Prague ONCO
ONCOLOGY COOPERATION

Kontroverze v terapii karcinomu rekta.

Dytrych P. [1] Hoskovec D. [1], Krška Z. [1], Černý V. [2]

- [1] -1. Chirurgická klinika VFN a 1. LF UK
- [2] - Radiodiagnostická klinika VFN a 1. LF UK

29.–31. 1.2020 PRAHA

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aneb
jak využít radioterapii.

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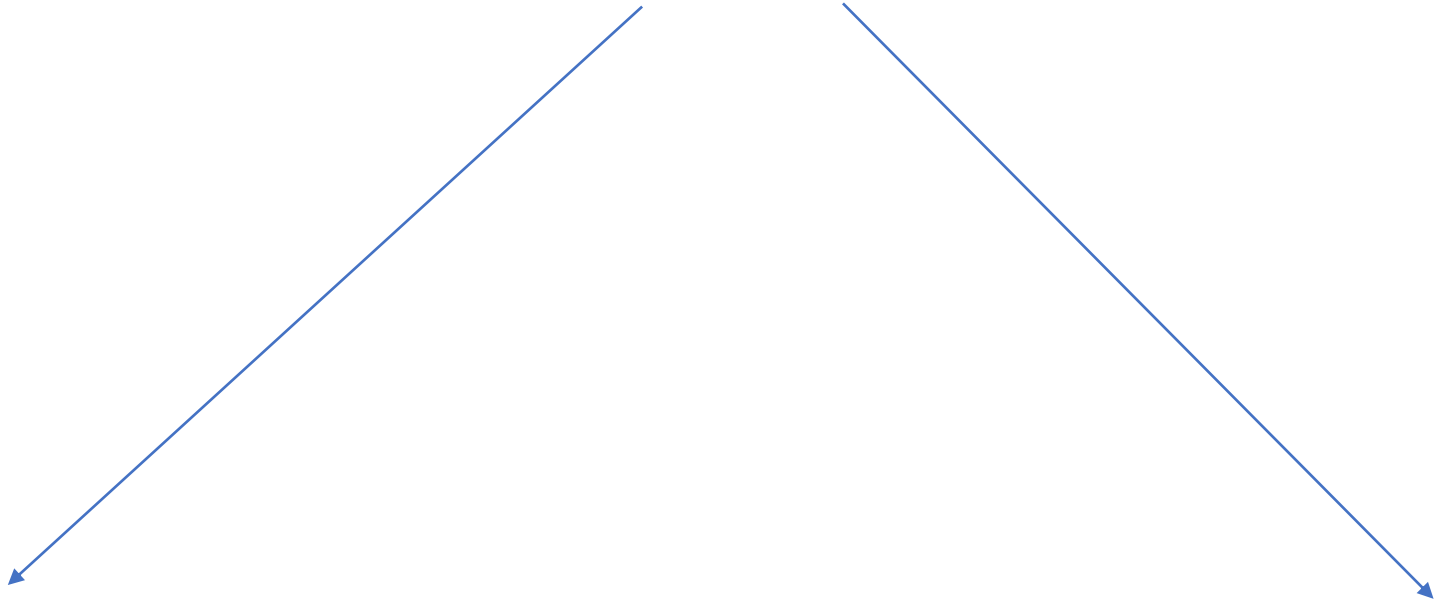
Jak využít radioterapii.

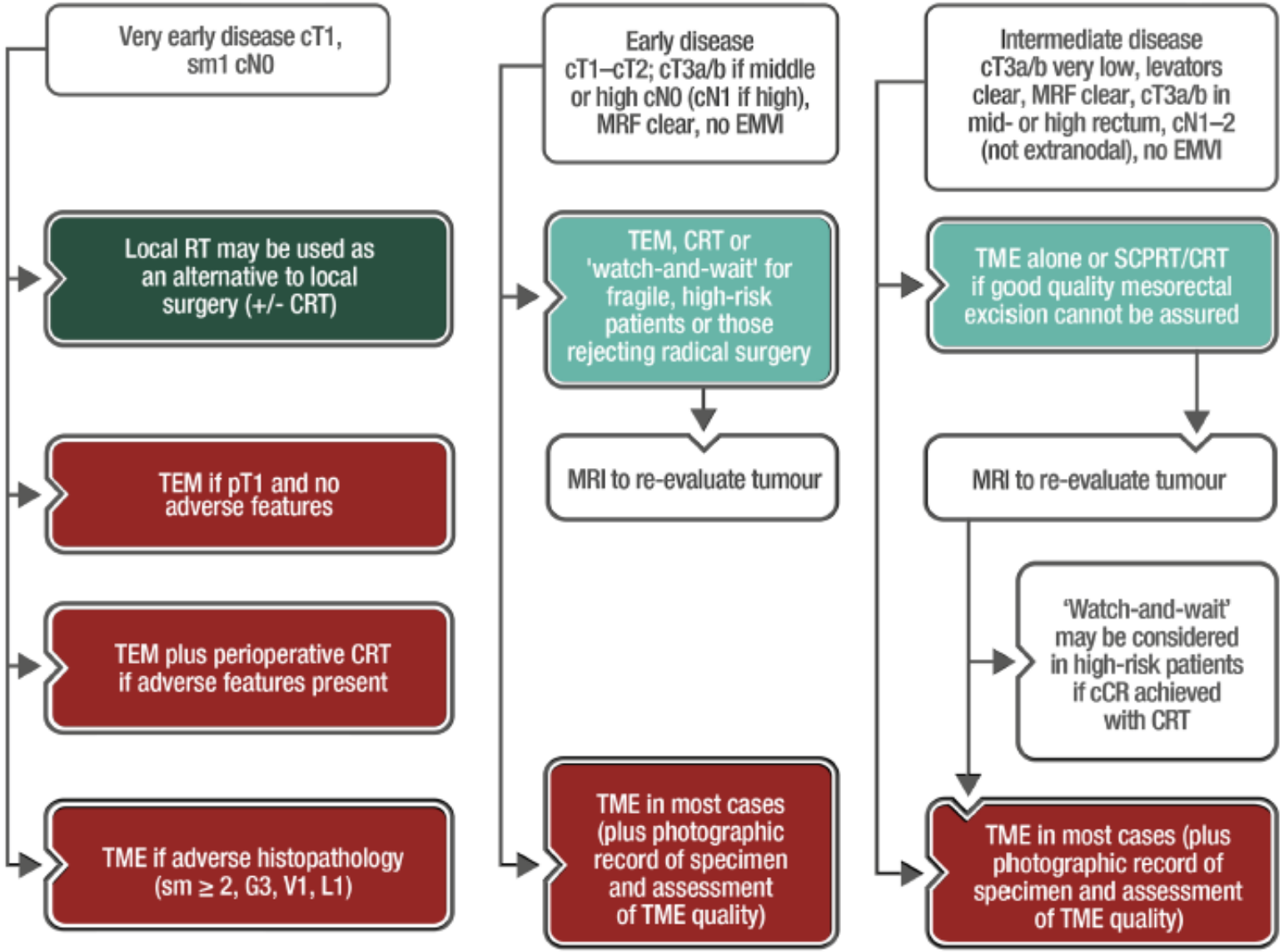


- umožnit rektum šetřící výkon
- minimalizovat nežádoucí efekt

CLINICAL PRACTICE GUIDELINES

Treatment recommendations

Very early, early and intermediate disease



ESMO

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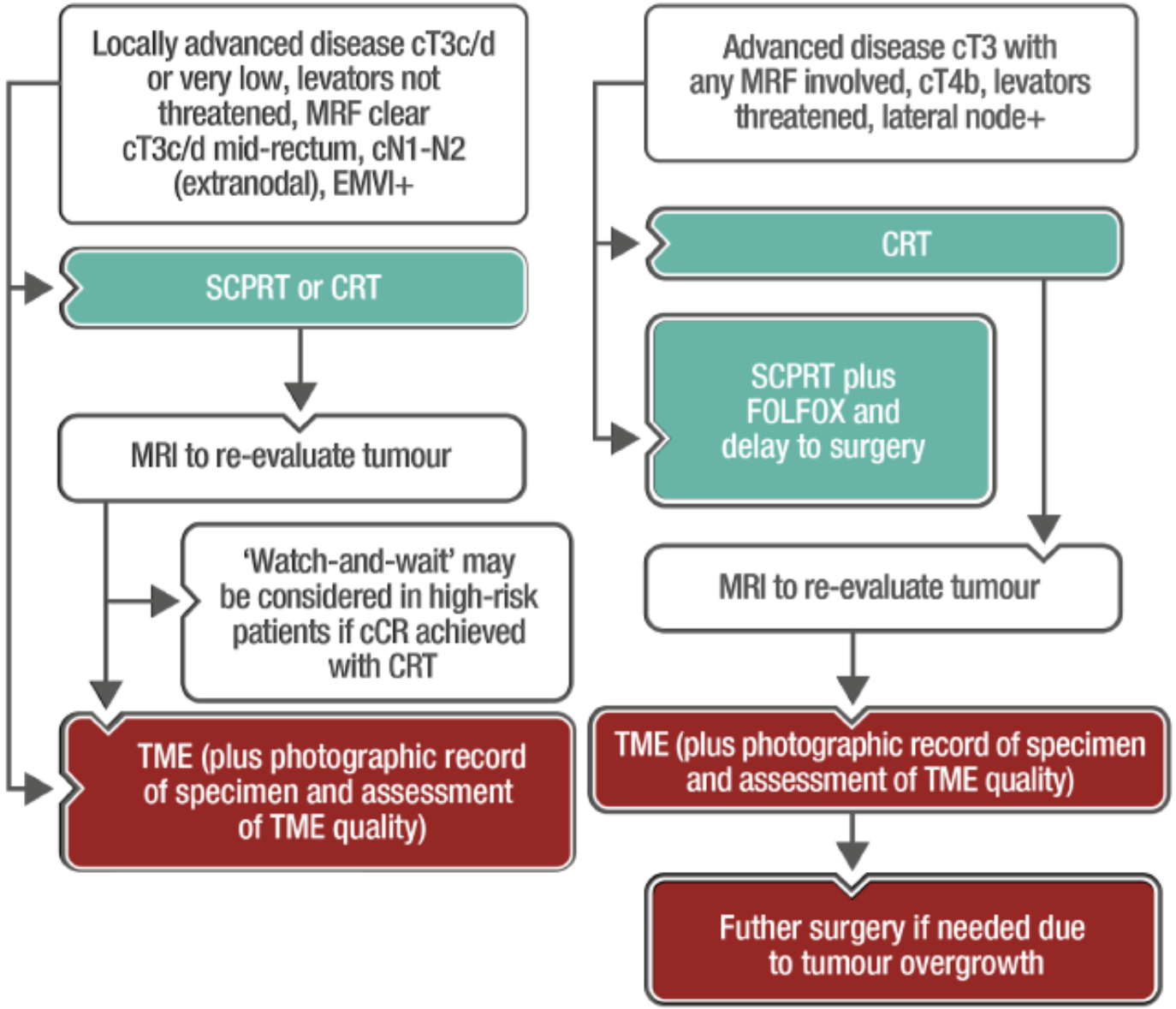
CLINICAL PRACTICE GUIDELINES

