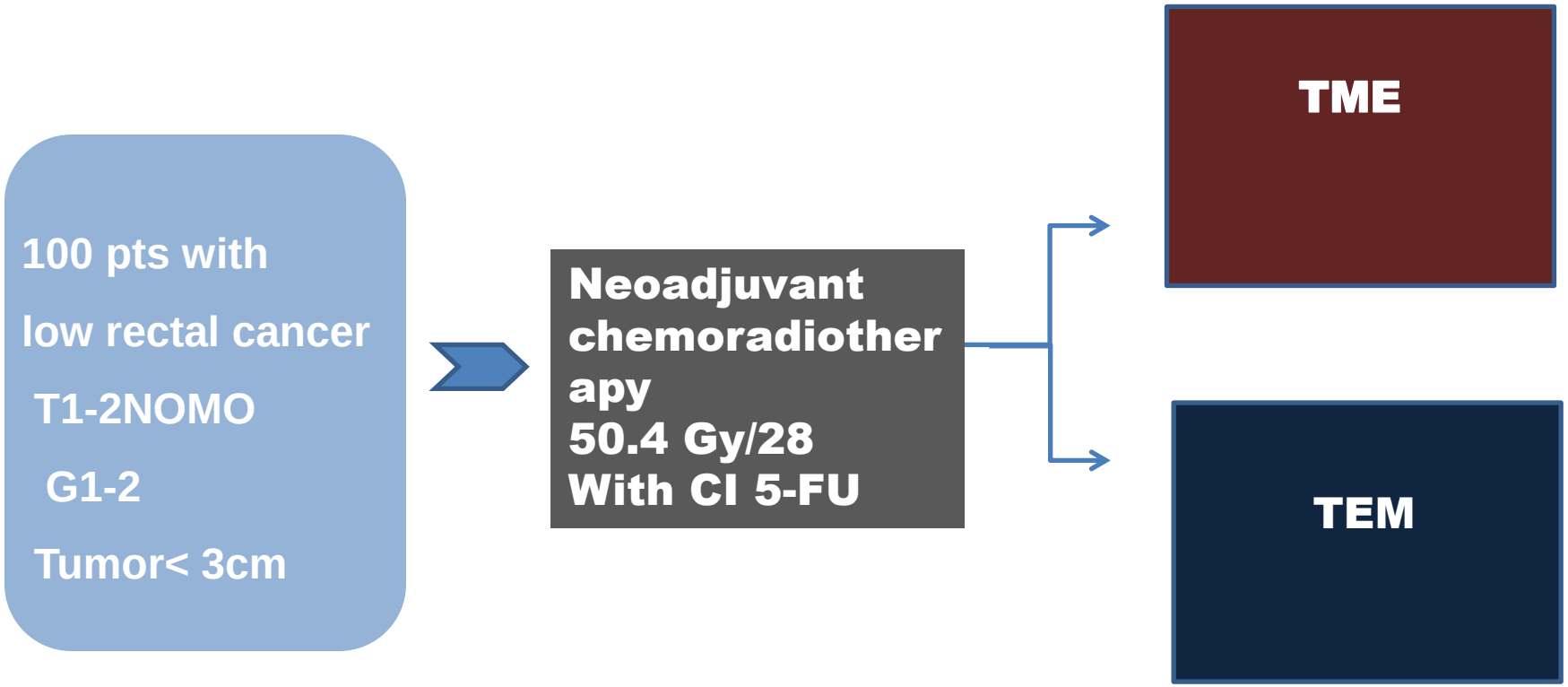
Randomized clinical trial of local resection *versus* total mesorectal excision for T2 rectal cancer after neoadjuvant therapy (URBINO Trial)



