County Durham and Darlington NHS
NHS Foundation Trust

Complete Biological Response to Neoadjuvant Therapy in Rectal Cancer: A Local Review

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Background

- Total mesorectal excision has transformed the standard of care of rectal adenocarcinoma
  - Reduction of local recurrence rates from 50% to 4-22%.[1]
- Care is further improved with addition of adjuvant and neoadjuvant chemoradiotherapy (CRT)[2]

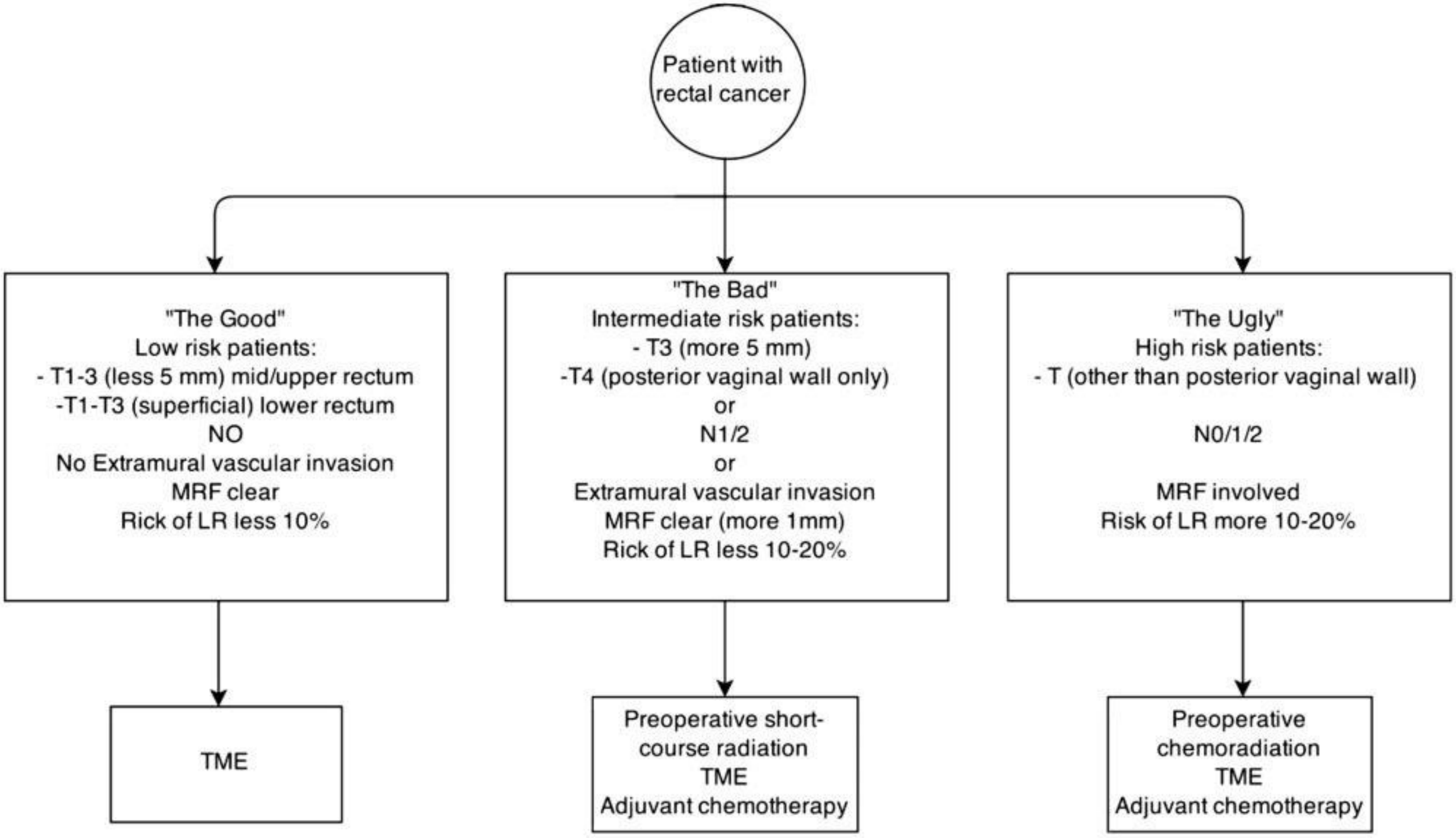
Background

- German Rectal Cancer trial
  - Patients with T3-T4 tumours and N+ have a lower local recurrence rate with preoperative CRT compared to surgery alone (4% vs. 13%).[3]