Treatment recommendations

Locally advanced and advanced disease



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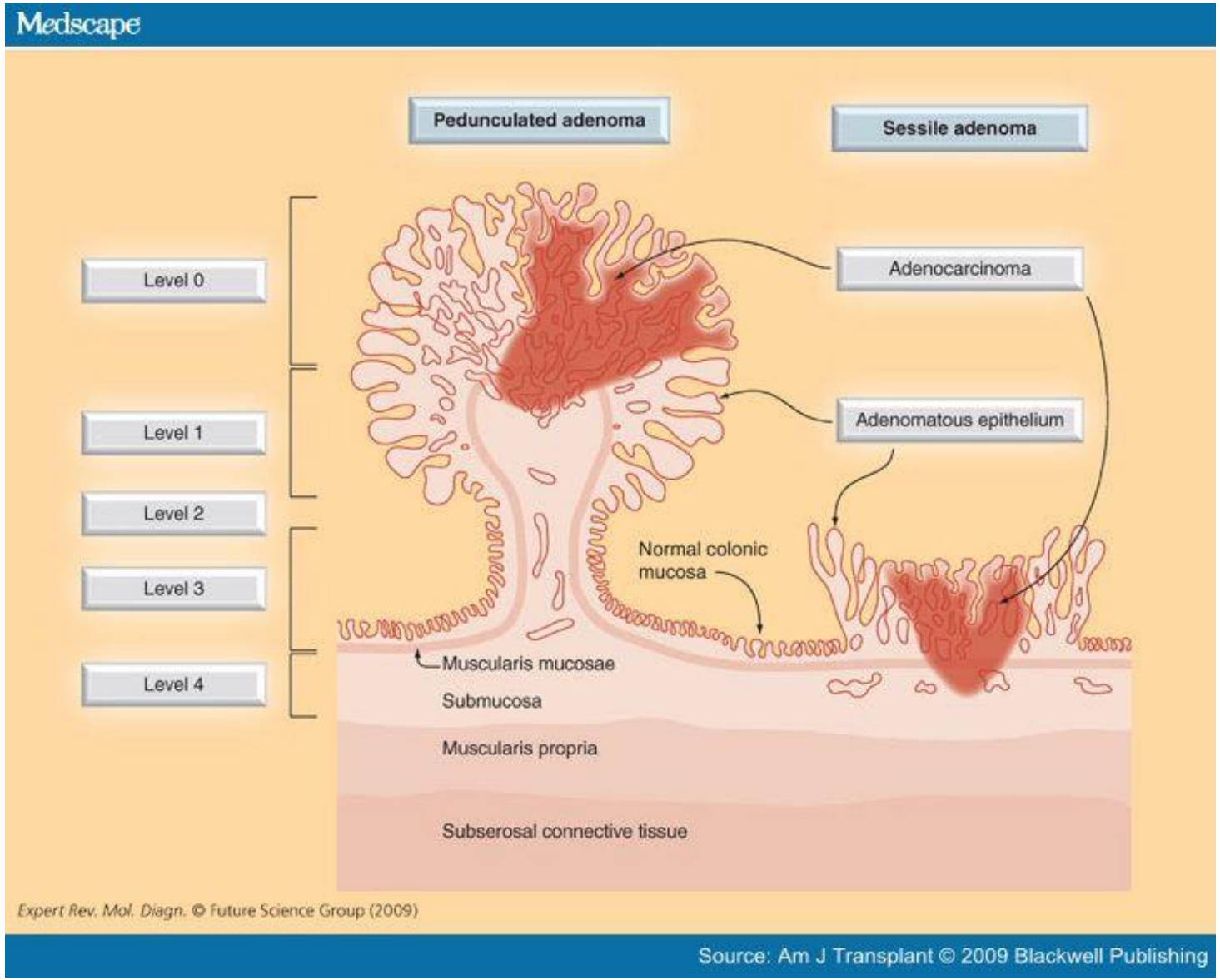
Část 1.

Jak ušetřit rektum?



T1 …….LN +

Sm1 – 2%
Sm2 – 8%
Sm3 – 23%

T1 **low risk**

Author	No. Pts	LN + Low Risk	analysis of Sm depth	Signifficance of Sm
Kikuchi 1995	64 Sm 1	**0 %**	yes	yes
Blumberg 1999	42 low risk T1	**7%**	no	-
Okabe 2004	304 T1	-	yes	yes
Ueno 2004	56 low risk T1	**0%**	yes	yes
Hassan 2005	78 low risk T1	**5,1**%	no	-
Rasheed 2007	48 T1	-	yes	**no**
Kobayashi 2010	101 low risk T1	**1%**	no	-
Saraste 2012	128 T1	**6%**	yes	**no**

Qualitative predictive markers of LN involvement: LVI, grade (budding)
Quantitative predictive markers of LN involvement: (width), depth of Sm invasion

X T1 High risk - Sm2-3
G 3-4
L 1
V1
tumor -budding

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

Articles included in systematic review

n = 22 804 pts

local excision + adjuvant therapy (long-course chemoradiation or radiotherapy)

Median follow-up was 51 months (range 1–165).
LR:
5.8% (95% CI 3.0–9.5) for pT1
13.8% (95% CI 10.1–17.9) for pT2
33.7% (95% CI 19.2–50.1) for pT3

overall median disease-free survival was 88% (range 50%–100%)
pooled overall morbidity of 15.1% (95% CI 11.0–18.7).

Meta-analysis of oncological outcomes after local excision of pT1–2 rectal cancer requiring adjuvant (chemo)radiotherapy or completion surgery

W. A. A. Borstlap[1], T. J. Coeymans[1], P. J. Tanis[1], C. A. M. Marijnen[3], C. Cunningham[4], W. A. Bemelman[1] and J. B. Tuynman[2]

BJS 2016; **103**: 1105–1116

14 studies …….. 405 pts adjuvant (chemo)radiotherapy
7 studies ……. 130 pts completion TME

weighted average **local recurrence** rate for locally excised pT1/pT2, CHRT vs. TME
14% (95% c.i. 11 to 18) X **7%** (4 to 14)
weighted averages for **distance recurrence**
9 % (6 to 14) X **9%** (5 to 16)

LR for **pT1** were **10%** (4 to 21) and **6%** (3 to 15)
LR for **pT2** were **15%** (11 to 21) and **10%** (4 to 22)

Local excision - ypT0,1, 2

Surg Endosc. 2008 Feb;22(2):352-8

A prospective randomized study with a 5-year minimum follow-up evaluation of transanal endoscopic microsurgery versus laparoscopic total mesorectal excision after neoadjuvant therapy

G. Lezoche · M. Baldarelli · Mario · A. M. Paganini · A. De Sanctis · S. Bartolacci · E. Lezoche

	TEM ($n = 35$)	LR ($n = 35$)	Statistical test	p Value
Gender, male: n (%)	23 (66)	20 (57)	Chi-square test	0.461[a]
Age (years): median (25–75th %tile)	67 (61–70)	65 (60–69)	Wilcoxon test	0.360[b]
Follow-up (months): median (25–75th %tile)	84 (71–97)	84 (76–96)	Wilcoxon test	0.416[b]
Radiotherapy downstage: n (%)				
pT0	11 (32)	10 (29)	Chi-square test	0.939[a]
pT1	6 (17)	7 (20)		
pT2	18 (51)	18 (51)		

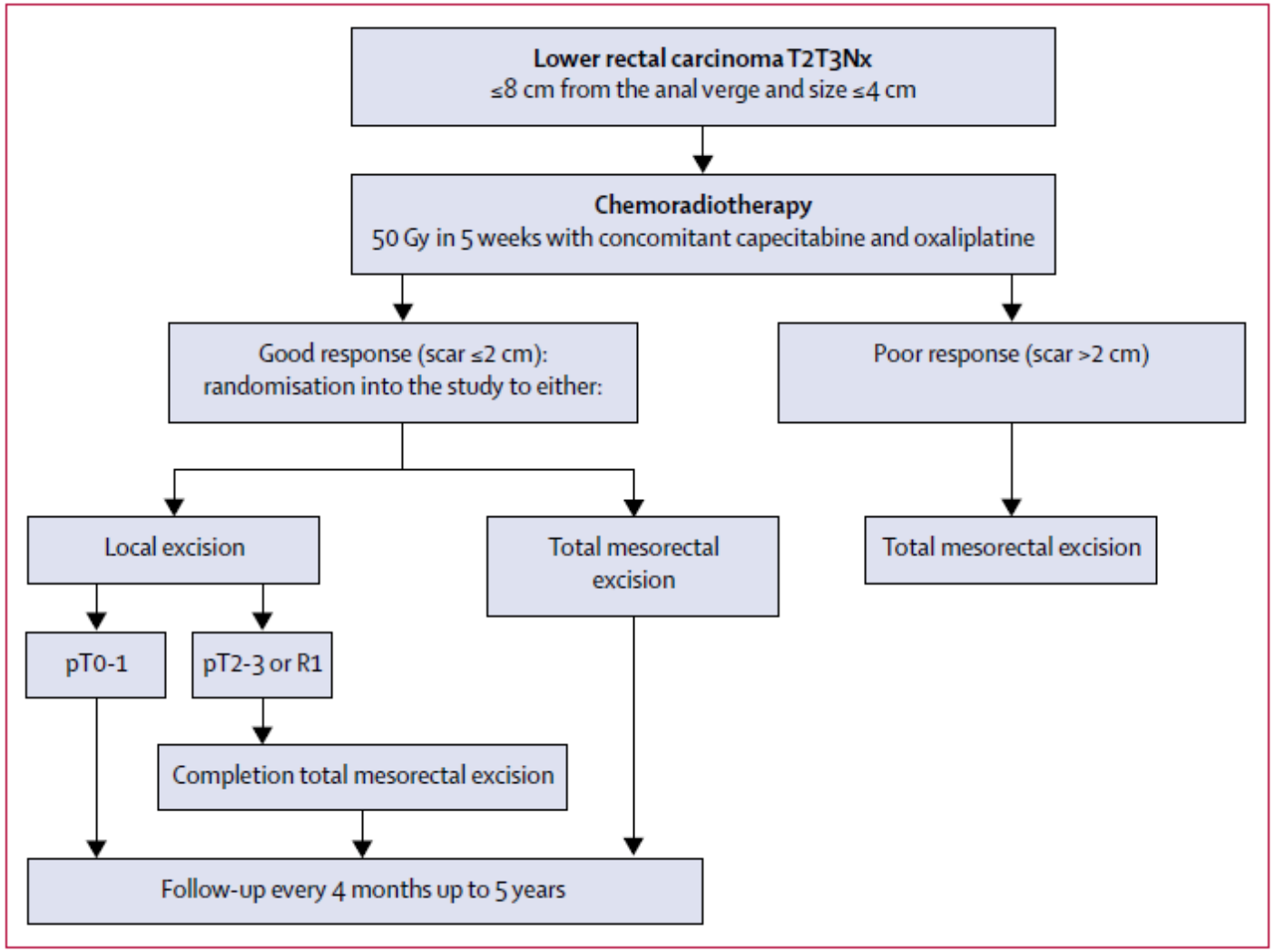
LR 6% (2) **LR 3% (1)**
DR 0 **DR 3% (1)**

Ongoing study: ACOSOG Z6041 (USA), GRECCAR 1, GRECCAR 2 (France), CONTEM (UK, France, Denmark , Sweden) , CARTS (Netherlans).

Organ preservation for rectal cancer (GRECCAR 2): a prospective, randomised, open-label, multicentre, phase 3 trial

Eric Rullier, Philippe Rouanet, Jean-Jacques Tuech, Alain Valverde, Bernard Lelong, Michel Rivoire, Jean-Luc Faucheron, Mehrdad Jafari, Guillaume Portier, Bernard Meunier, Igor Sileznieff, Michel Prudhomme, Frédéric Marchal, Marc Pocard, Denis Pezet, Anne Rullier, Véronique Vendrely, Quentin Denost, Julien Asselineau, Adélaïde Doussau

Lancet, Volume 390, ISSUE 10093, P469-479, July 29, 2017



The primary endpoint was a composite outcome of death, recurrence, morbidity, and side-effects at 2 years after surgery, to show superiority of local excision over total mesorectal excision in the modified intention-to-treat (ITT) population.

