The oncological and functional risks of the organ preservation experimental treatment approach in rectal cancer

C Cocco Martins MD
CHO Torres Vedras
CHLC Lisbon
Portugal
Disclosures

No disclosures to declare
Outline

• Standard treatment for rectal cancer
• Non standard treatments
  Oncological and Functional risks
• Wait and See approach
• Conclusions
Standard treatment of rectal cancer

- Anterior resection
- Abdominoperineal resection
- Neoadjuvant CRT in T3-T4
- Pelvic exenteration
Oncological results
standard treatment at 5y

- T1-T2 N0
  local recurrence ≤ 2%

- T3-T4 after CRT
  local recurrence < 10%
  survival 70%
  sphincter sparing surgery > 70%

- TME alone 10% local recurrence
- R0 local recurrence 5.6%
- 10-20% cCR after CRT
What has been changing

• Earlier diagnosis
• Improvements in imaging and radiation techniques
• Improvements in staging
  - tumor
  - margins
  - ganglia
  - circunferential 1mm
distal <1cm
never positive?
• New techniques (laparoscopy, TEM, robotic)
• Downstaging with neoadjuvant CRT
Have made possible

- Local excision
- Coloanal anastomosis
- Inter/partial sphincteric resection

Reconstruction
- J pouch
- straight
Anastomosis
- hand sewn
- stapled

WAIT AND SEE APPROACH
Difficulties in evaluating results

- Series are not homogeneous
- Distance to the anal verge is not clearly specified
- Functional results are not clearly evaluated
Local treatment

• T1 low risk / Selected T2 after CRT best choice
• Many possibilities
  open/endoscopic/robotic/laparoscopic
• Local recurrence higher than standard, variable 6-30%
• Overall survival > 80% at 5 y
• adjuvant CRT after local excision of T2 tumors or T1 with adverse prognostic factors?
• Salvage surgery
  Multivisceral pelvic resection
  morbidity 34%
  R0 79-84%
  5y disease free survival 53-59%
Bordeaux Group
Low rectal cancer

• Type I  supraanal tumor
  >1 cm anal ring  CAA

• Type II juxta anal tumor
  < 1cm from anal ring  pISR

• Type III intra anal tumor
  Internal sphincter invasion  tISR

• Type IV transanal tumor
  APR
  IV A  levator ani muscles
  IV B  external sphincter
  IV C  levator ani+ external sphincter

Rullier E et al Dis Colon Rectum 2013; 56;5(2560-67)
Doi:10.1097/DCR.0b013e31827c4a8c
Oncological outcome in the Bordeaux series

- at 5 y
- Local recurrence 8%
- Distant recurrence 26%
- Overall survival 77%
- Disease free survival 64%
- No difference in results for patients type I to III
- As expected for type IV worse results

Rullier E Dis Colon Rectum 2013;56;560-567
Intersphincteric resection  ISR

- 14 retrospective studies from 84; systematic review
- Mean distance of tumor to the anal verge -31mm
- 1289 patients: open and laparoscopic
- Median follow-up 56 months
- R0 in 97%
- Mean local recurrence rate 6.7% (0-23%)
- Mean 5y overall survival 86.3%
- Disease free survival 78.6%

Martin ST et al BJS2012Jn13
Functional results in ISR

- Only 8 studies report functional outcome
- Mean number of bowel motions 2.7
- 51% perfect continence
- 29% fecal soiling
- 23.8% Incontinence to flatus
- 18.6%-urgency

Martin HM, Winter DC-BJS2012, May; 99(5):603-12
Coloanal anastomosis

- Tumors 1-2 cm dentate line
- distal even < 5mm
- TME and preoperative RT
- Distal margin doesn’t matter if RT?
- Strategies for improving distal margin in T1 (RT,intersphincteric resection) may be unnecessary

Pahlman L, Bujko et al. WCDis 2013 Apr;15(4):e166-74
About functional risks

- Quality of life seem preserved
- But functional results are not so good

- HOW MUCH CONTINENCE AND FREQUENCY COMPROMISE DOES ANYONE ADMIT TO AVOID COLOSTOMY?

Low anterior resection syndrome

• 10-20% after sphincter sparing surgery
  Urgency
  incontinence
  various degrees of evacuatory dysfunction

• Worse
  anastomosis 3 cm from the anal verge
  30% straight coloanal anastomosis
  with J pouch  5.5% to 8.5% (worse with time)

*The Lancet Oncology, 2012*
Volume 13, Issue 9, Pages e403-e408
Low anterior resection syndrome

• Can be preventable?
  manometry

• Treatable?
  Loperamide
  Bulking agents
  Laxatives
  Irrigation
  Biofeedback
Urinary and sexual dysfunction

• Mainly caused by surgery (1)
• Only 9% of women and 39% of men remember discussing sexual effects of treatment (2)
• Dysfunction exists despite global quality of life

What is the impact of neoadjuvant chemoradiation in functional outcomes?