- Now standard practice is to give CRT followed by surgery for certain stages of rectal cancer

European management of rectal cancer [4-6]

LR= local recurrence; MRF = mesorectal fascia; TME =total mesorectal excision



What to do about complete local clinical / Pathological response (cCR / cPR) to preoperative CRT?

- Complete pathological response (cPR) to preoperative CRT in rectal adenocarcinoma after TME is 8-27% [7-9]
- cPR is achievable even in patients with a T4 cancer [7-9]
- cCR can negate the need for surgery with reduced morbidity and mortality associated with surgery

cCT surveillance compared to surgical excision

- Patients initially presenting with cT3 cN0 disease had an overall 97% 5-year survival and a disease free survival of 84%, comparable to contemporaneous reviews of cPR patients treated with invasive surgery. [9-11]
    - Within these series, 5% of patients developed a local recurrence within 2 years of initial treatment and underwent salvage surgery.
- This is comparable to a recent Philadelphia series, which achieved an 89% disease free survival over 5 years.[12]
    - This included clinical complete response in patients with stage IV disease (T3N1M1)
- Studies by Maas based in the Netherlands, and Smith in New York, demonstrated a disease free survival of 89% and 88%, and overall survival of 100% and 97% respectively. [8, 13]

Aims of this audit

- To ascertain the local incidence of cCR and cPR of patients with rectal carcinoma who have received preoperative radiotherapy
- Accuracy of MRI and pathological specimen reporting
- Short term surgical outcomes of all patients undergoing rectal cancer surgery

Study period

- 1st January 2015 - 31st April 2017

- All patients with a diagnosis of adenocarcinoma of the rectum discussed at Darlington colorectal MDT