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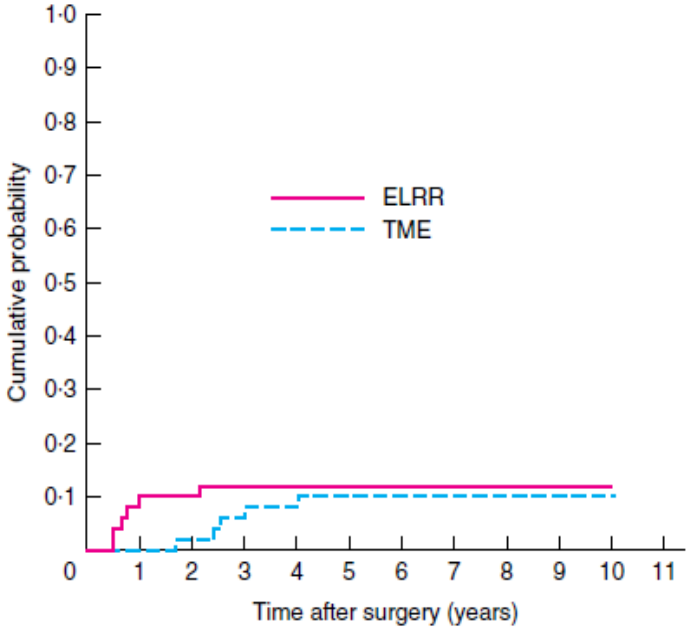
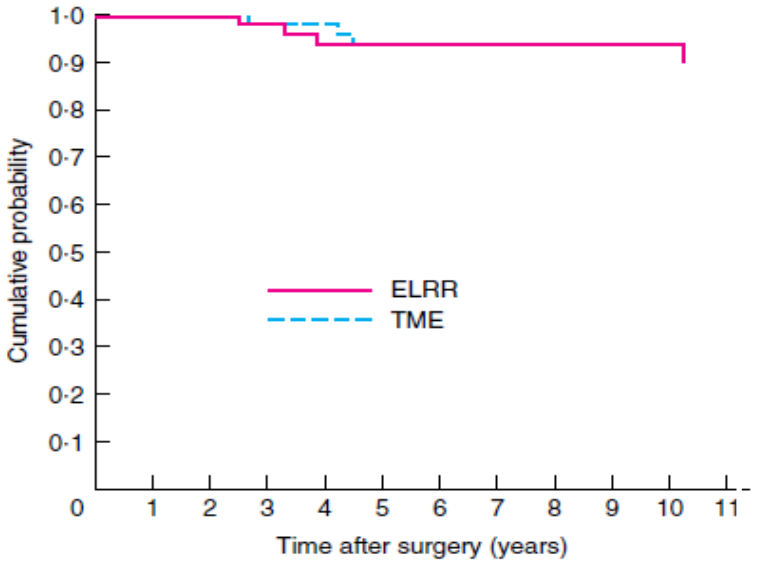


No. at risk											
ELRR	50	45	45	44	43	43	40	37	34	30	19
TME	50	50	49	46	44	43	39	36	32	29	22

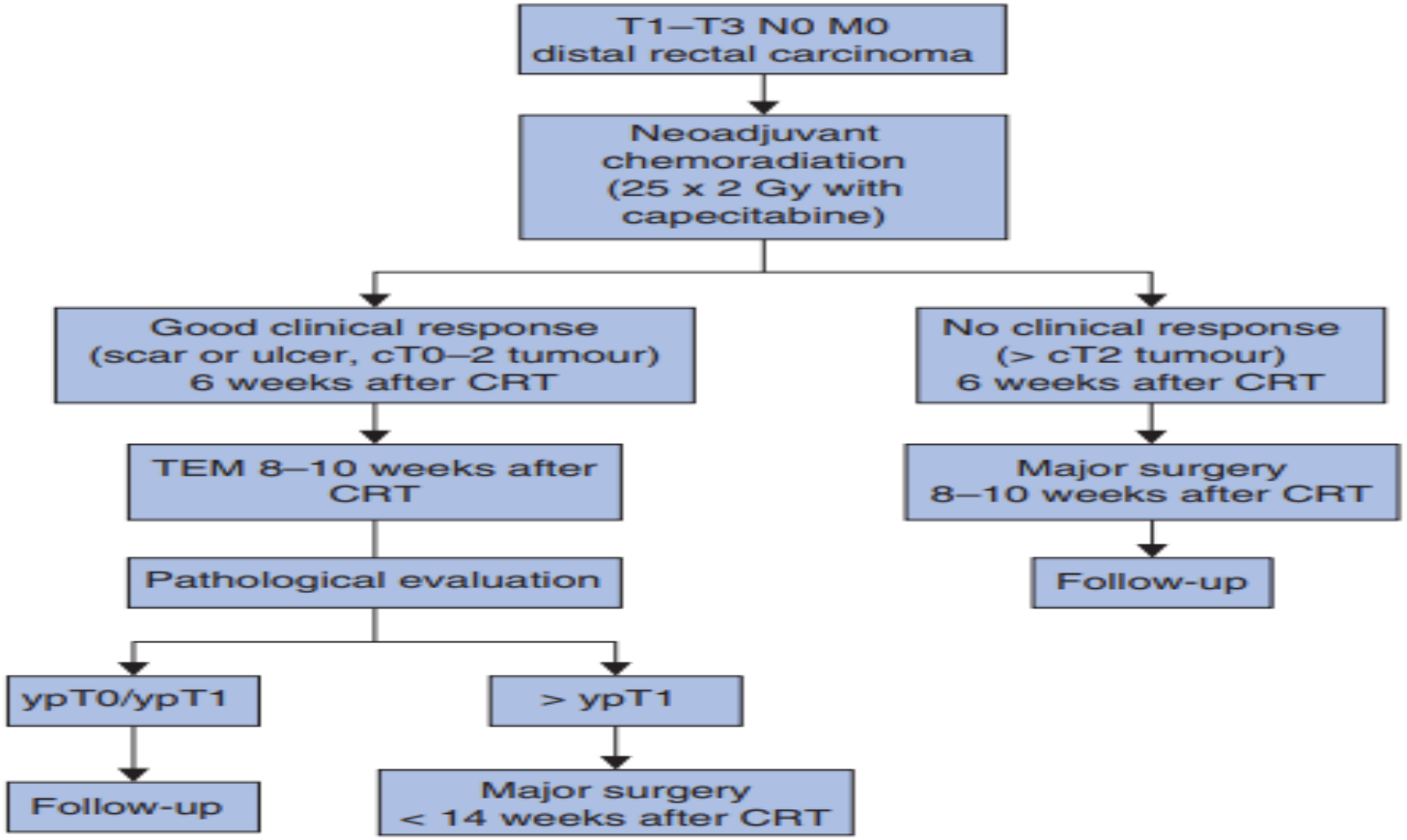
Fig. 2 Cumulative probability of developing recurrence or metastases according to type of operation. ELRR, endoluminal locoregional resection; TME, total mesorectal excision. $P = 0{\cdot}686$ (log rank test)