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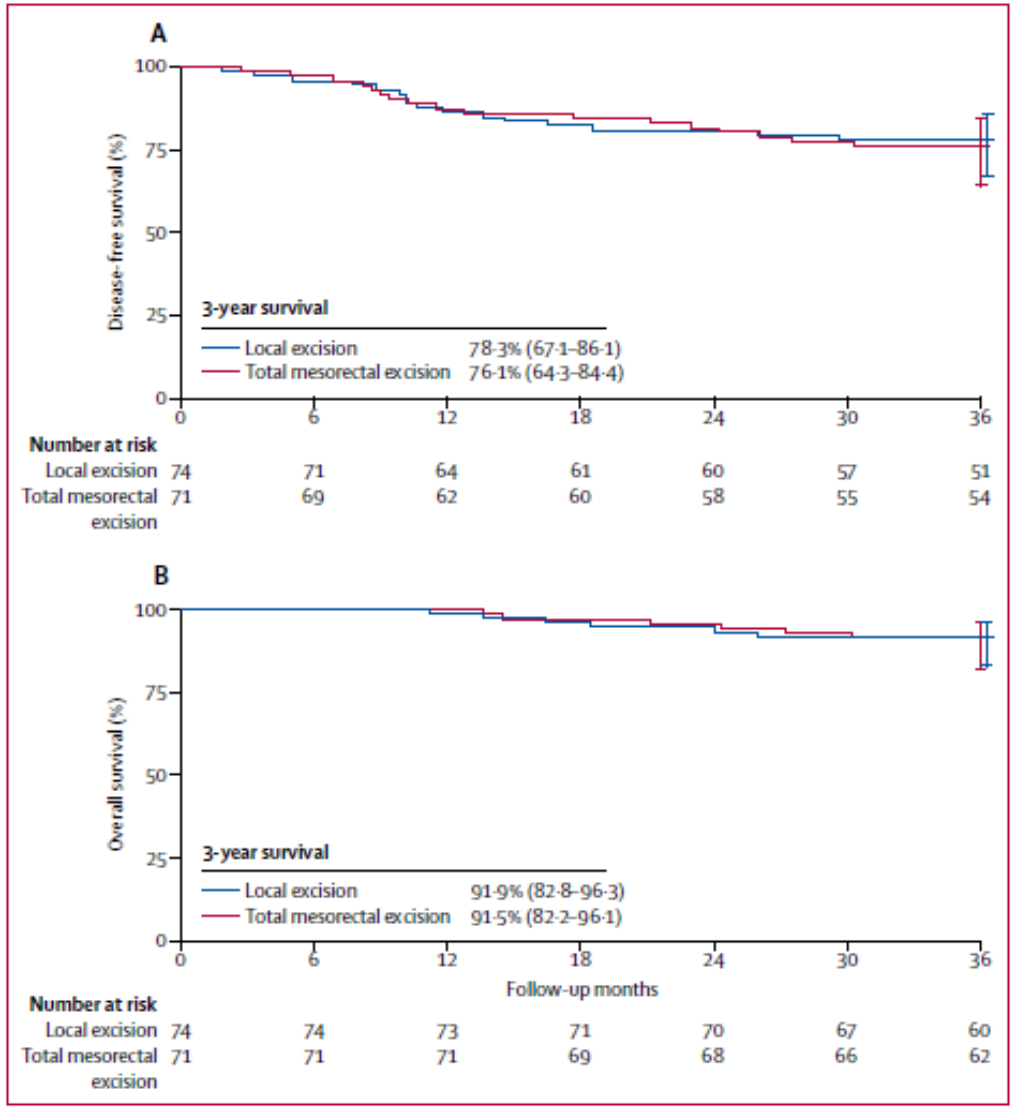

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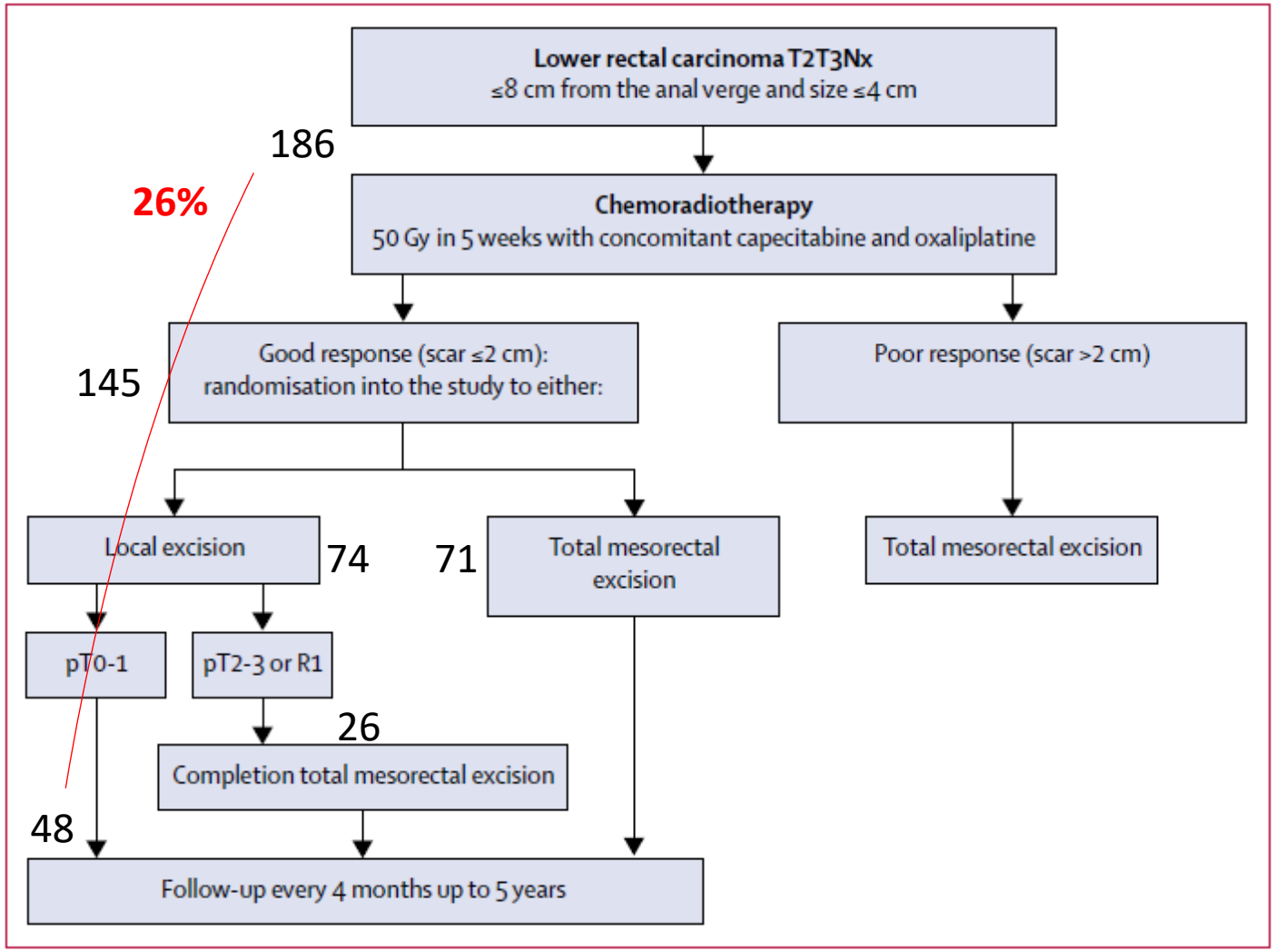
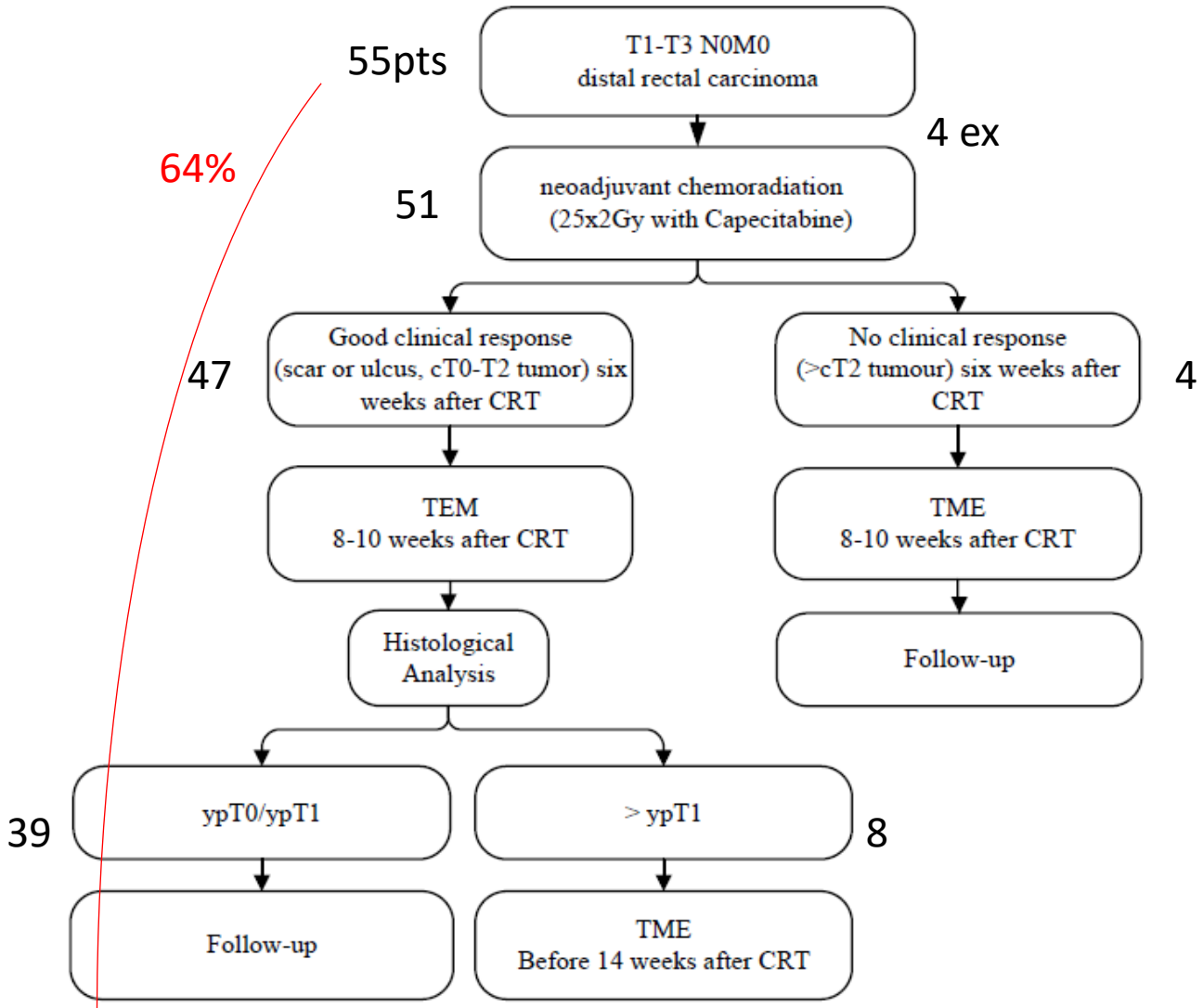


At 2 years in the modified ITT population, one or more events from the composite primary outcome occurred in 41 (56%) of 73 patients in the local excision group and 33 (48%) of 69 in the total mesorectal excision group (odds ratio 1·33, 95% CI 0·62–2·86; p=0·43).

Substantial proportion of patients analyzed in the local excision group eventually underwent a completion TME. Major morbidity or adverse effects were experienced in 78% of these patients compared with 29% of patients who underwent local excision alone and 38% of patients who underwent only TME surgery after CRT.

Long-term Oncological and Functional Outcomes of Chemoradiotherapy Followed by Organ-Sparing Transanal Endoscopic Microsurgery for Distal Rectal Cancer

The CARTS Study JAMA Surg. 2019 Jan; 154(1): 47–54.