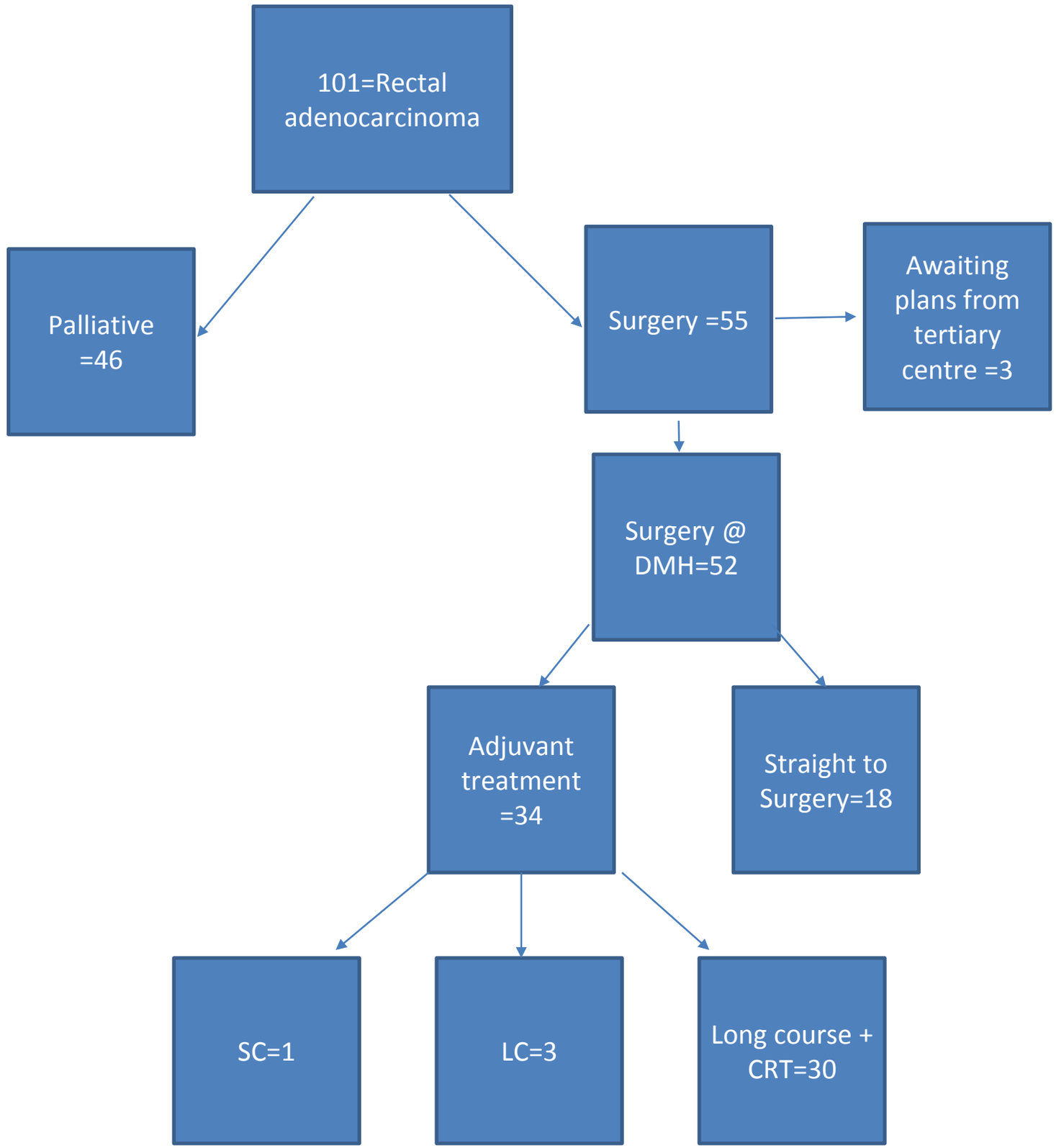
Data collection

- Patient details obtained via Cancer Services Department at Darlington Memorial Hospital

- Data extracted from iSOFT computer software

Patient demographics

- 102 patients (67 male; 36 female)
- Median age 71 years (range 36 - 95 years)
- Median tumour height on MRI 6.5cm (2.3 - 15cm)


101=Rectal adenocarcinoma
Palliative =46
Surgery =55
Awaiting plans from tertiary centre =3
Surgery @ DMH=52
Adjuvant treatment =34
Straight to Surgery=18
SC=1
LC=3
Long course + CRT=30

