Early Rectal Cancer - Surgical options
Organ Preservation?

Chinna Reddy
Colorectal Surgeon
Western General, Edinburgh
What is Early rectal cancer?

pT1T2N0M0

Predictors for LN involvement:
- Size
- Depth
- Intramural Lymphatic invasion
- Vascular invasion
- Tumour differentiation

Kikuchi levels:
sm 1: invasion of superficial third of submucosa by neoplastic cells
sm 2: invasion of middle third of submucosa by neoplastic cells
sm 3: invasion of deep third of submucosa by neoplastic cells
Surgery for rectal cancer

- Current gold standard of treatment is radical surgery with TME - anterior resection or APR
- Local recurrence - 3 - 6% over 5 yrs in pT1 tumours
- Mortality - 3-4%
5% postop deaths
30-40% morbidity
40% permanent stoma
Conclusions

The 30-day post-operative mortality rate is falling across England. There is, however, significant variation in post-operative mortality across the population with it being greater in the elderly, among men, the socioeconomically deprived, those with advanced stage disease at diagnosis or with additional co-morbidities and among those operated upon as emergencies.

Figure 1: 30-day post-operative mortality in relation to year of diagnosis

Figure 2: 30-day post-operative mortality in relation to patient age
Rationale for Local excision

- 49-62% Screen detected tumour are “early” (T1/T2)
- Radical (TME) Surgery 3-6% relapse
- Radical surgery evolved to treat locally advanced Dx
- TME Morbidity
- Mortality 65-74 yr 4.6%, 75-84 yr 13.4%
- Fl >50%
- LARS 30-40%
- Local resection with salvage if required?
What about the Lymph nodes?

Risk of nodal metastasis

Nascimbeni R, Burgart LJ, Nivatvongs S, Larson DR.  
*Dis Colon & Rectum* 2002

Pick two.”

An evening with
Keith Bontrager

September 28, 2013
7:30 p.m.

801 Ridge Road
Wilmette, Illinois
847.920.9360
velosmith.com
History of local excision

• Morson 1980
• Local excision
• T1 20% recur, T2 40% recur
Evolution TEMS

- Operating microscope
- Access lower rectum
- Polyps
- Early rectal cancer
The Principles
Marking
Excision
Advantages

- Minimally invasive

- The stereoscope provides a magnified three-dimensional image allows an optimal view of the tumour and thus facilitates an extremely precise dissection

- Instruments can reach further into the rectum than other forms of local excision

- Reduced length of stay
TEMS at the Western General
Alternatives

TAMIS

Robot
TEMS for adenomas

- Outcomes favorable
- Low recurrence if out
- Margin less of an issue
- Piecemeal not good

Who should be followed up after transanal endoscopic resection of rectal tumours?
Speake D, Lees N, McMahon RF, Hill J.
Adenoma
TEMS for Early rectal Ca
Pre op Workup

- Endoscopy
- DRE
- ERUS
- MRI
- Staging CT scan
- Discussion
MDT Discussion In Early Rectal Cancer

- Technical feasibility - size, position
- Will full thickness excision affect subsequent treatment options? - Conevert AR to APR
- Risk of Lymph node metastases - histology, staging
A predictive model for local recurrence after transanal endoscopic microsurgery for rectal cancer

S. P. Bach¹, J. Hill², J. R. T. Monson³, J. N. L. Simson⁴, L. Lane⁵, A. Merrie⁷, B. Warren⁶ and N. J. McC. Mortensen⁵, on behalf of the Association of Coloproctology of Great Britain and Ireland Transanal Endoscopic Microsurgery (TEM) Collaboration

- 487 patients
- 21 centres
- 5 yr DFS 81% T1, 70% T2
- pT1 Sm1 L0, V0 <5%
- All recurrences were salvaged if fit

![Table]

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<th>Depth of invasion</th>
<th>Lymphatic invasion</th>
<th>Maximum tumour diameter (cm)</th>
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</tr>
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Is TEMS alone adequate?

- pT1 Low risk (well differentiated, no lymphovascular invasion, less than 3-4cm, Sm1-2)

- Local excision is deemed sufficient

- TEMS CURES EARLY TUMOURS
Early Cancer Scenario

Male 60’s
- Transplant
- T2
- 3cm
- Transplant in field SCPRT
- Steroid/Tac

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What if the pathology is Unfavourable?

- Early completion surgery - TME/APR
Is there a place for Radiotherapy following local excision?