No. at risk											
ELRR	50	50	50	48	45	45	41	38	35	31	19
TME	50	50	50	49	48	44	39	36	32	29	22

Fig. 3 Cumulative probability of cancer-related survival according to type of operation. ELRR, endoluminal locoregional resection; TME, total mesorectal excision. $P = 0{\cdot}687$ (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 %**

M. Verseveld1,2, E. J. R. de Graaf1, C. Verhoef2, E. van Meerten3, C. J. A. Punt5, I. H. J. T. de Hingh6, I. D. Nagtegaal7, J. J. M. E. Nuyttens4, C. A. M. Marijnen9 and J. H. W. de Wilt8, on behalf of the CARTS Study Group

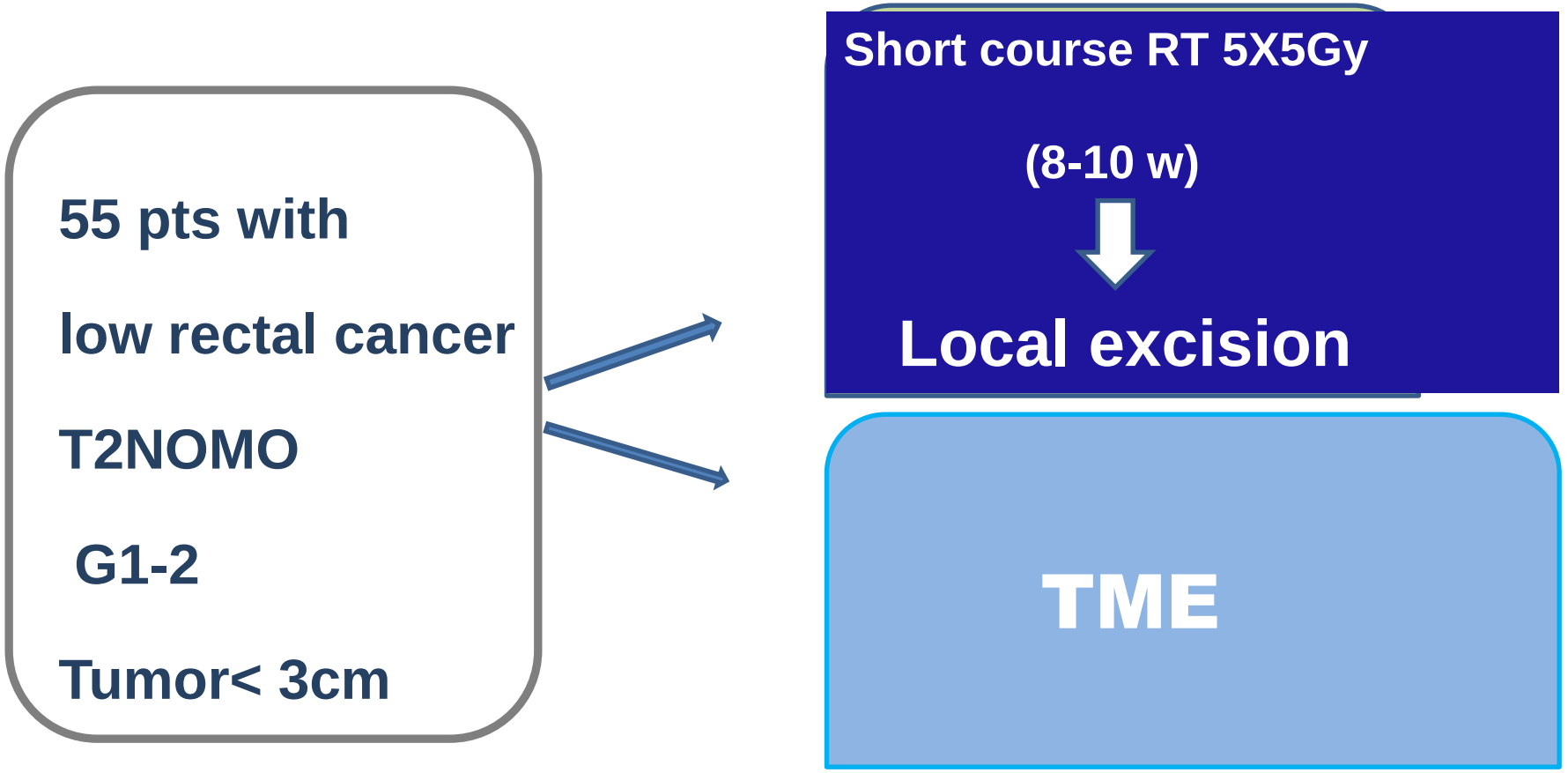
Chemoradiation therapy for rectal cancer in the distal rectum followed by organ-sparing transanal endoscopic microsurgery (CARTS study)