35 OK + 4 LR (10%) ➡ TME

Characteristic	Patients (N = 55)
Age, median (interquartile range), y	64 (39-82)
Male, No. (%)	30 (55)
Tumor size, median (interquartile range), cm	3.4 (3.0-5.0)
Clinical tumor category, No. (%)	
cT1	10 (18)
cT2	29 (53)
cT3	16 (29)
Clinical node category, No. (%)	
cN0	50 (91)
cN1	5 (9)
Distance to anal verge, median (interquartile range), cm	3.5 (2.0-6.0)
Median follow-up	53 m

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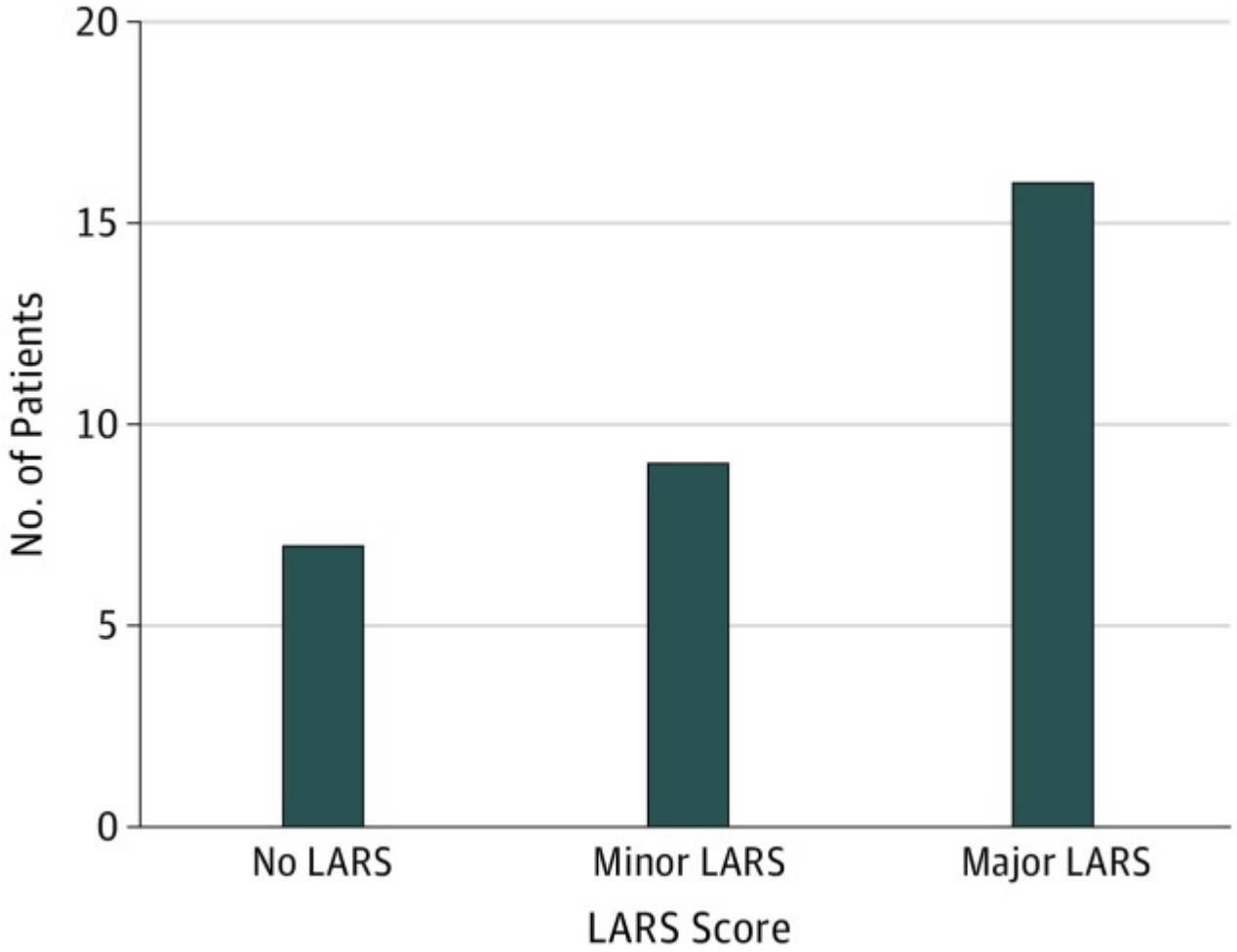

Low anterior resection syndrome scores were retrieved from 32 of 35 patients (91%) who underwent successful organ-preserving treatment

These scores were retrieved 48 to 68 months after surgical treatment.

Research Article

Digestive Surgery

Dig Surg 2020;37:39–46
DOI: 10.1159/000496434

Received: May 31, 2018
Accepted: December 19, 2018
Published online: June 11, 2019

Quality of Life and Bowel Dysfunction after Transanal Endoscopic Microsurgery for Rectal Cancer: One Third of Patients Experience Major Low Anterior Resection Syndrome

Maarten van Heinsbergen[a] Jeroen W. Leijtens[b] Gerrit D. Slooter[c]
Maryska L. Janssen-Heijnen[d, e] Joop L. Konsten[a]

Table 1. Patient characteristics and univariate analyses of associations between patient, tumour and treatment characteristics, on the one hand, and major LARS, on the other hand, in patients who underwent TEM

Associated factor	Patients, *n* (%)	Unadjusted OR (95% CI)	*p* value
Age at follow-up, years, median (range)	72 (49–86)	1.03 (0.96–1.10)	0.401
Gender, *n* (%)			
Male	35 (63.6)	Reference	
Female	20 (36.4)	4.00 (1.20–13.36)	0.024
Marital status			
Married	40 (72.7)	Reference	
Single/widowed	15 (27.3)	1.76 (0.51–6.10)	0.374
TNM stage			
T0N0	7 (12.7)	1.67 (0.23–12.22)	0.615
T1N0	39 (70.9)	0.38 (0.83–1.70)	0.203
T2N0	9 (16.4)	Reference	
Tumour height (distance from anal verge)			
High rectum (10–14.9 cm)	15 (27.3)	Reference	
Mid rectum (5–9.9 cm)	21 (38.2)	1.10 (0.25–4.86)	0.900
Low rectum (<5 cm)	19 (34.5)	1.60 (0.37–7.02)	0.530
Tumour location			
Anterior	17 (23.0)	2.67 (0.36–19.71)	0.337
Left Lateral	15 (20.3)	2.00 (0.28–14.20)	0.488
Posterior	19 (25.7)	2.00 (0.30–13.17)	0.471
Right Lateral	10 (13.5)	Reference	
Specimen size (cm^2), median (range)	8.60 (1.70–38.50)	1.01 (0.95–1.07)	0.815
Specimen thickness, mm, median (range)	8 (2–30)	1.10 (1.01–1.20)	0.023
Interval since treatment, years, median (range)	4.3 (2.5–8.0)	1.01 (0.97–1.04)	0.912
Neo-adjuvant therapy			
No neo-adjuvant therapy	38 (69.1)	Reference	0.037
(Chemo) radiotherapy	17 (30.9)	3.63 (1.08–12.17)	
ASA grade			
Grade I–II	45 (81.8)	Reference	
Grade III–VI	10 (18.2)	0.95 (0.21–4.22)	0.945
Complication (Clavien-Dindo)			
Grade 0 (no complication)	47 (85.5)	Reference	
Grade I–II	4 (7.3)	0.79 (0.08–8.22)	0.840
Grade III–IV	4 (7.3)	2.36 (0.30–18.44)	0.414

LARS, low anterior resection syndrome; TEM, transanal endoscopic microsurgery.

Received: May 31, 2018
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Major

Research Article

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55 respondents (75.3%) could be included for the analyses
The median interval since treatment was 4.3 years

“Major LARS” was observed in 29%
“minor LARS” in 26%
Female gender (OR 4.00; 95% CI 1.20–13.36)
neo-adjuvant chemoradiotherapy (OR 3.63; 95% CI 1.08–12.17) (major LARS: 50% CRT+TEM vs. 22% TEM)
specimen thickness in millimetres (OR 1.10 for each mm increase in thickness; 95% CI 1.01–1.20)

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Bowel Function 14 Years After Preoperative Short-Course Radiotherapy and Total Mesorectal Excision for Rectal Cancer: Report of a Multicenter Randomized Trial

Tina Yen-Ting Chen,[1] Lisette M. Wiltink,[2] Remi A. Nout,[2]
Elma Meershoek-Klein Kranenbarg,[3] Søren Laurberg,[1] Corrie A.M. Marijnen,[2]
Cornelis J.H. van de Velde[4]

Major LARS was reported by 46% of all patients
56% PRT plus TME vs. 35% TME

Clin Colorectal Cancer. 2015 Jun;14(2):106-14

Research Article

Digestive Surgery

Dig Surg 2020;37:39–46
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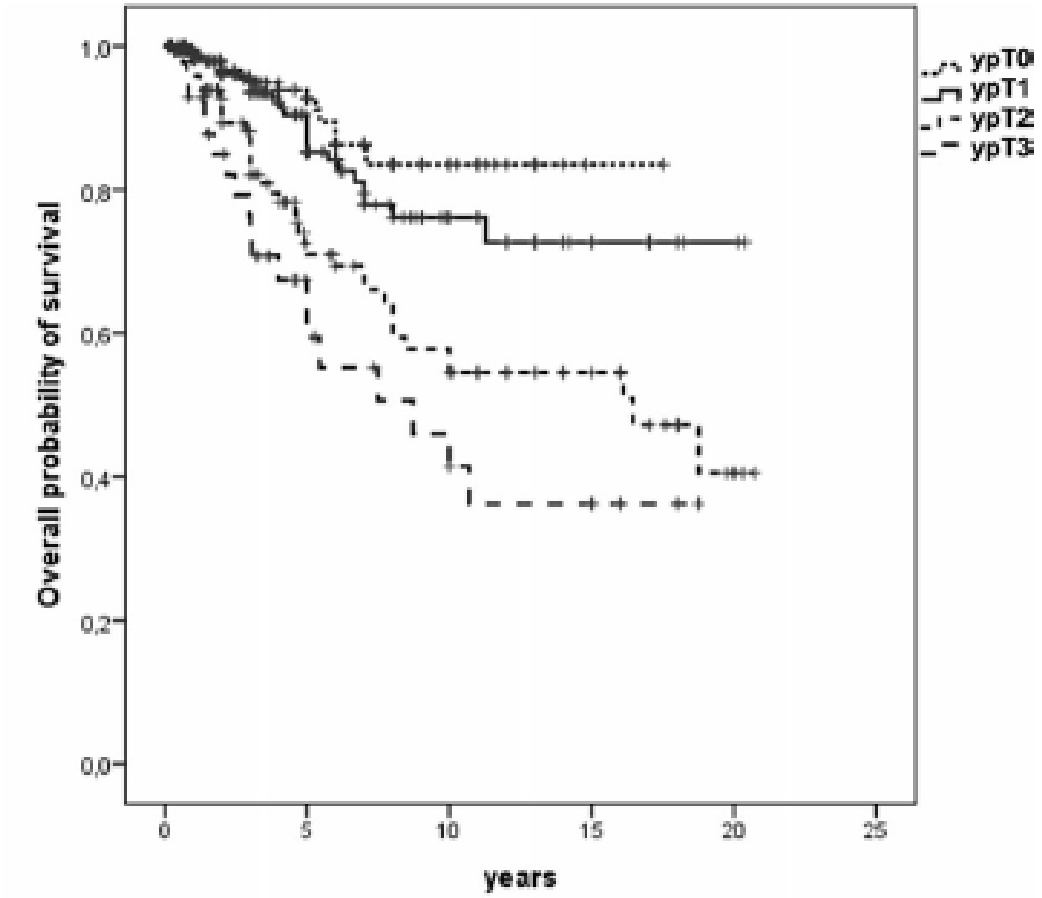
Quality of Life in Rectal Cancer Patients After Chemoradiation: Watch-and-Wait Policy Versus Standard Resection – A Matched-Controlled Study

Diseases of the Colon & Rectum: October 2017 - Volume 60 - Issue 10 - p 1032-1040

Major LARS - 1/3 pts after nCRT + watch and wait

Author	*n*	Local recurrence (%)	Systemic recurrence (%)	Overall survival (%)	Median follow-up (months) (range)
Coco 2013 [9]	22	1 (4.5)	2 (9)	19 (86.4)	99 (32–173)
Bujko 2013 [12]	89	13 (16.0)[a]	8 (9)	77 (86.5)	26.1 (2.4–85)
Guerrieri 2014 [7]	297	7 (2.4)	13 (4.4)	297 (100)	60.8 (12–243)
Stipa 2014 [8]	43	15 (34.9)	9 (20.9)	16 (37.2)	48 (3.7–252)
Perez 2014 [13]	23	3 (13)	6 (26.1)	20 (86.9)	44 (3–89)
Arezzo 2014 [10]	14	2 (14.2)	0	14 (100)	17.6 (1.6–55.5)
Restivo 2015 [11]	29	4 (13.8)	3 (10.3)	20 (69)	19.7 (3–214)
Total	517	45 (8.7)	41 (7.9)	463 (89.5)	38,8 (1.6–252)



Individual participant data pooled-analysis of risk factors for recurrence after neoadjuvant radiotherapy and transanal local excision of rectal cancer: the PARTTLE study

A. Arezzo[1] · G. Lo Secco[1] · R. Passera[2] · L. Esposito[1] · M. Guerrieri[3] · M. Ortenzi[3] · K. Bujko[4] · R. O. Perez[5] · A. Habr-Gama[5] · F. Stipa[6] · M. Picchio[6] · A. Restivo[7] · L. Zorcolo[7] · C. Coco[8] · G. Rizzo[8] · M. Mistrangelo[1] · M. Morino[1]

Techniques in Coloproctology (2019) 23:831–842

		Univariate		Multivariate	
		OR (95% CI)	p	OR (95% CI)	p
Age	>70 vs ≤70 years	1.20 (0.65-2.22)	0.553		
Gender	M vs F	0.58 (0.32-1.08)	0.086	0.66 (0.32-1.36)	0.259
cT	3-4 vs 1-2	1.13 (0.61-2.11)	0.699		
ypT	*3 vs 1-2*	*9.20 (4.72-17.93)*	*<0.001*	*4.79 (2.25-10.16)*	*<0.001*
ypT			<0.001		
	2 vs 0-1	4.91 (2.28-10.58)	<0.001		
	3 vs 0-1	15.60 (6.83-35.67)	<0.001		
Tumor grade	high vs low	0.88 (0.33-2.38)	0.801		
Tumor size	>40 vs ≤40 mm	0.71 (0.34-1.48)	0.365		
Distance from anorectal junction	>60 vs ≤60 mm	0.86 (0.46-1.61)	0.638		
Preoperative CRT	*no vs yes*	*5.69 (3.02-10.71)*	*<0.001*	*3.68 (1.78-7.62)*	*<0.001*
Tumor size post RT	*>10 vs ≤10 mm*	*9.52 (3.93-23.08)*	*<0.001*	*5.86 (2.33-14.74)*	*<0.001*
Dehiscence	yes vs no	1.06 (0.43-2.60)	0.905		
RT dose	LC vs SC	0.39 (0.20-0.76)	0.006		
Time between CRT and surgery	>8 vs ≤8 weeks	1.44 (0.68-3.03)	0.337		

CRT: chemo-radio therapy, RT: radiotherapy, LC: long course radiotherapy, SC: short course radiotherapy

Univariate and multivariate logistic regression for local recurrence

(NCT02945566; NCT02514278; NCT02505750; NCT01060007; NCT02860234).