Complete Clinical response

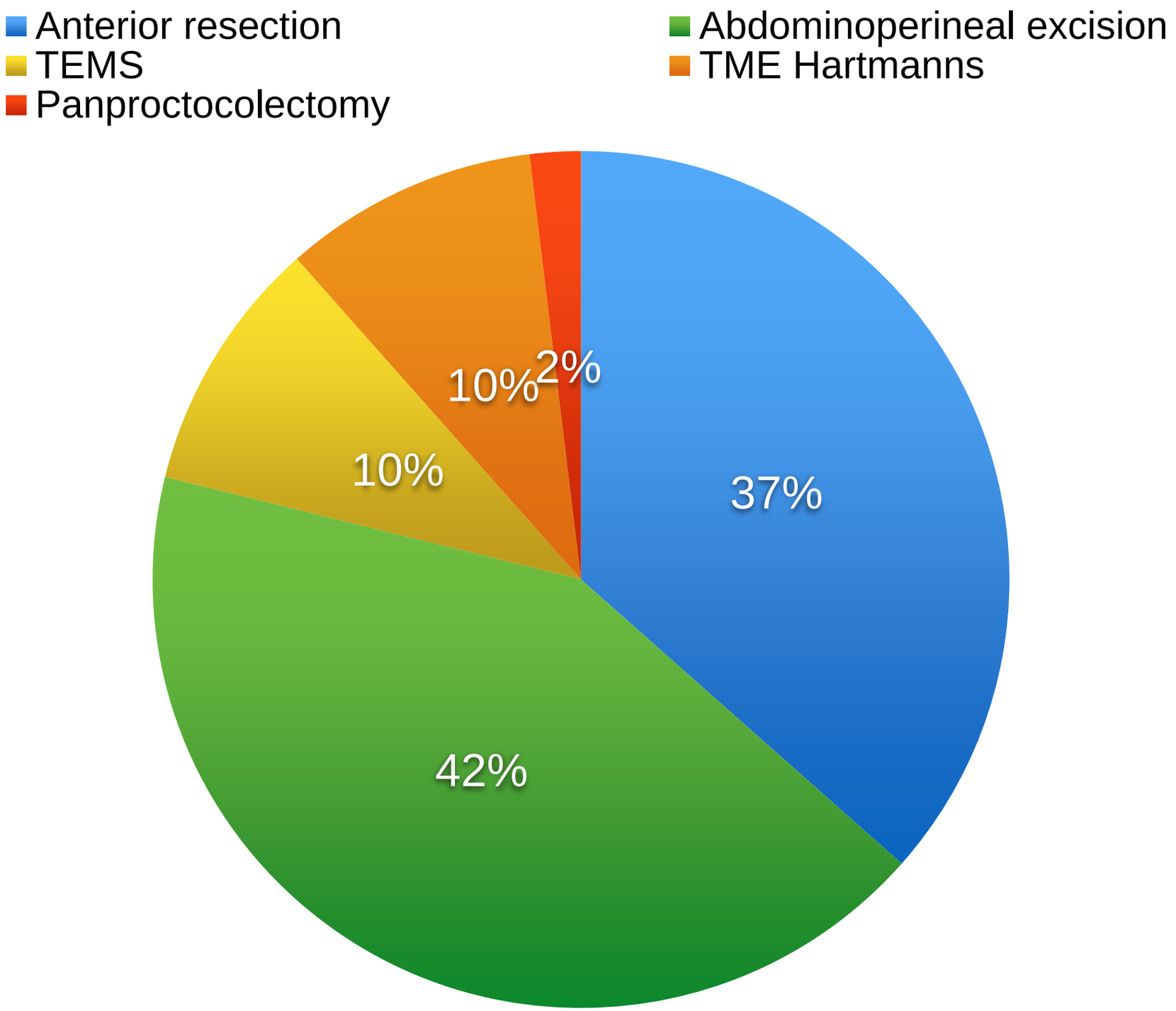
- 5 patients
- Only one is currently under surveillance
- Three patients had residual tumour on surgical specimen
- 3 patients had T2N0
- 1 patient had TxN1

Complete pathological response

- 5 Patients

Pre Treatment TNM (MRI)	Post Treatment TNM (MRI)	Post Treatment TNM (Path)
T4 N2 V1	T2 N0 V0	T0 N0 V0
T3 N2 V1	T2 N0 V0	T0 N0 V0
T3 N2 V1	T3 Nx V1	T0 N0 V0
T4 N2 V1	T3 N0 V1	T0 N0 V0
T2 N0	T2N0	T0 N0 V0

Type of operations



Operative outcomes

- Conversions
  - 2 (4%)
    - 1 AR, 1 TME Hartmanns
- Anastomosis leak
    - 15% (n=3)
  - Median LOS 9 days (Range 0-41)
  - 0% 30 day mortality

How do we follow up cCR?

- No consensus on when or how to investigate patients with cCR
  - Evidence ranges from 4 - 6 weeks until 24 weeks [8,10,11,14]
- How do we define cCR
  - Absence of cancer on proctoscopy?
  - Negative biopsy?
  - Clear anorectal ultrasound?