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

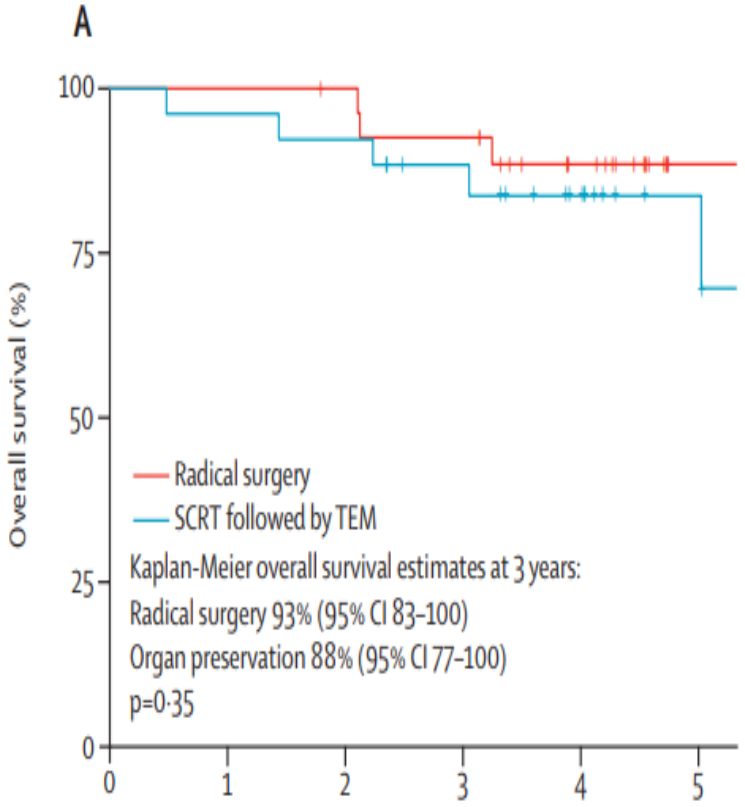
Organ preservation in early rectal cancer using short course RT

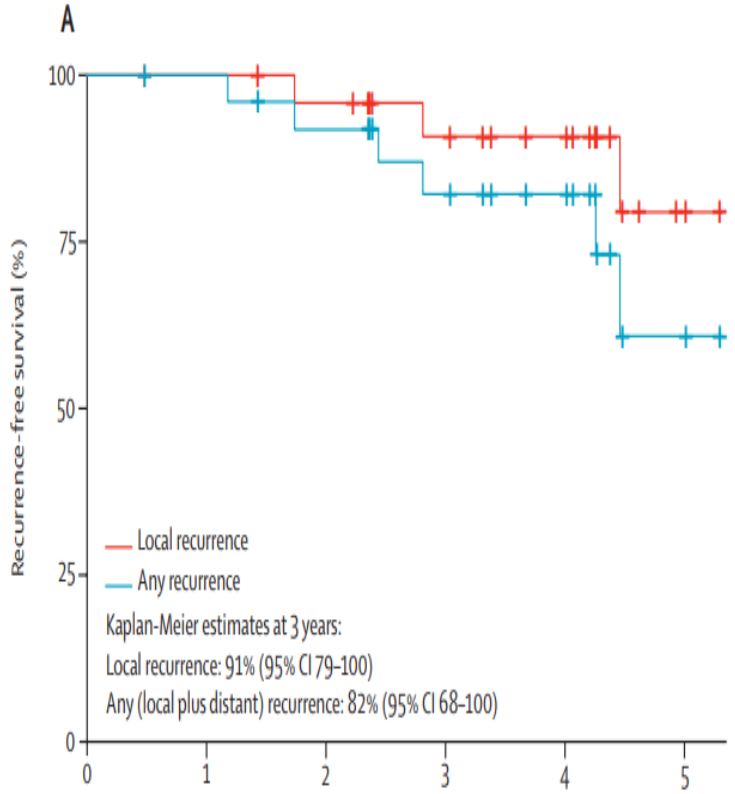
Radical surgery versus organ preservation via short-course radiotherapy followed by transanal endoscopic microsurgery for early-stage rectal cancer (TREC): a randomised, open-label feasibility study