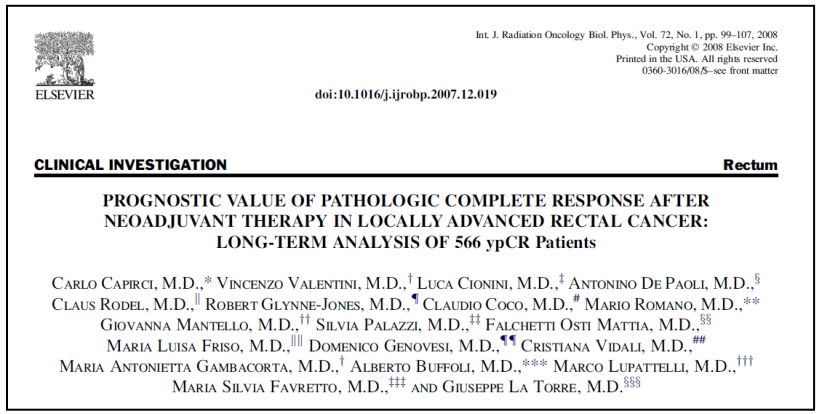
Local excision – the only therapy of pCR - results.

Author	Year	Number of ypT0 pts	Follow-up (months)	No. of Local Recurrencies	No. of Distant Recurrencies
Kim	2001	17	24	0	0
Schell	2002	8	48	0	1 (12%)
Ruo	2002	3	29	0	0
Hershmann	2003	7	33	0	0
Bonnen	2004	14	42	0	1(7%)
Stipa	2004	7	37	0	NR
Caricato	2006	3	NR	0	0
Borschitz	2007	7	24	0	0
Lezoche	2008	11	84	0	0
Nair	2008	19	64	1 (5%)	1(5%)
Huh	2008	4	91	0	1 (25%)
Kundel	2010	14	48	0	0
Callender	2010	23	63	0	1
Issa	2012	23	87	0	0
Noh	2014	10	75	1	0
Total		**170**	**24-91 (avrg. 58)**	**2 (1,2%)**	**5 (2,9%)**

pCR - Outcomes of different therapeutical approaches.

watch and wait (ycCR)	LR 4-6%	DR 0-8,1%
Local excision (ypT0)	LR 1,2%	DR 2,9%
LAR/APR+ TME (ypCR)	LR 0,5-3,3%	DR 8,9-11%
Local excision of T1 low risk	LR 0-7% (11-18%)	

527 pts s pCR …….. N+ v 6,6%



Int. J. Radiation Oncology Biol. Phys., Vol. 72, No. 1, pp. 99–107, 2008
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0360-3016/08/$–see front matter

ELSEVIER

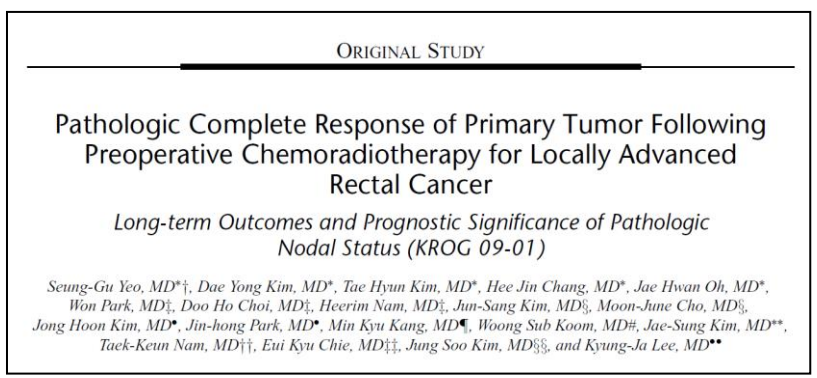
doi:10.1016/j.ijrobp.2007.12.019

CLINICAL INVESTIGATION **Rectum**

PROGNOSTIC VALUE OF PATHOLOGIC COMPLETE RESPONSE AFTER NEOADJUVANT THERAPY IN LOCALLY ADVANCED RECTAL CANCER: LONG-TERM ANALYSIS OF 566 ypCR Patients

Carlo Capirci, M.D.,[*] Vincenzo Valentini, M.D.,[†] Luca Cionini, M.D.,[‡] Antonino De Paoli, M.D.,[§] Claus Rodel, M.D.,[‖] Robert Glynne-Jones, M.D.,[¶] Claudio Coco, M.D.,[#] Mario Romano, M.D.,[**] Giovanna Mantello, M.D.,[††] Silvia Palazzi, M.D.,[‡‡] Falchetti Osti Mattia, M.D.,[§§] Maria Luisa Friso, M.D.,[‖‖] Domenico Genovesi, M.D.,[¶¶] Cristiana Vidali, M.D.,[##] Maria Antonietta Gambacorta, M.D.,[†] Alberto Buffoli, M.D.,[***] Marco Lupattelli, M.D.,[†††] Maria Silvia Favretto, M.D.,[‡‡‡] and Giuseppe La Torre, M.D.[§§§]

333 pts s pCR …….. N+ v 8,7%



ORIGINAL STUDY

Pathologic Complete Response of Primary Tumor Following Preoperative Chemoradiotherapy for Locally Advanced Rectal Cancer

Long-term Outcomes and Prognostic Significance of Pathologic Nodal Status (KROG 09-01)

Seung-Gu Yeo, MD†, Dae Yong Kim, MD*, Tae Hyun Kim, MD*, Hee Jin Chang, MD*, Jae Hwan Oh, MD*, Won Park, MD‡, Doo Ho Choi, MD‡, Heerim Nam, MD‡, Jun-Sang Kim, MD§, Moon-June Cho, MD§, Jong Hoon Kim, MD•, Jin-hong Park, MD•, Min Kyu Kang, MD¶, Woong Sub Koom, MD#, Jae-Sung Kim, MD**, Taek-Keun Nam, MD††, Eui Kyu Chie, MD‡‡, Jung Soo Kim, MD§§, and Kyung-Ja Lee, MD••*

Table 1 Summary of patient demographics comparing surgical resection with watch and wait in rectal cancer.

Study	Design	Mean time (weeks)[a]	Patients		Age (years)		Male : Female		Mean follow-up (months)	
			W&W (*n*)	Control (*n*)	W&W (*n*)	Control (*n*)	W&W	Control	W&W (*n*)	Control (*n*)
Maas *et al*, 2011[8]	Prospective	6.5	21	20	65	64	14 : 7	16 : 4	25	35
Dalton *et al*, 2012[15]	Retrospective	6								
Smith *et al*, 2015[14]	Retrospective	12	18	30	62.3	60.4	15 : 3	20 : 10	68.4	46.3
Habr Gama *et al*, 2004[7]	Prospective	8	71	22	58.1	53.6	12 : 10	18 : 14	48	28
Smith *et al*, 2012[13]	Retrospective	4–10	32	57	70	60	18 : 14	27 : 30	42	47.7
Araujo *et al*, 2015[24]	Retrospective	12	42	69	63.6	60.1	17 : 25	34 : 35	46.7	49.9
Lai *et al*, 2015[12]	Retrospective	n/a	18	26	67.6	63.8	15 : 3	12 : 14	49.4	42.3
Li *et al*, 2015[16]	Retrospective	n/a	30	92	62	56	18 : 12	60 : 32	58	58
Nahas *et al*, 2016[23]	RCT	8.7	4	2	n/a	n/a	n/a	n/a	33.2	28.2

[a] Mean time to response evaluation.
W&W, watch and wait.

Royal College of Surgeons
ADVANCING SURGICAL CARE

REVIEW ARTICLE

Ann R Coll Surg Engl 2019; **101:** 441–452
doi 10.1308/rcsann.2019.0018

Systematic review and meta-analysis on outcomes of salvage therapy in patients with tumour recurrence during 'watch and wait' in rectal cancer

J On[1], J Shim[2], EH Aly[1]

LR 30/248 – 12%
DR 12/248 - 6%

Of 248 patients who followed the watch and wait strategy, 10.5% had salvage therapy for recurrent disease. No statistical heterogeneity was found in the results. The relative risk of overall mortality in the salvage therapy group was 2.42 (95% confidence interval 0.96–6.13) compared with the group who had conventional surgery, but this was not statistically significant (P > 0.05).

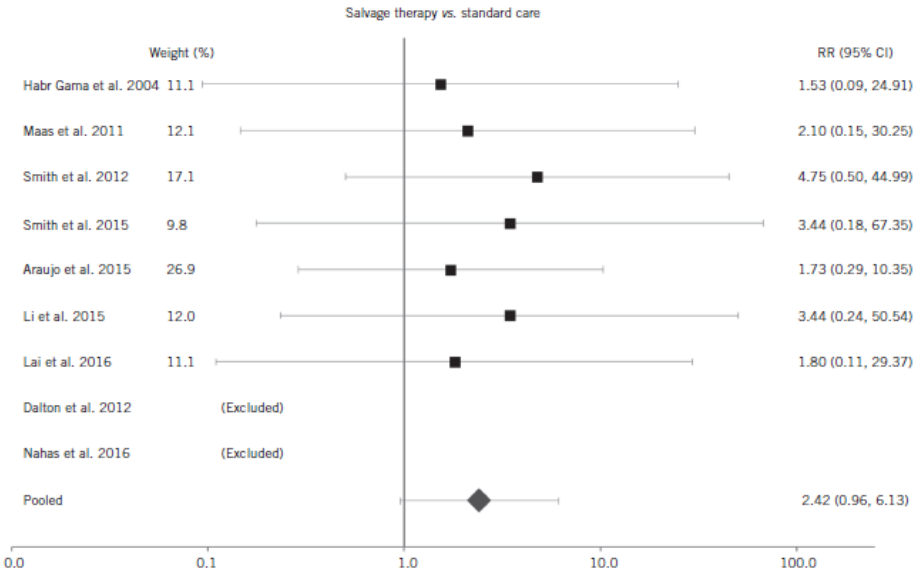


Figure 3 Forest plot of random effects meta-analysis demonstrating the overall risk of mortality in patients who had salvage therapy versus patients who had standard treatment. Overall effect size is not statistically significant ($P = 0.06$).

Část 2.

Jak ušetřit rektum od radioterapie?

CRM, LN

MRC CR07 and NCIC-CTG C016 studie

- 1350 pts, Stádium I–III
- randomizace k nRCT či primární chirurgii
- selektivně pooperační RCT u posit . CRM (<1 mm)

3-y DSF 77.5% vs. 71.5%, p=0.013)

LR 4.4% vs. 10.6%, p<0.0001

2009, Lancet 373:811–820

Dutch TME trial, 12-year follow-up

81% pacientů s patologicky *negativním CRM profitovalo z nRCT*:

LR 5% vs. 11%

10-yr LR:
stage cI: 1% vs. 3% stage cII: 4% vs.7%
stage cIII: 5 vs.17%.
(p<0.0001):

2011, Lancet Oncol 12:575–582

Pooled analysis of 5 European randomized clinical trials

N status - signifikantní prediktivní faktor nejen pro DR a OS ale i pro LR

5y LR - 12,9%
5y DR - 30.8%
5y OS - 30,4%

2011, J Clin Oncol 29:3163–3172

European Journal of Surgical Oncology 44 (2018) 1241–1246

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Clinical lymph node staging in colorectal cancer; a flip of the coin?

