

When to take your decision? Before or after nCRT?



Ahmed M. Hussein, MCh,DrCh

Past-Chairman Unit of Colon & Rectal Surgery
University of Alexandria, EGYPT

When to take your decision? Before or after nCRT?

Is it possible to change operative strategy after nCRT in low rectal cancer?



When to take your decision? Before or after nCRT?

Tumor Response After nCRT



Before Treatment



After radiotherapy



At 12 wks follow up



When to take your decision? Before or after nCRT?

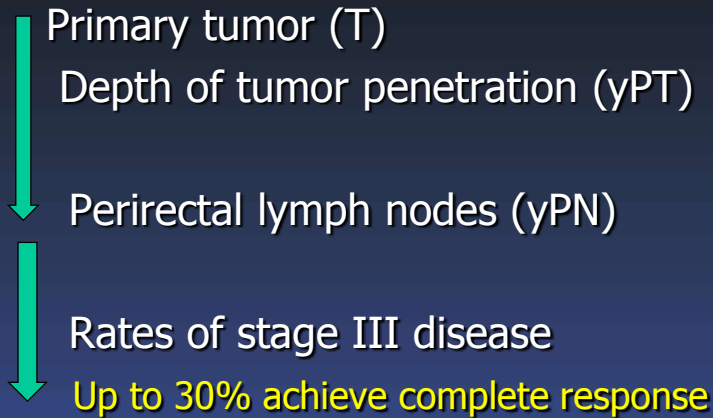
When to assess tumor response?

- ▶ Effect of nCRT on tumor is time dependant
- ▶ Standardized time to assess tumor response is after 12 weeks

Kalady , Lavery, Fazio Ann Surg 2009



Effect of nCRT in Rectal Cancer Downstaging and Downsizing



Disease Free Survival

▶ pCR	83%
▶ Incomplete Response	65%

Long-term outcome in patients with a pathological complete response after chemoradiation for rectal cancer: a pooled analysis of individual patient data.

Lancet 2010



When to take your decision? Before or after nCRT?

Pathologic Complete Response ?



When to take your decision? Before or after nCRT?

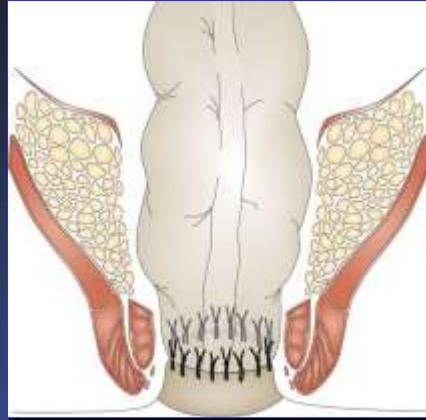
Is it acceptable to submit a patient to
a considerably morbid surgery
without removing one cancer cell?



When to take your decision? Before or after nCRT?

nCRT & Colorectal or Coloanal anastomosis

- ▶ Increase frequency
- ▶ Need of temporary stoma
- ▶ Risk of anastomotic leak, stricture...etc
- ▶ Morbidity up to 38%
- ▶ Fecal incontinence up to 20%
- ▶ Impotence (15%) and urinary problems (20%)



When to take your decision? Before or after nCRT?

APR

Permenant Stoma???
Bad Healing!!!!



1- Wait and See after Complete Clinical Response



CCR (Wait and see)

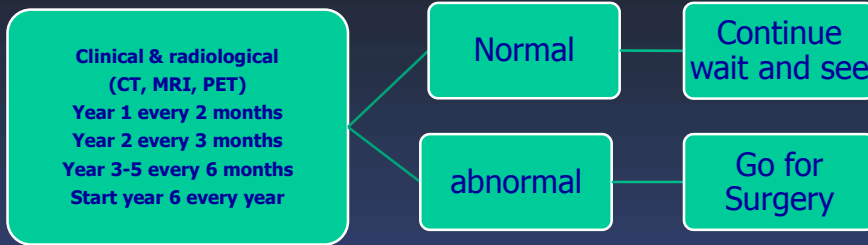
- ▶ No more than whitening of the mucosa, teleangiectasia with mucosal integrity
- ▶ No palpable masses or nodules
- ▶ No radiological evidence of extra-rectal disease (MRI, PET,CT)

Habr Gama 2010 DCR



When to take your decision? Before or after nCRT?