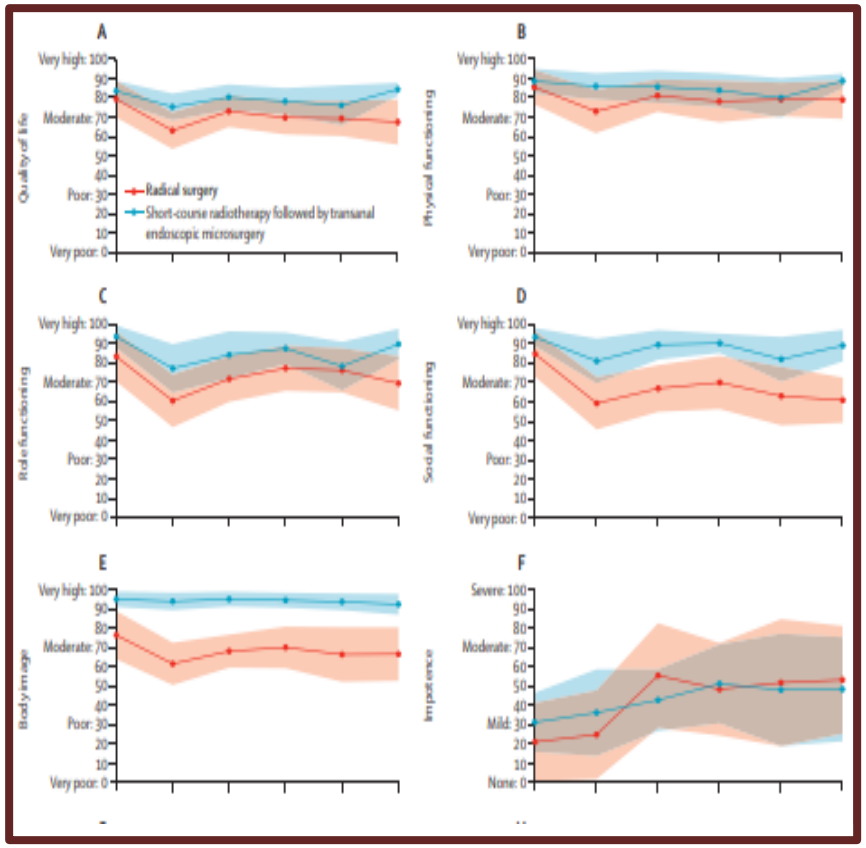
TREC study

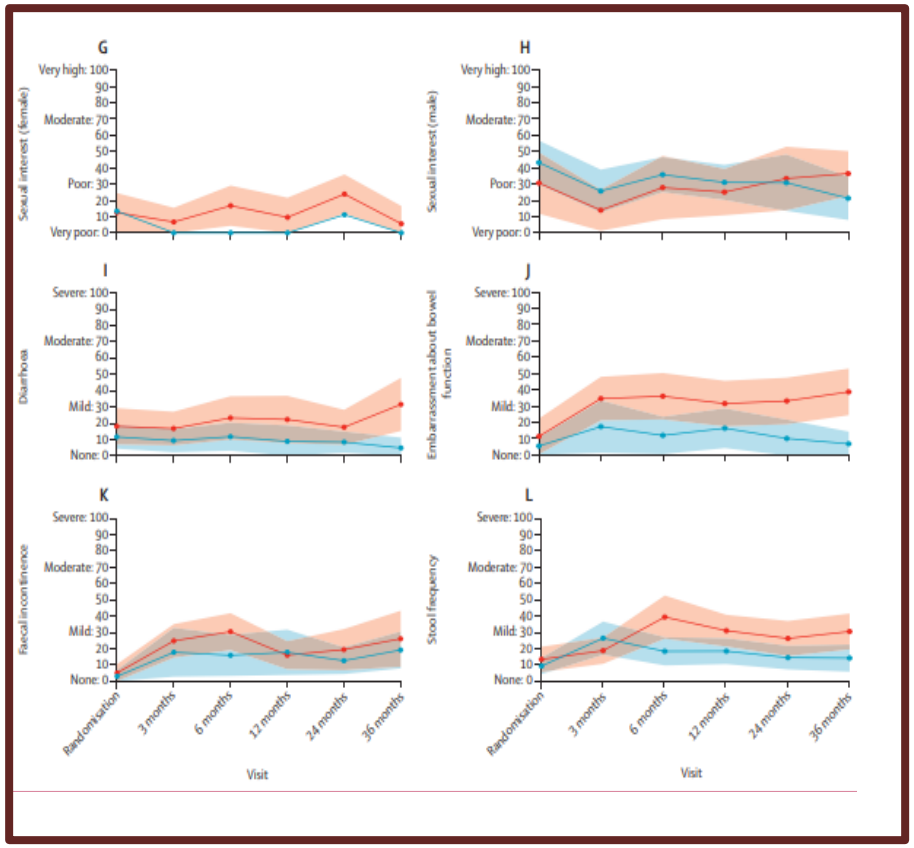
Organ preservation was achieved in 70% randomised patients