Nelleke P.M. Brouwer [a, *], Rutger C.H. Stijns [b], Valery E.P.P. Lemmens [c, d], Iris D. Nagtegaal [e], Regina G.H. Beets-Tan [f, g], Jurgen J. Fütterer [b], Pieter J. Tanis [h], Rob H.A. Verhoeven [d], Johannes H.W. de Wilt [a]

Clinical lymph node diagnosis (cN) compared to pathological lymph node diagnosis (pN) for patients diagnosed with colon cancer or rectal cancer between 2011 and 2014, who received no preoperative treatment.

		Pathological lymph node diagnosis	
		pN+	pN-
Colon			
	cN+	3058[a] (59)	2108[c] (41)
	cN-	4456[b] (29)	11105[d] (71)
Rectum			
	cN+	248[A] (56)	192[C] (44)
	cN-	402[B] (24)	1257[D] (76)

Note. Data are absolute numbers with percentages between parentheses.

Parameters of clinical lymph node staging in patients without neoadjuvant treatment.

Colon cancer	Rectal cancer
Sensitivity = a/(a+b)*100% = 41%	Sensitivity = A/(A+B)*100% = 38%
Specificity = d/(c+d)*100% = 84%	Specificity = D/(C+D)*100% = 87%
PPV = a/(a+c)*100% = 59%	PPV = A/(A+C)*100% = 56%
NPV = d/(b+d)*100% = 71%	NPV = D/(B+D)*100% = 76%

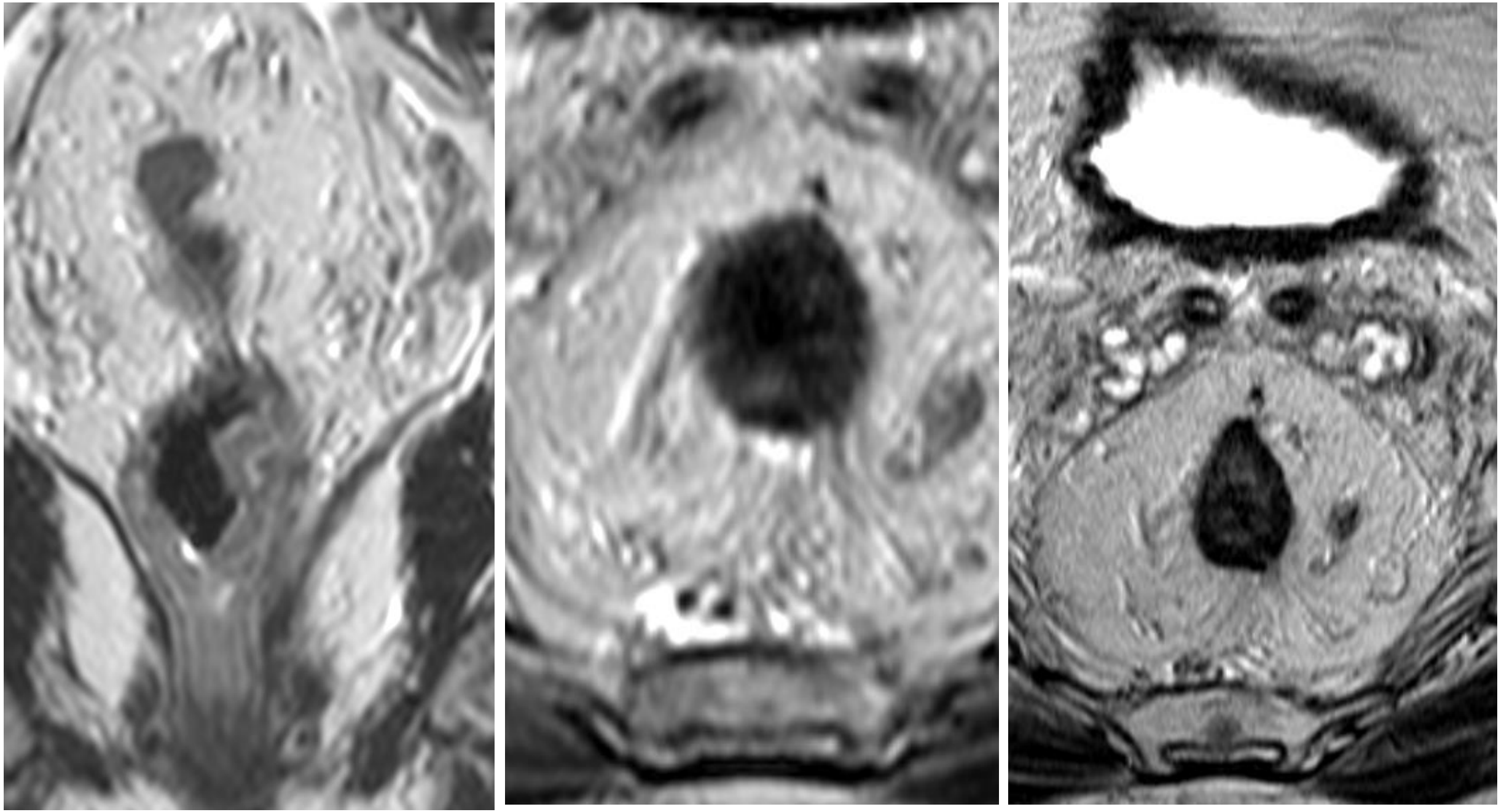
Clinical lymph node staging (cN) compared to pathological lymph node staging (pN) for patients diagnosed with rectal cancer between 2011 and 2014, who received short neoadjuvant radiotherapy scheme (5 × 5 Gy) and 0–10 days from the start of radiotherapy until resection.

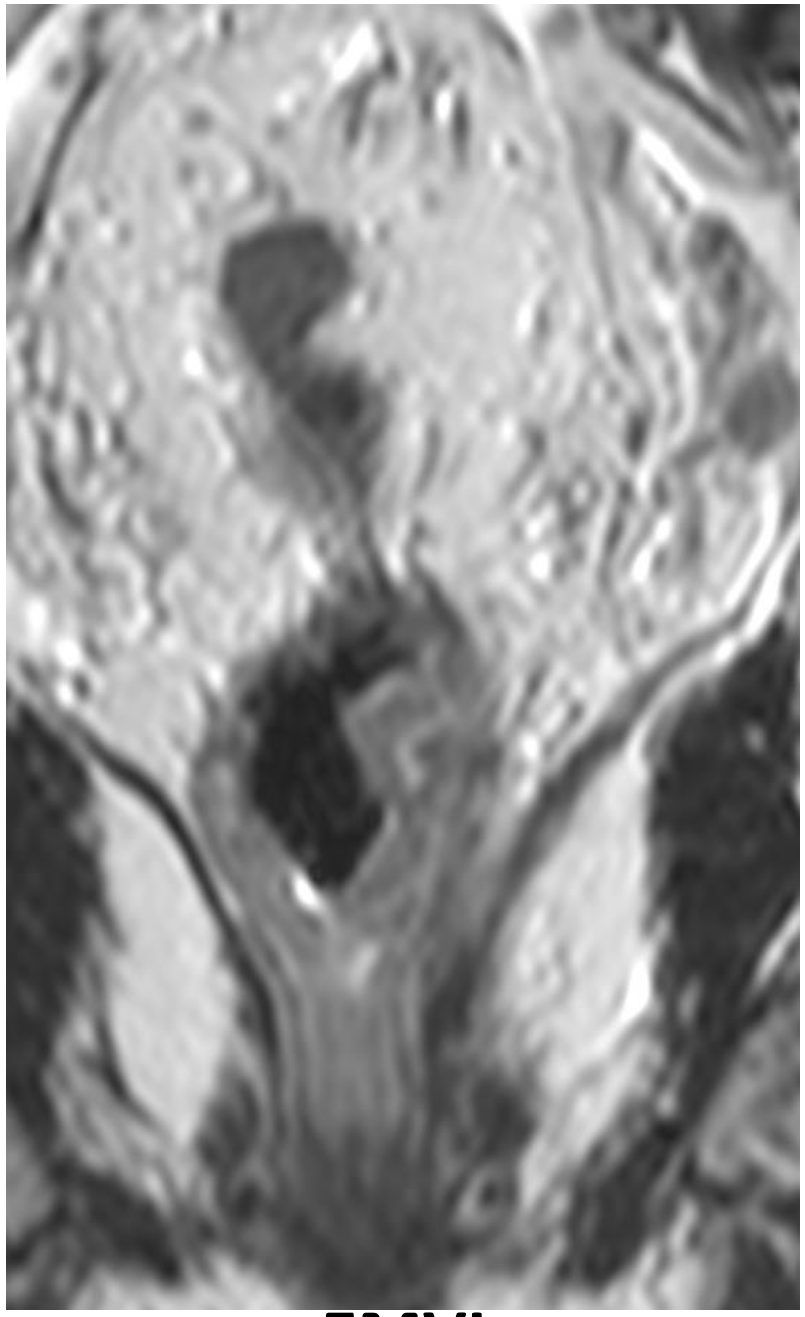
	Pathological lymph node diagnosis	
	pN+	pN-
cN+	460[a] (47)	525[b] (53)
cN-	360[c] (25)	1060[d] (75)

Note. Data are absolute numbers with percentages between parentheses.

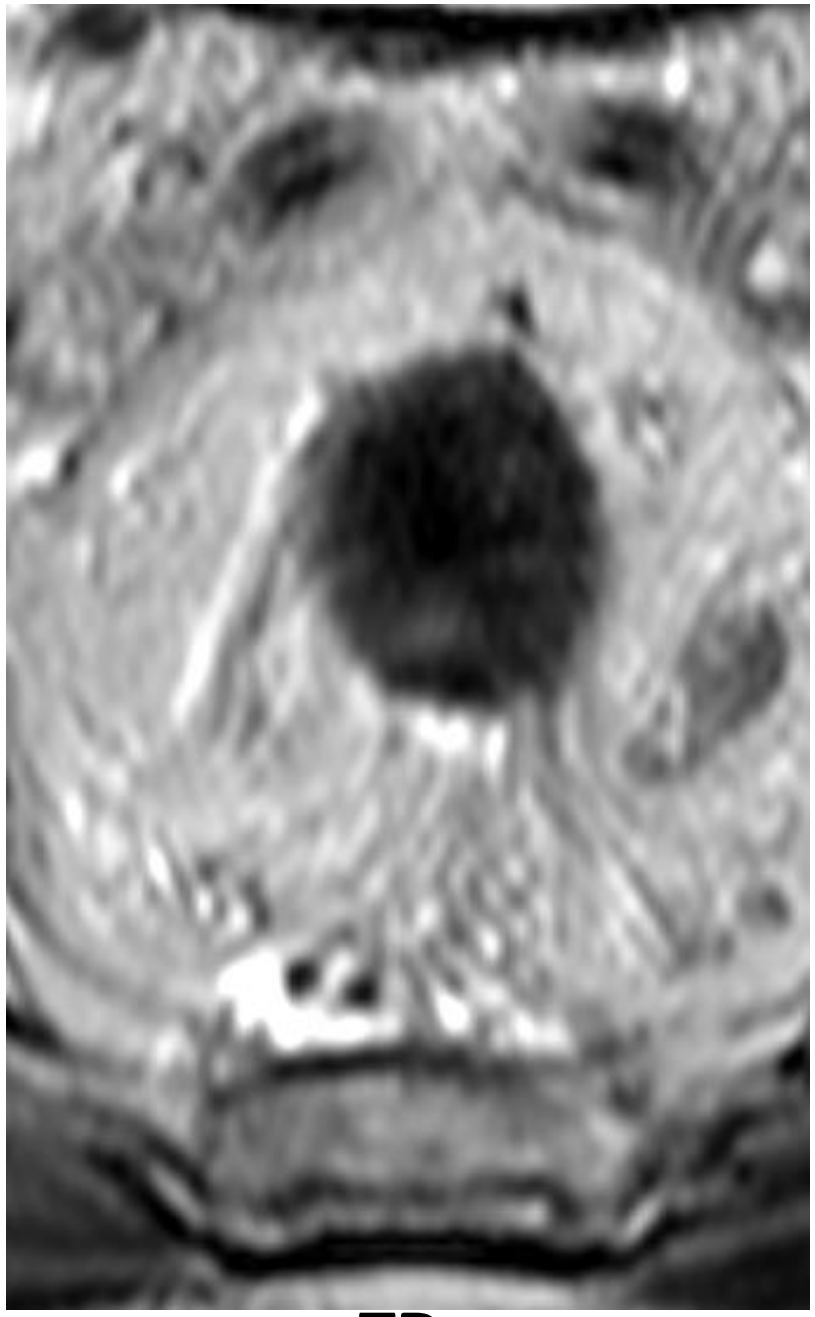
Parameters of clinical lymph node staging in rectal cancer patients treated with short neoadjuvant radiotherapy.