Habar Gama Follow-up Protocol



When to take your decision? Before or after nCRT?

ORIGINAL CONTRIBUTION

Watch and Wait Approach Following Extended Neoadjuvant Chemoradiation for Distal Rectal Cancer: Are We Getting Closer to Anal Cancer Management?

Angelita Habr-Gama, M.D., Ph.D.¹ • Jorge Sabbaga, M.D., Ph.D.^{1,2}
Joaquim Gama-Rodrigues, M.D., Ph.D.¹ • Guilherme P. São Julião, M.D.³
Igor Proscurshim, M.D.¹ • Patricia Batista Aguilár, M.D., Ph.D.^{4,5}
Wladimir Nadalin, M.D., Ph.D.^{6,7} Rodrigo O. Perez, M.D., Ph.D.^{1,4,8}

- ▶ Incomplete CR → Immediate surgery
- ▶ CCR → Watch & Wait



Habar Gama Results

- ▶ 47 patients had initial complete clinical response.
- ▶ 8 developed local re-growth within the first 12 months
- ▶ 4 patients developed late local recurrences (>12 months of follow-up).
- ▶ 35 patients **never** underwent surgery



Local recurrences after wait and see: Are they salvageable?

Local recurrence after complete clinical response and watch and wait in rectal cancer after neoadjuvant chemoradiation: impact of salvage therapy on local disease control.

Habr-Gama A, et al. *Int J Radiat Oncol Biol Phys.* 2014 Mar 15;88(4):822-8.



Local recurrences after wait and see: Are they salvageable?

- ▶ Local recurrence developed in 31% of (90) patients with initial CCR
- ▶ Salvage therapy is possible in $\geq 90\%$ of recurrences
 - ▶ 94% local disease control
 - ▶ 78% organ preservation



Nonoperative Management of Rectal Cancer With Complete Clinical Response After Neoadjuvant Therapy

James D. Smith, MD, Jeannine A. Ruby, MD,* Karyn A. Goodman, MD,† Leonard B. Saltz, MD,‡
José G. Guillem, MD,* Martin R. Weiser, MD,* Larissa K. Temple, MD,* Garrett M. Nash, MD,*
and Philip B. Paty, MD**

- ▶ Annals of Surgery 2012



NOM

- ▶ 32 patients
- ▶ 6 local failure
 - ▶ of them 3 have distant recurrence
- ▶ 81% avoided rectal resection
- ▶ Salvage surgery for local recurrence
- ▶ No further local recurrence FU 17 ms



NOM

2-year disease free survival

- ▶ NOM group 88%
 - ▶ Rectal resection/pCR group 98%
- P = 0.27

Overall survival

- ▶ NOM group 96%
 - ▶ Rectal resection/pCR group 100%
- P= 0.56



What is against wait and see?

- ▶ No definition of CCR
- ▶ You can't be sure that LNs are free
- ▶ You can't be sure that there is no residual tumors
- ▶ No correlation between clinical and pathological complete response
- ▶ You can only diagnose complete pathologic response after resection
- ▶ You don't know if you are helping or harming your patient!! (No Randomized trials)

Julio Garcia 2011



DISEASES OF COLON & RECTUM

ORIGINAL CONTRIBUTIONS

Complete Clinical Response After Preoperative Chemoradiation in Rectal Cancer: Is a "Wait and See" Policy Justified?