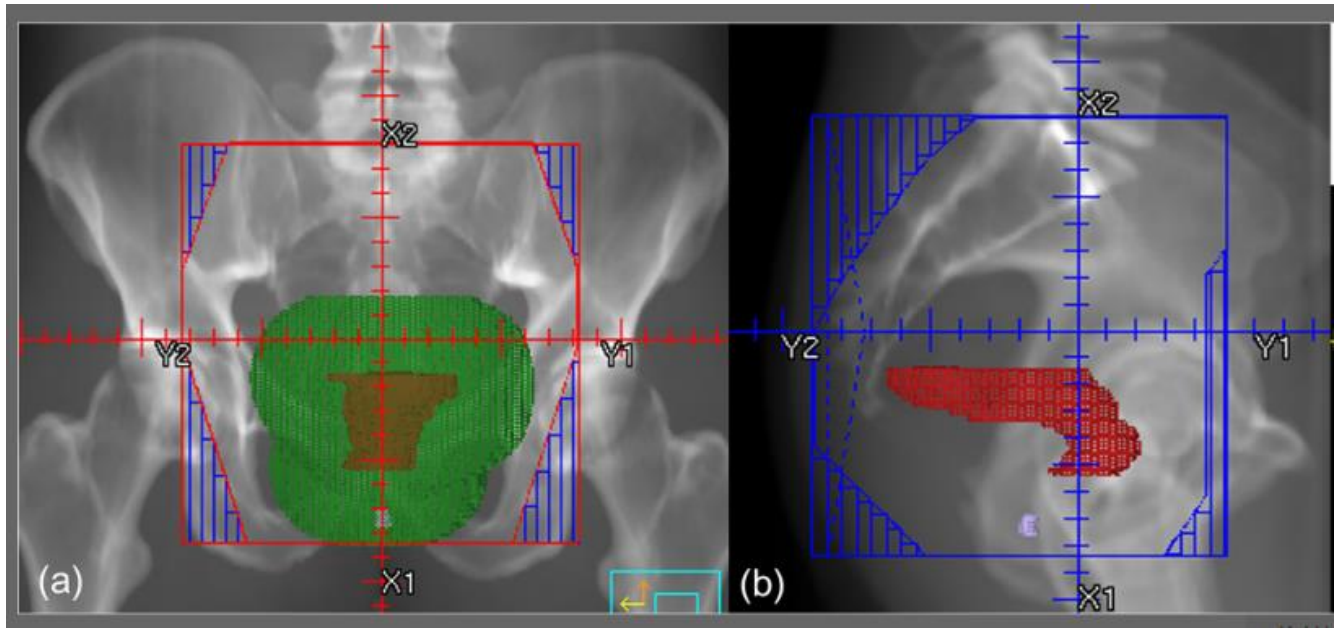
Quality of life



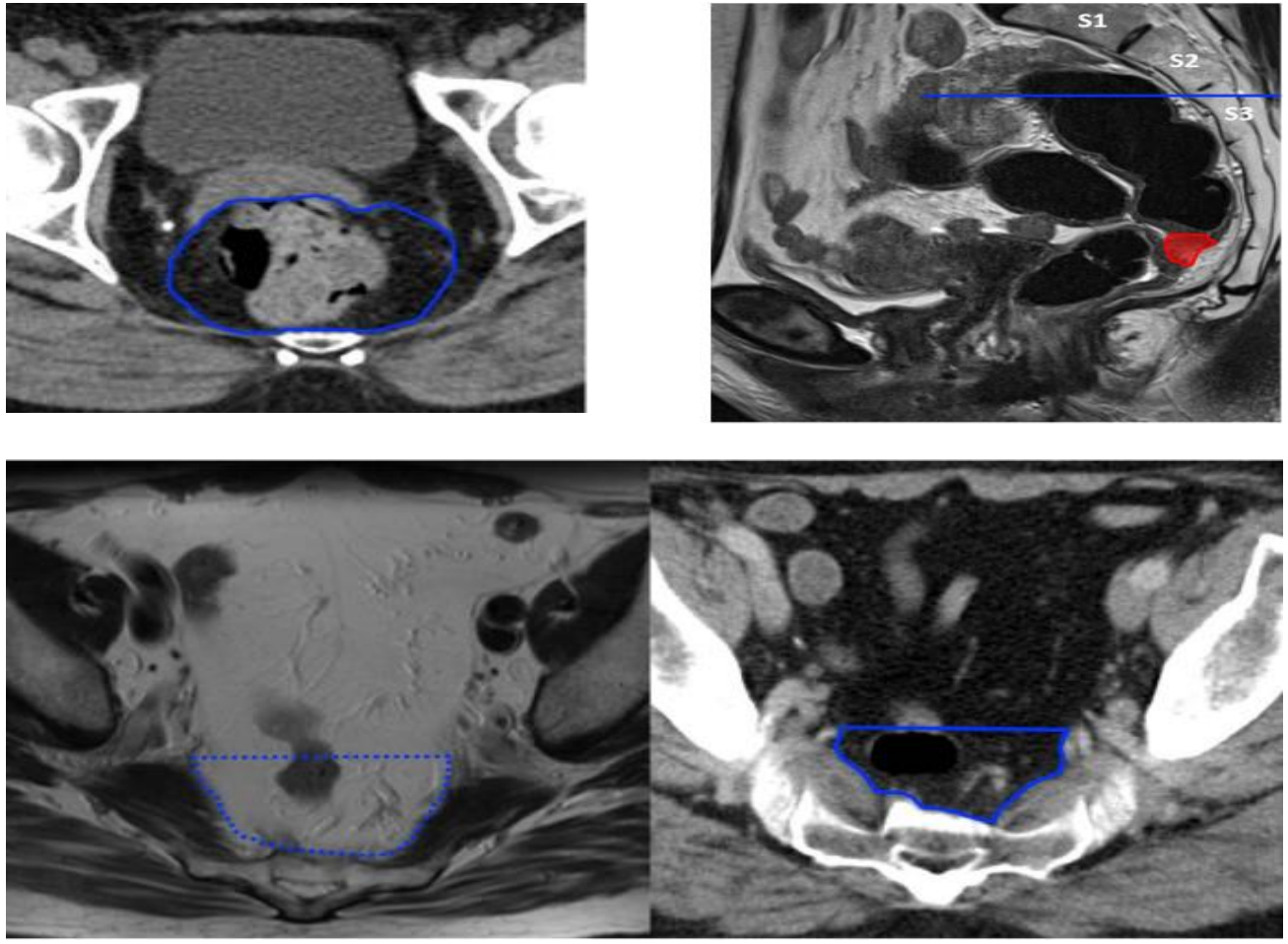


Short-course radiotherapy and transanal endoscopic microsurgery is associated with lower acute and late side effects than total mesorectal excision , with minimal impact on patients' QOL

Radiation therapy in locally advanced Rectal cancer

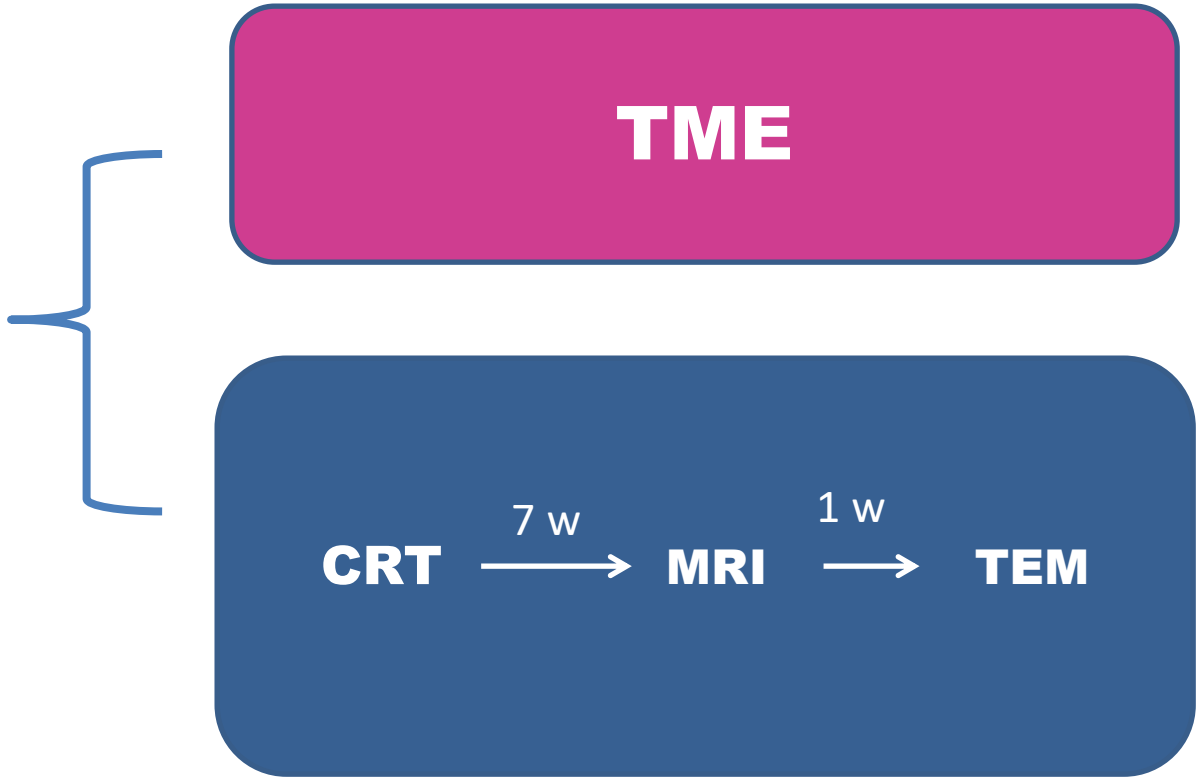


Mesorectal radiotherapy for early rectal cancer: A novel target volume (STAR-TREC)



Chemoradiotherapy and local excision versus total mesorectal excision in T2-T3ab,N0,M0 rectal cancer, phase III prospective trial (TAU-TAM)

162 patients with adenocarcinoma ≤10 cm from anal verge
Superficial T2-T3–N0
Lesion ≤4 cm



Chemoradiotherapy and local excision versus total mesorectal excision in T2-T3ab,N0,M0 rectal cancer, phase III prospective trial (TAU-TAM)

	CRT TEM	TME	
Post -Operative morbidity	20.7%	50.6%	p < 0.001
Pathological complete response	44 .3 %		
Organ -preservation	**82.7%**		