Sensitivity = a/(a+b)*100% = 56%, Specificity = d/(c + d)*100% = 67%, PPV = a/(a+c)*100% = 47%, NPV = d/(b + d)*100% = 75%.

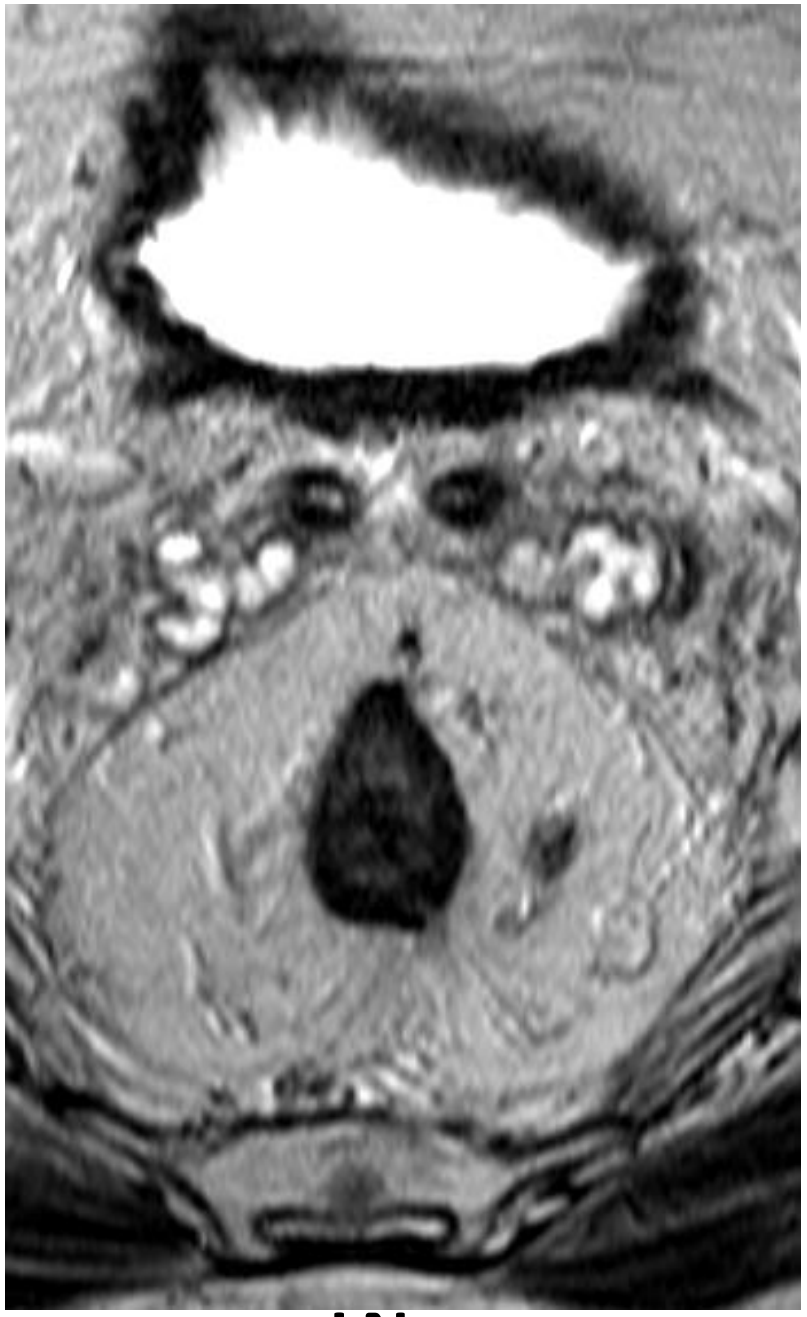




EMVI



TD



LN

IVYSPRING INTERNATIONAL PUBLISHER

Journal of Cancer

2018; 9(8): 1466-1475. doi: 10.7150/jca.23311

Research Paper

Survival Contradiction Between Stage IIA and Stage IIIA Rectal Cancer: A Retrospective Study

Shaobo Mo[1,2*], Weixing Dai[1,2*], Wenqiang Xiang[1,2*], Ben Huang[1,2], Yaqi Li[1,2], Yang Feng[1,2], Qingguo Li[1,2✉], Guoxiang Cai[1,2✉]

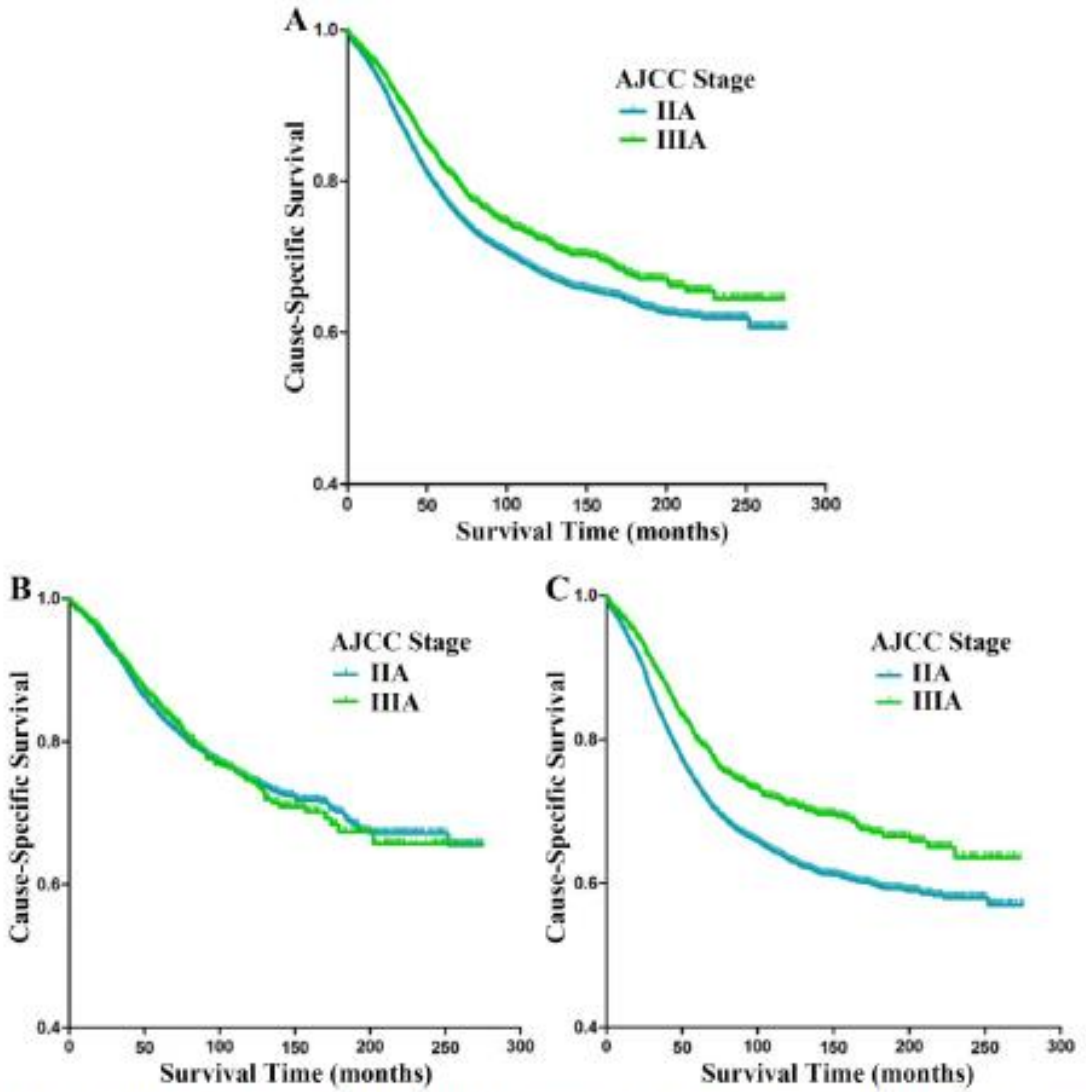


Fig. 1. Cause-specific survival (CSS) stratified by stage IIA and IIIA rectal cancer (A-C) in SEER database. (A) Kaplan-Meier curves for stage IIA and stage IIIA rectal cancer patients. (B) Kaplan-Meier curves for stage IIA and stage IIIA rectal cancer patients with at least 12 lymph nodes harvested. (C) Kaplan-Meier curves for stage IIA and stage IIIA rectal cancer patients with fewer than 12 lymph nodes harvested.

SEER database

IIa – 13551 pts
IIIa – 3237 pts

IIa (T3N0M0)
IIIa (T1-2, N1-2a, M0)

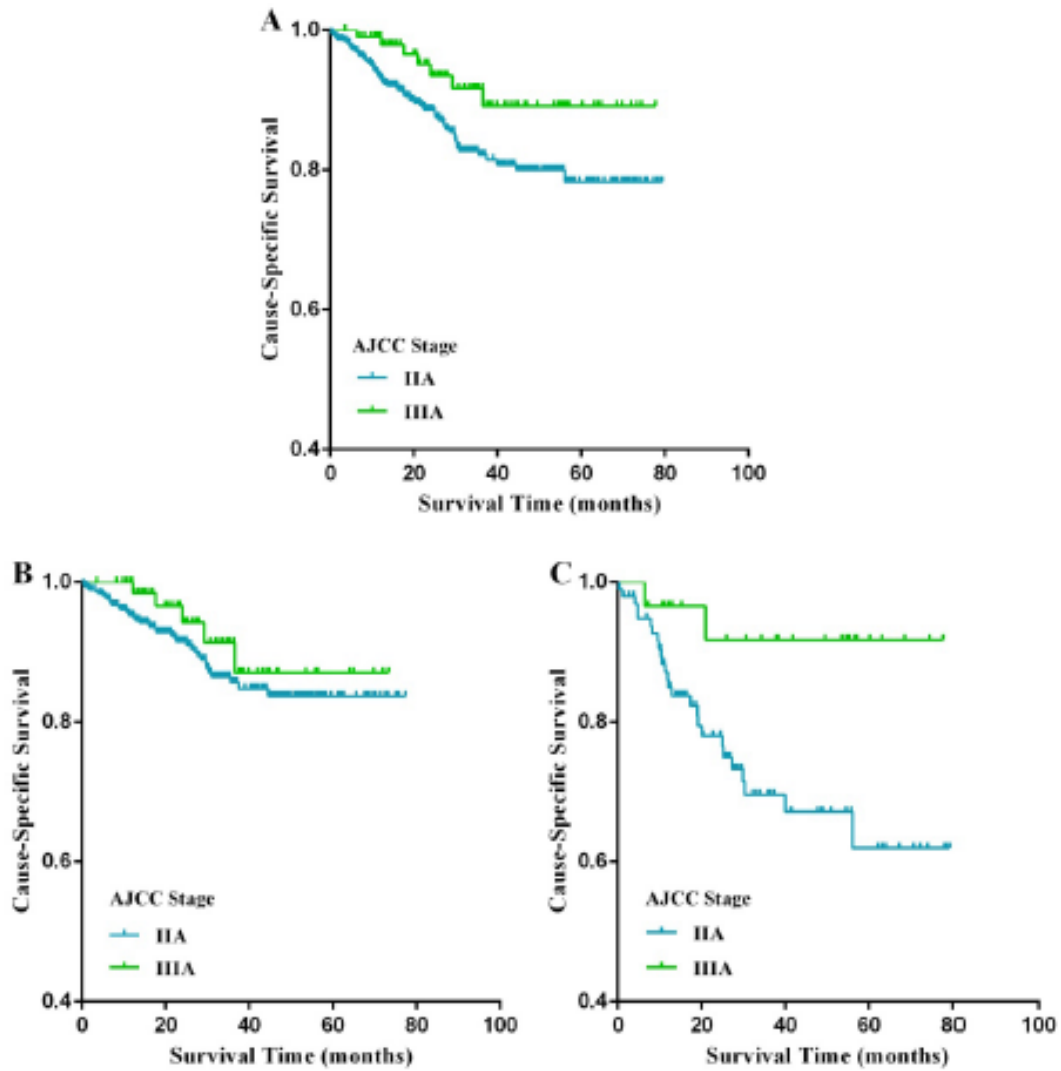


Fig. 3. Cause-specific survival (CSS) stratified by stage IIA and IIIA rectal cancer (A-C) in the FUSCC cohort. (A) Kaplan-Meier curves for stage IIA and stage IIIA rectal cancer patients. (B) Kaplan-Meier curves for stage IIA and stage IIIA rectal cancer patients with at least 12 lymph nodes harvested. (C) Kaplan-Meier curves for stage IIA and stage IIIA rectal cancer patients with fewer than 12 lymph nodes harvested.