- Multivariate analysis in ISR patients
- Predictors of continence
  - Distance of the tumor to the anal ring
  - Distance of the anastomosis to the anal verge
- Not significant*
  - Age
  - Extent of internal sphincter resection (others do not agree**)

- Quality of life maintained
- Improved function over time

*Denost Q et al Dis Colon Rectum 2011;54;963-8
**Barisic G et al colorectal Dis 2011;13:638-43
Functional results in DUTCH TME TRIAL radiation plus TME

- 597 patients excluded local recurrence
- at 5 y
  - 68% day incontinence
  - 32% incontinence at night
- These were 24% responders, 15% more than non irradiated

Pads for incontinence
  - 56% of irradiated
  - 33% of operated, n irradiated

- Irradiated patients >impaired in daily life and social activity
- Irradiated patients without stoma <satisfied than non irradiated
- With stoma radiated equally satisfied as non irradiated

Some patients would prefer stoma

A Dutch Colorectal Cancer Group Study JCO23;6199-6206
How to measure

- MSK scale (1)
- Low anteriorsyndrome score (2)
- Jorge and Wexner scale (3)

etc

1-Temple L et al  Dis Col Rectum July 2005:1353
3-Vaizey C et al-Gut 1999,44:77-80
Wait and See
When?

- Habr Gama series, 361 patients, 122 cCR at 8w
- Small tumors T1-t2? Included cT1-T3, local recurrence in first year excluded, from 7 cm anal verge

- cCR to neoadjuvant at 1y, without biopsy, 99 patients (28%) absence or fany residual scar no mass or ulcer after clinical, endoscopic and radiological assessment and CEA

- At 5y from those with cCR at 1y (28%) local recurrence rate 5%; survival 93%

Habr Gama A, Perez ANN Surgery 2004; 240: 711-717
Maastricht series

- 192 patients cT4,cT3, of which 21 had a cCR after CRT (biopsy)
- 10 were distal tumors that would require APR
- Results were identical

Maas M, Beets-Tan et al. JCO 2011; 294633-4640
Oncological risks

• An inadequate choice of patient
  Unexpected aggressive situation
    local progression
    distant metastases
  Inadequate evaluation and remanescent tumor after chemoradiation or radiation
    de novo tumor

• Bad results with salvage surgery?
Pitfalls in evaluation of pathologic response

- 220 patients / 276 1997-2010
- 19 of 31 patients with complete pCR had residual mucosal abnormalities consistent with incomplete response
- In tumors downstaged to pT0/1 residual mucosal abnormalities and had a 2% risk of positive nodes

Smith FM, Chang H-BJS
2012; 99: 993-1001
Accuracy of evaluation of response

- Timing of response evaluation after CRT: 8-12 weeks; plateau at 12w
- Criteria:
  - Clinical examination
  - Endoscopic ultrasound
  - NMI
  - Carcinoembrionc antigen (CEA)
  - PET
- Timing for follow up:
  - 4-6 weeks first y
  - every 2 m second y
  - annual after 4y
Wait and See evaluation
Glynne Jones

• 30 publications, 9 series, 650 patients
• All series heterogeneous
  Staging
  Inclusion criteria
  Study design
  Rigour of followup

• Not suitable for downshifted T3-T4 at the moment
• DO PATIENTS GO WORSE IF THEY RECUR?
• Need for more observational studies

Glynne Jones BJS 2012;99:897-909
Some ongoing studies

• Deferral of Surgery (UK)
• Danish Colorectal Cancer Group

European Network for Watchful Waiting

Glynne Jones BJS 2012,99,897-909
In conclusion

• Patient selection, stratification of approach by location and stage are crucial in rectal cancer
• For local treatment technique depends on local expertise but even so expected rate of local recurrence is > than with standard treatment
• Quality of life evaluation is prone to a subjective bias of expectation and not synonymous of good function so specific tools for bowel, urinary and sexual function should be systematically applied
• Would manometric or other evaluations help in preventing dysfunction and be routinely applied?
• The wait and see approach is promising, time and resource consuming, and there is an urgent need for data
• An European Registry seems a good idea
• There is an urgent need for prognostic markers to obviate on a too much aggressive neoadjuvant therapy in early cancer to obtain organ preservation or loose some downstaged patients because fear of recurrence