- Currently no evidence of adequate quality to recommend it

- Rectal Preserving Treatment for Early Rectal Cancer. A Multi-centred Randomised Trial of Radical Surgery Versus Adjuvant Chemoradiotherapy After Local Excision for Early Rectal Cancers (TESAR)
TESAR Trial

Local radical resection
No neoadjuvant treatment, cN0M0 based on pelvic MRI and CT-thorax/abdomen

Low Risk Early Rectal Cancer
T1 < 3 cm, well to moderately differentiated, no lymphatic or vascular invasion

Medium Risk Early Rectal Cancer
T1 size 3-5 cm with any other histological characteristics, or size < 3 cm with poor differentiation and/or vascular invasion and/or lymphatic invasion.
T2, well/moderate differentiated, No lymphatic or vascular invasion, size < 3cm

High Risk Early Rectal Cancer
T1 > 5cm; T2 > 3cm and/or poorly differentiated and/or lymphatic or vascular invasion

Baseline Pelvic MRI, CT-abdomen, X-thorax/CT-thorax (1-4 weeks after local radical excision)

Randomisation

No further treatment

Adjuvant Chemoradiotherapy (start 4-8 weeks after local excision)

Completion TME surgery (start 4-8 weeks after local excision)

Extensive Follow-up
Sigmoidoscopy at 6, 24 and 36 months
Colonoscopy at 12 and 48 months
MRI at 6, 18, 36 and 60 months
CT abdomen/chest or ultrasound: 6, 12, 24 and 36 months, CEA every 3 months

Regular Follow-up
Expanding the role of Organ Preservation in Early Rectal Cancer

- Neoadjuvant treatment followed by TEMS

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<td>Salvage</td>
<td>1 in TEMS group</td>
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Lyon Trial

- CRT
- T2/T3
- 201 patients
- 2 weeks delay 10% pCR
- 6 week delay 26% pCR

Lessons using CRT for advanced disease
Habr Gamma IJROBP 2014

CRT n=183

12 WEEKS

- cCR n=90
- EARLY REGROWTH n=17
- FTLE n=5
- TME n=9
- Unresect n=3

1 YEAR

- cCR n=73
- LATE REGROWTH n=11
- FTLE n=2
- Brach n=1
- TME n=5
- Unresect n=3

SUSTAINED

- cCR n=62
- ORGAN PRESERVATION n=70
- UNRESECTABLE n=6

34%
38%
3%
Multicentre study of short-course radiotherapy and transanal endoscopic microsurgery for early rectal cancer

C. J. Smart¹, S. Korsgen², J. Hill³, D. Speake⁵, B. Levy⁶, M. Steward⁷, J. I. Geh², J. Robinson⁷, D. Sebag-Montefiore⁸ and S. P. Bach¹

- Frail or declined surgery
- 63 patients
- SCPRT 8-10 weeks delay
- 66% Downstaging
- pCR 32%
- ypT1 36%
- ypT2 30%
- LR 6.5%, Distant 4.8%

SCPRT and TEMS cohort study
Manchester, Chichester, Bradford and Birmingham

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<td>0</td>
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<td>0</td>
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<td>Mean follow up (range)</td>
<td>18 (12-30)</td>
<td>12 (6-30)</td>
<td>15 (3-36)</td>
<td>12</td>
</tr>
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A multicentre study of SCRT and TEMS for early rectal cancer. Smart et al. BJS 2016
CARTS

- 25x2 gy
- 55 patients
- 47 TEM
- 2 Deaths toxicity
- ypT0-1 30/47
- ypT2 15/47
- ypT3 0
- 9 ypT2 Declined op 3 LR
- 1pT1 LR
TREC Trial

RECTAL CANCER STAGED AS T1-2 N0

Clinical Equipoise Patient Consent

YES

RANDOMISE

NO

RadicAl Surgery

TME/APE

ORGAN PRESERvATION

SCPRT

8-10 WEEKS

TEMS
Saving the rectum by watchful waiting or TransAnal surgery after (chemo)Radiotherapy versus Total mesorectal excision for early Rectal Cancer

STAR TREC

Simon Bach
Queen Elizabeth Hospital Birmingham
On behalf of the Netherlands, Denmark and UK groups
New concepts for STAR-TREC

• Smaller radiotherapy fields to reduce toxicity

• Opportunities for watch and wait

• Moved away from mandatory TEMS for rectal sparing treatment
**Inclusion Criteria**

- Biopsy proven adenocarcinoma

- mrT1-T3b (<= 5mm extramural spread) V0 N0 CRM-ve

- The *multidisciplinary team considers that* TME, CRT, SCPRT and TEMS are all reasonable and feasible treatments
STARTREC – Study design
Phase II/III clinical trial

- cT1-T3b N0
  - Radical Surgery
    - TME
  - Organ preservation
    - 5x5 Gy
  - Organ preservation
    - CRT
    - evaluation
      - Good response
        - CCR
          - W&W
        - Not CCR
          - TEM
            - high risk conversion TME
      - Poor response
        - TME