R. Glynn-Jones, M.B.B.S., F.R.C.R.,¹ • M. Wallace, M.S., F.R.C.S.,² • J. L. L. Livingstone, M.S., F.R.C.S.,² • J. Meyrick-Thomas, M.A., M.B.B.S., F.R.C.S.²

¹ Centre for Cancer Treatment, Mount Vernon Hospital, Northwood, Middlesex, United Kingdom
² Watford General Hospital, Watford, Hertfordshire, Middlesex, United Kingdom

The rationale of a "wait and see" policy relies on retrospective observations, which are currently insufficient to support this policy except in patients who are:
Unfit for or **Refuse** radical surgery



When to take your decision? Before or after nCRT?

2- From APR to SP after Complete or Incomplete Clinical Response



When to take your decision? Before or after nCRT?

Downsizing & Sphincter Preservation

- ▶ Tumor down-staging
 - ▶ Increases rate of sphincter preservation
 - ▶ German Rectal Cancer Trial & (NSABP) R-03 trial

Sauer R, Becker H, Hohenberger W, et al: Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med 351:1731-1740, 2004.



Downsizing & Sphincter Preservation

- ▶ Tumor down-staging
 - ▶ No difference in sphincter preservation
 - ▶ 2 Systematic Reviews

- Bujko K, Kepka L, Michalski W, Nowacki MP. Does rectal cancer shrinkage induced by preoperative radio(chemo)therapy increase the likelihood of anterior resection? A systematic review of randomised trials. *Radiother Oncol.* 2006;80:4-12.
- Wong RK, Tandan V, De Silva S, Figueredo A. Pre-operative radiotherapy and curative surgery for the management of localized rectal carcinoma. *Cochrane Database Syst Rev.* 2007(2):CD002102



World J Surg (2015) 39:1248-1256
DOI 10.1007/s00268-014-2930-3

World Journal
of Surgery

ORIGINAL SCIENTIFIC REPORT

Changing Operative Strategy from Abdominoperineal Resection to Sphincter Preservation in T3 Low Rectal Cancer after Downstaging by Neoadjuvant Chemoradiation: A Preliminary Report

Khaled M. Madbouly · Ahmed M. Hussein

ASCRS 2014



Why SP Surgery?

- ▶ Not to lose the golden chance of cure if CCR
- ▶ T1 have 5% MLN
 - ▶ MLN % increases in T2 & T3
- ▶ No permanent Stoma
- ▶ Free CRM and DRM



- ▶ Alexandria Main University Hospital
- ▶ Health Insurance Hospitals
- ▶ Between 1/2010 & 12/2014



Methods

- ▶ Prospective study: 45 pts (SP) 26 control (APR)
- ▶ Inclusion criteria:
 - ▶ T3
 - ▶ <1 cm distance between the top of the anal sphincter and the distal edge of the tumor
- ▶ Exclusion Criteria:
 - ▶ Mucinous carcinoma
 - ▶ Distant metastasis



Methods

- ▶ Preoperative nCRT
- ▶ Final decision about sphincter preservation was intra-operative
- ▶ Surgery was done 8–12 weeks after completion of nCRT
- ▶ **Criteria for changing operative strategy to SP:**
 - ▶ Tumor downsizing that leaves ≥ 1 cm distal safety margin above the anal sphincters
 - ▶ Free potential CRM in MRI



Tumor Response

	n	%
ycCR	12	27
TRG4 (ypCR)	10	22
TRG3	11	24
TRG2	14	31
TRG1	10	22



Study Group

- ▶ 36 Pts TME & CAA
 - ▶ 6 Pts ISRR (partial resection of IAS)
- ▶ 9 Pts TME & CRA



Oncologic outcome

- ▶ Mean follow up 57 months
- ▶ CA specific 87.5%
- ▶ Overall survival 79%



Oncologic outcome

	SP	APR	p
Overall Recurrence	6/45	3/26	0.99
	13.3%	11.5 %	
Local Recurrence	4/45	1/26	0.64
	8.8%	3.8%	
Mean time for Recurrence (ms)	27.2	31.8	0.06