Chemo-Radiotherapy in Early Rectal cancer

- Neoadjuvant
- **Adjuvant**
- Definitive

Adjuvant chemo-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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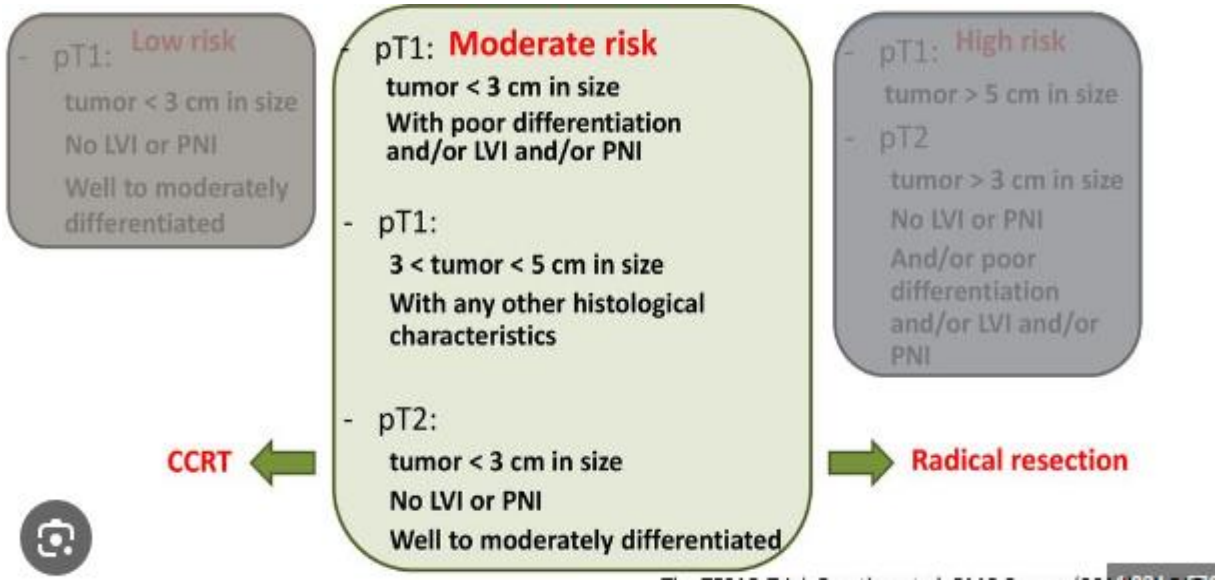
Adjuvant chemoradiotherapy instead of radical resection after local excision for high-risk early rectal cancer



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


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 ≥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 withearly-stage rectal cancer but underdeveloped in the widerpatient 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 ofan organ preservation approach for treatment of early-stage rectal cancer in fit patients because of insufficienthigh quality evidenc

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 shoul

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 ≥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 ctal 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 µm)

- 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 patientwith low-risk tumours, who could have been treated with local excision only7,8.

Advantages of neoadjuvant

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

- In this trial, the clinical target volume has been tailored to the early staged disease of the included patients. This mesorectal irradiation volume includes the mesorectum and pre-sacral lymph nodes at the level of the tumour, two centimetres below and cranially up to the S2-3 interspace level. In contrast to conventional irradiation volumes, the lateral lymph nodes and the nodes along the superior rectal artery are excluded. As a result, the dose to the bowel, bladder, anal sphincter and the neurovascular plexus in the lower pelvis is substantially decreased, especially when combined with modern irradiation techniques, such as dynamic arc therapy. These lower doses are expected to lead to decreasing acute and late toxicity and beneficial functional outcomes. The implementation of this novel target volume will be accompanied by an extensive quality assurance program in the STAR-TREC trial. Recurrence patterns from the trial will inform us on the safety of this mesorectal CTV and ultimately, facilitate further treatment refinement to achieve optimum oncological efficacy with the lowest toxicity and b

- esection is advocated. In early stage tumours (C)RT can lead to OP in more than 50% when combined with local excision [13–16]. Unfortunately, this (C)RT can be accompanied by toxicity, morbidity and even mortality [14,15,17]. However, all available data on toxicity and mortality, are based on conventional radiotherapy techniques, with large treatment volumes, including large elective LN regions. In early stage rectal cancers, such as those included in the STARTREC trial, a smaller tailored CTV is expected to be oncologically safe.

- Early stage rectal cancer has a favourable prognosis for patients treated with total mesorectal excision (TME) [1]. Only 2% and 12% of patients experience local or distant failure [2–4]. However, resection of a low rectal tumour requires a permanent stoma in approximately 40% of cases while many more patients will have a temporary stoma [5–7]. Complications of surgical resection include anastomotic leaks, autonomic nerve damage leading to urinary incontinence or retention, sexual dysfunction and faecal incontinence.

- Patients with low risk early rectal cancers do not undergo preoperative radiotherapy in most countries. Local control rate of 98% after surgery in this group underlines that removal of only the mesorectal envelope is sufficient in most patients [2–4]. Irradiating only this mesorectal envelope should therefore also be sufficient