- Week 11-13 – central review
- Week 16-20 – central review
## Consent

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<th>TEMS</th>
<th>Resection</th>
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<tr>
<td>Mortality</td>
<td>&lt;1%</td>
<td>&gt;1% c possum</td>
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<tr>
<td>Radiotherapy</td>
<td>Toxicity of rads</td>
<td>Not for early cancer</td>
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<tr>
<td>Morbidity</td>
<td>Low</td>
<td>High</td>
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<tr>
<td>Stoma</td>
<td>Very unlikely</td>
<td>Possible/Likely</td>
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<tr>
<td>Recurrence</td>
<td>Higher risk</td>
<td>Lower risk</td>
</tr>
<tr>
<td>Evidence</td>
<td>Emerging</td>
<td>Well recognised</td>
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National issues

- Training
- ERUS
- Early rectal cancer group
- Database
- Trials
- PROMS
Magnetic Resonance Tumour Regression Grade (mrTRG) as a Novel Biomarker to Stratify Management of Good And Poor Responders to Chemoradiotherapy: A Rectal Cancer Multicentre Randomised Control Trial

The TRIGGER Feasibility Trial

Protocol Version: 3.0
Protocol Date: 26 November 2015
IRAS Number: 156408
EudraCT Number: 2015-001009-40
ISRCTN: Date registered: CTA number:
REC Number: 15/I/LO/1836
Sponsors Number: CCR 4326
mrTRG

• High resolution MRI images to determine proportion of tumour that has become fibrotic (low intensity) v remaining residual intermediate signal intensity

• mrTRG Grades

1  -2  -3  -4  -5

Good       Bad
TRIGGER - Protocol

Rectal Cancer
1) Biopsy - adenocarcinoma
2) Baseline MRI
3) Chemoradiotherapy
4) Eligible & Consent

1:2 Randomisation

Control arm
- Repeat MRI
- Clinical assessment and baseline MRI
- Surgery
- Adjuvant Therapy
- FOLFOX**
- 24 weeks

Intervention arm
- Repeat MRI and REASSESS (mrTRG)
- Good Response
  - mrTRG I&II
  - Deferral of surgery
  - Adjuvant Therapy
  - FOLFOX
  - 12 weeks
  - Repeat MRI (mrTRG)
  - Surgery

- Poor Response
  - mrTRG III-V
  - FOLFOX**
  - 12 weeks

+Recommended CRT regimen – 45Gy/25# and Capecitabine
++Recommended post-treatment regime – FOLFOX regimen
#Randomise following MRI assessment but before the MRI is report at the MDT.
*MRI to assesses disease progression only
** TME surgery if patient declines deferral of surgery
mrTRG - performed at 6 weeks post-CRT
mrTRGb - performed 12 weeks into ‘up-front’ FOLFOX treatment
Options

**TEMS**
Risk determined by pathology
Low - Close surveillance
Inter/High - Salvage TME

**TME/APR**
TEMS/TREC/STARTREC
? Watch and wait ycCR
Salvage TME

**TME/APR +/- Neoadjuvant CRT**
TRIGGER
Summary

- TEMS has an established role in early stage cancer
- TEMS alone can be recommended for small (<3cm) pT1 Sm1 tumours with favourable histological features
- Other pT1 and pT2 tumours - TEMS alone is not adequate treatment and should be combined with additional treatment including neoadjuvant therapy and/or rescue surgery and should be performed in the context of a clinical trial.
- In case of ycCR, local excision of the scar can be considered an alternative to TME surgery with close surveillance for yPT0-1
- Wait and see for yCR should only be performed in the controlled setting of a trial.

Decision making should be tailored to individual patients needs to balance the goals of maximising life expectancy and quality of life.
Personalised Approach

Patient preference

KARDÅSH
Designed by Kanye West

IKEA
Design and Quality
IKEA of Sweden
Acknowledgements

- Doug Speake
Exclusion Criteria

- Maximum tumour diameter >4cm
- MRI evidence of EMVI
- MRI evidence of Node +ve
- Mesorectal fascia threatened (<=1mm clearance)
- Definite evidence of metastatic disease (patients with indeterminate lesions agreed by the MDT are eligible)
- Anterior tumour above peritoneal reflection on MRI
Consensus

Clinical stage
• Local excision is safe for cT1N0M0
• For cT2N0M0 - TME should be offered. Local excision following neoadjuvant CRT in context of trials, unfit pts or refusing major surgery

Pathological stage (pT)
• pT1 low risk - local excision is deemed sufficient
• pT1 high risk - completion TME. Rectal preservation with neoadjuvant CRT in trials, unfit pts or pt choice
Summary /Consensus

• Based on clinical stage
• Local excision is a safe approach for cT1N0M0 rectal cancer
SCRT and TEM for early disease
## SCPRT and delay

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