Oncologic outcome Salvage APR

- ▶ 3/4 patients with local recurrence underwent salvage APR with free safety margins
- ▶ Follow-up after salvage surgery for 31, 33, and 37 months revealed no recurrences



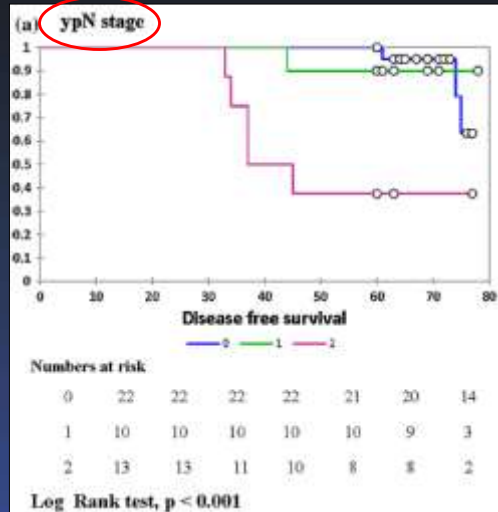
Oncologic Outcome

- ▶ Kaplan–Meier analysis (study group)
 - ▶ Disease-free Survival 87%
 - ▶ Overall Survival 88.9 %
- ▶ Univariate analysis for factors affecting recurrence:
 - ▶ N2 stage
 - ▶ Low TRG
 - ▶ Pathologic response



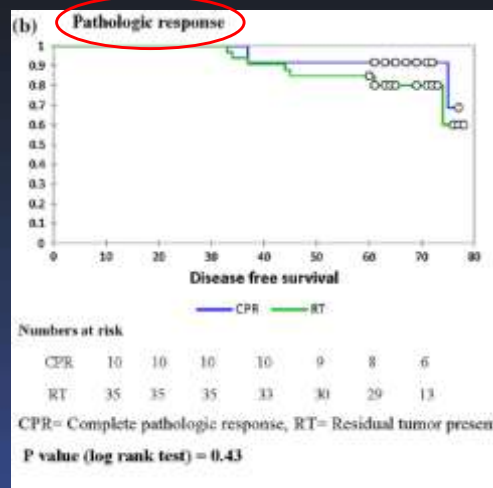
When to take your decision? Before or after nCRT?

Factors affecting recurrence

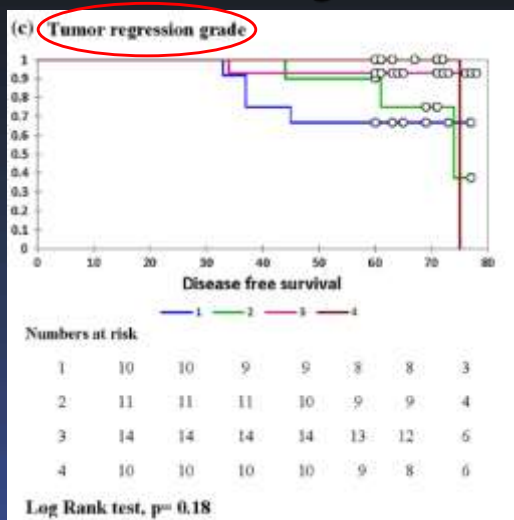


When to take your decision? Before or after nCRT?

Factors affecting recurrence



Factors affecting recurrence



Conclusions

- ▶ Changing operative strategy from APR to SP after downstaging by nCRT:
 - ▶ T3 low rectal cancer
 - ▶ Favorable histopathology
 - ▶ Motivated patients
 - ▶ Good sphincter function
 - ▶ Strict follow-up



Conclusions

- ▶ Disease-free survival rates are comparable to patients having their decision made before nCRT
- ▶ Early diagnosis of recurrence and salvage surgery with free resection margins can be achieved



Thank You for Your Kind Attention