Inaccuracies with investigations in detecting true cCR

- Digital rectal examination NPV 21-24%.[15-17]
- Endoscopic assessment with biopsy NPV 69%, although FPV is 0%.[18]
- MRI-large meta analysis demonstrated 50% sensitivity and 91% specificity for T stage and 19% sensitivity and 94% specificity for T0 tumours.[19]
- With addition of DWI In context of post CRT sensitivity has risen to 84% (T stage) and 85% (T0 stage).
- The use of T2 weighted MRI can provide accuracy of 92% of complete responders.
- MRI can over-stage nodal spread.[20]
- PET correctly identifying cCT in 60% however sensitivity of 97% for early distant metastasis[21]

Conclusions

- Complete pathological response to chemoradiotherapy for rectal cancer is becoming a common clinical entity
  - Our rates of cPR of 15% is comparable to the literature
  - 0% Correlation between cCR and cPR using MRI
  - Short term surgical outcomes are comparable with the literature[22]

Recommendations

- Tumour regression stage to be present on all post CRT MRIs – Achieved!
- Standardisation of CRT? – What are people doing?
- Given inaccuracy of local MRI reporting is it safe to adopt a surveillance policy? - ? Better MRI imaging ? Reporting MRI by specific GI Radiologist

Recommendations

- If surveillance is adopted for patients with cCR –

Should this be centralised?

Proposal

- 2 sites – North and South – RVI / DMH
- Electronic Database

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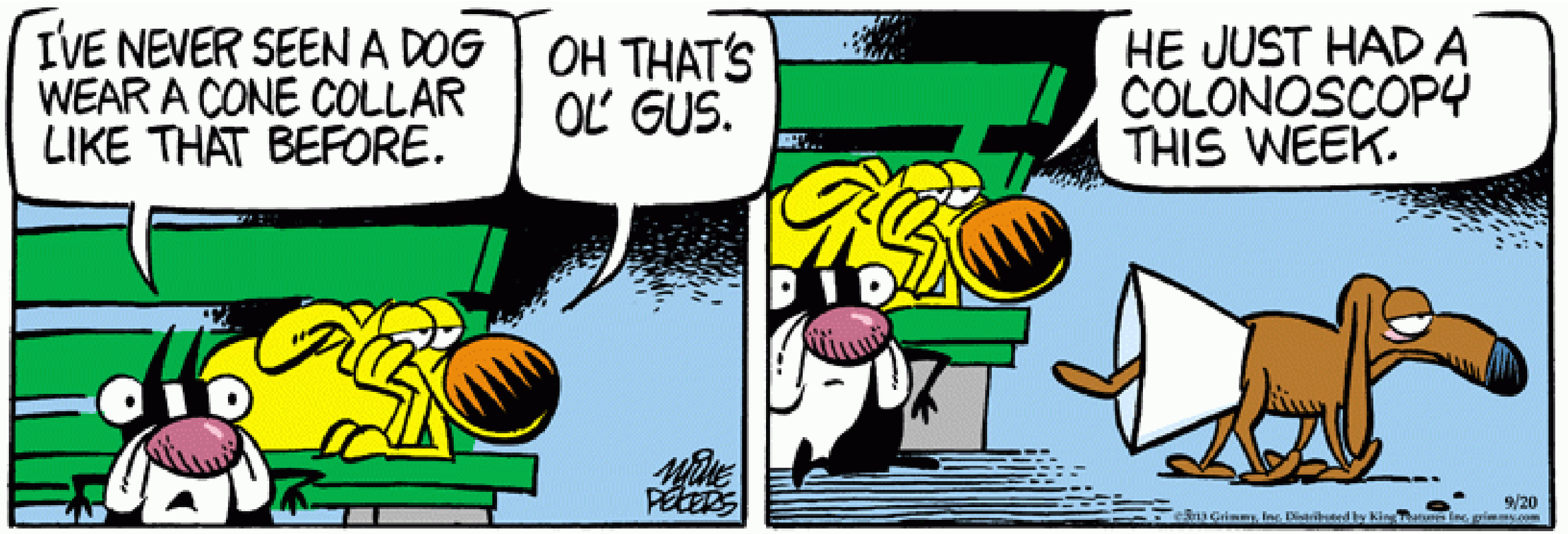
Questions?


I'VE NEVER SEEN A DOG WEAR A CONE COLLAR LIKE THAT BEFORE.
OH THAT'S OL' GUS.
HE JUST HAD A COLONOSCOPY THIS WEEK.
WAYNE PEDERS
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