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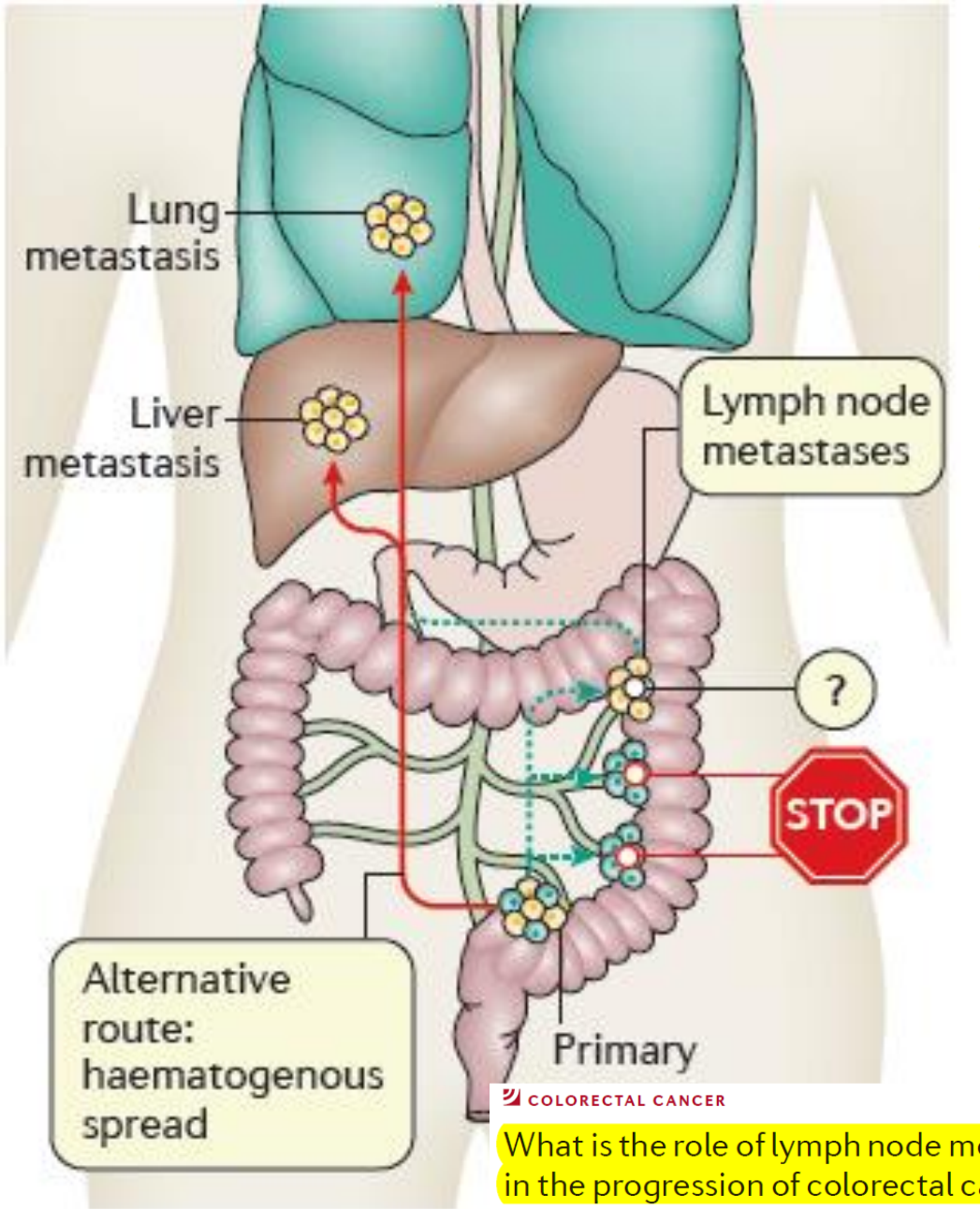
FUSCC database

IIa – 482 pts
IIIa – 103 pts

IIa (T3N0M0)
IIIa (T1-2, N1-2a, M0)



COLORECTAL CANCER

What is the role of lymph node metastases in the progression of colorectal cancer?

Iris D. Nagtegaal and Hans-Joachim Schmoll

Origins of lymphatic and distant metastases in human colorectal cancer

Kamila Naxerova,[1,2*] Johannes G. Reiter,[3] Elena Brachtel,[4] Jochen K. Lennerz,[4] Marc van de Wetering,[5,6] Andrew Rowan,[7] Tianxi Cai,[8] Hans Clevers,[5,6] Charles Swanton,[7,9] Martin A. Nowak,[3,10] Stephen J. Elledge,[2,11] Rakesh K. Jain[1]

Science 357, 55–60 (2017)

In 65% of cases, lymphatic and distant metastases arose from independent subclones in the primary tumor, whereas in 35% of cases they shared common subclonal origin.

If the numbers are extrapolated, these findings indicate that LNM might be directly involved in disease progression in only 13–20% of metastatic CRC cases.

Preoperative High-resolution Magnetic Resonance Imaging Can Identify Good Prognosis Stage I, II, and III Rectal Cancer Best Managed by Surgery Alone

A Prospective, Multicenter, European Study

Annals of Surgery. 253(4):711–719, APRIL 2011

Patients and Methods:

"Good" prognosis included MRI-predicted safe circumferential resection margins, with MRI-predicted **T2/T3a/T3b** (less than 5 mm spread from muscularis propria), **regardless of MRI N stage.**

MRI feature	*Good prognosis*	*Poor prognosis*
CRM	>1mm clear	<1mm involved
Low rectal <5cm	intersphincteric plane clear of tumor	intersphincteric plane involved by tumor
T stage	T1/T2, T3a<1mm, T3b, 1-5mm extramural spread	T3c>5mm extramural spread, T4
EMVI	negative	positive
N stage	any	any

Results: Of 374 patients followed up in the MERCURY study**, 122 (33%)** were defined as "good prognosis" stage III or less on MRI.

Overall and disease-free survival for all patients with MRI "good prognosis" stage I, II and III disease at 5 years was 68% and 85%, respectively.

The **local recurrence** rate for this series of patients predicted to have a good prognosis tumor on **MR was 3%.**

Preoperative High-resolution Magnetic Resonance Imaging Can Identify Good Prognosis Stage I, II, and III Rectal Cancer Best Managed by Surgery Alone

A Prospective, Multicenter, European Study

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TABLE 2. Final Pathology for the Study Patients (n = 122)

	Path TN Stage		
	Frequency (%)	Total	
Variable			
Path CRM	Clear	118 (96.7)	
	Involved	4 (3.3)	
Stage I or less			Actual no. of local recurrence
pT0N0	7 (5.7)		0
pT1N0	8 (6.6)		0
pT2N0	34 (27.9)	49	1
Stage II			
pT3aN0	20 (16.4)		0
pT3bN0	7 (5.7)		0
pT4N0	2 (1.6)	29	1
Stage III			
pT1N1	1 (0.8)		0
pT2N1	9 (7.4)		0
pT2N2	1 (0.8)		0
pT3aN1	8 (6.6)		1
pT3bN1	9 (7.4)		0 (2 = CRM_{+ve})
pT3bN2	7 (5.7)		1 (1 = CRM_{+ve})
pT3cN0	3 (2.5)		0
pT3cN1	4 (3.3)		0 (1 = CRM_{+ve})
pT4N1	2 (1.6)	44	0
	Total	122	

CRM indicates cross-reactive material.

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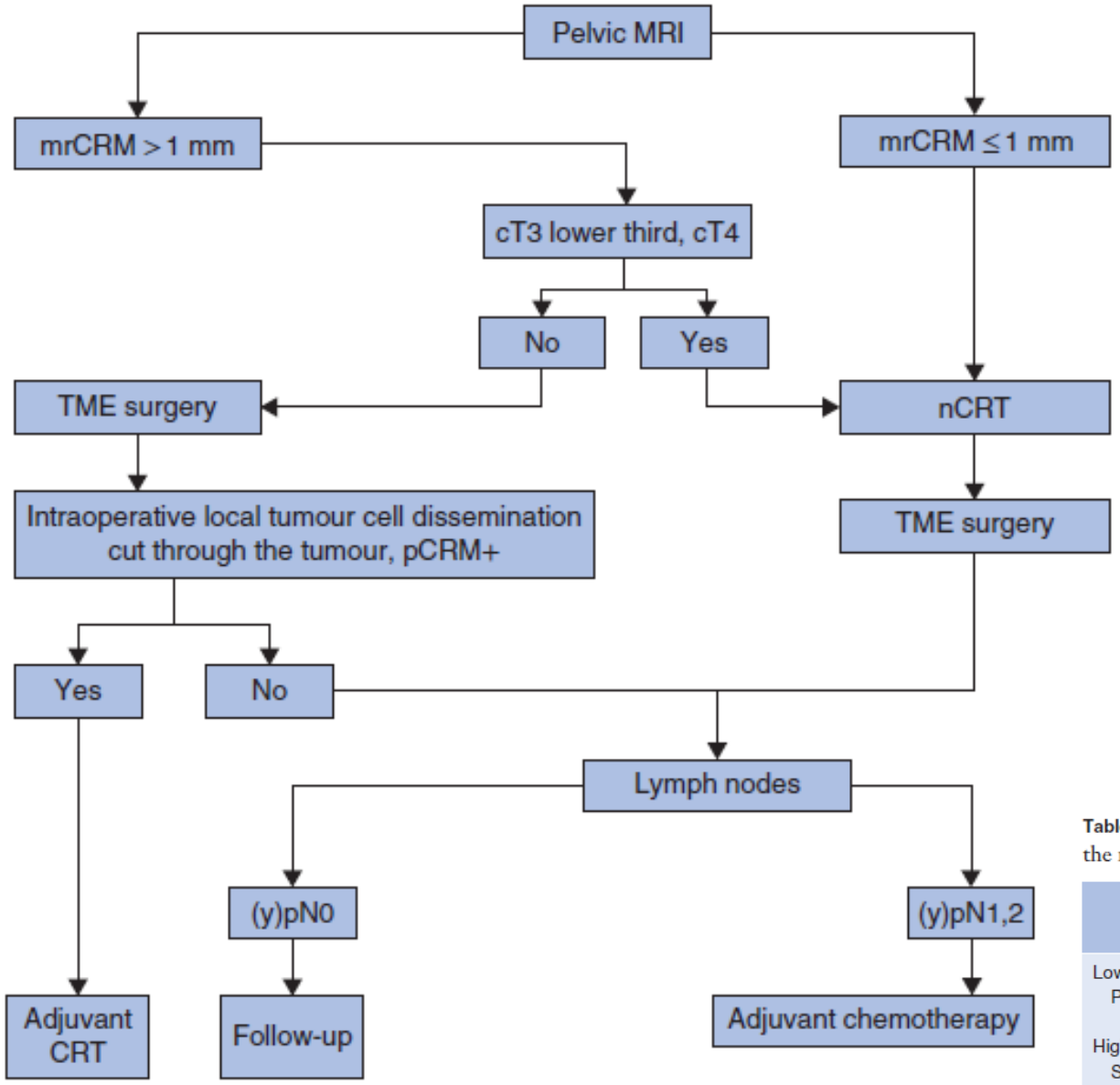


Oncological outcome after MRI-based selection for neoadjuvant chemoradiotherapy in the OCUM Rectal Cancer Trial

R. Ruppert[1], T. Junginger[2], H. Ptok[4], J. Strassburg[5], C. A. Maurer[10], P. Brosi[11], J. Sauer[7], J. Baral[8], M. Kreis[6], D. Wollschlaeger[3], P. Hermanek[9] and S. Merkel[9], on behalf of the OCUM group

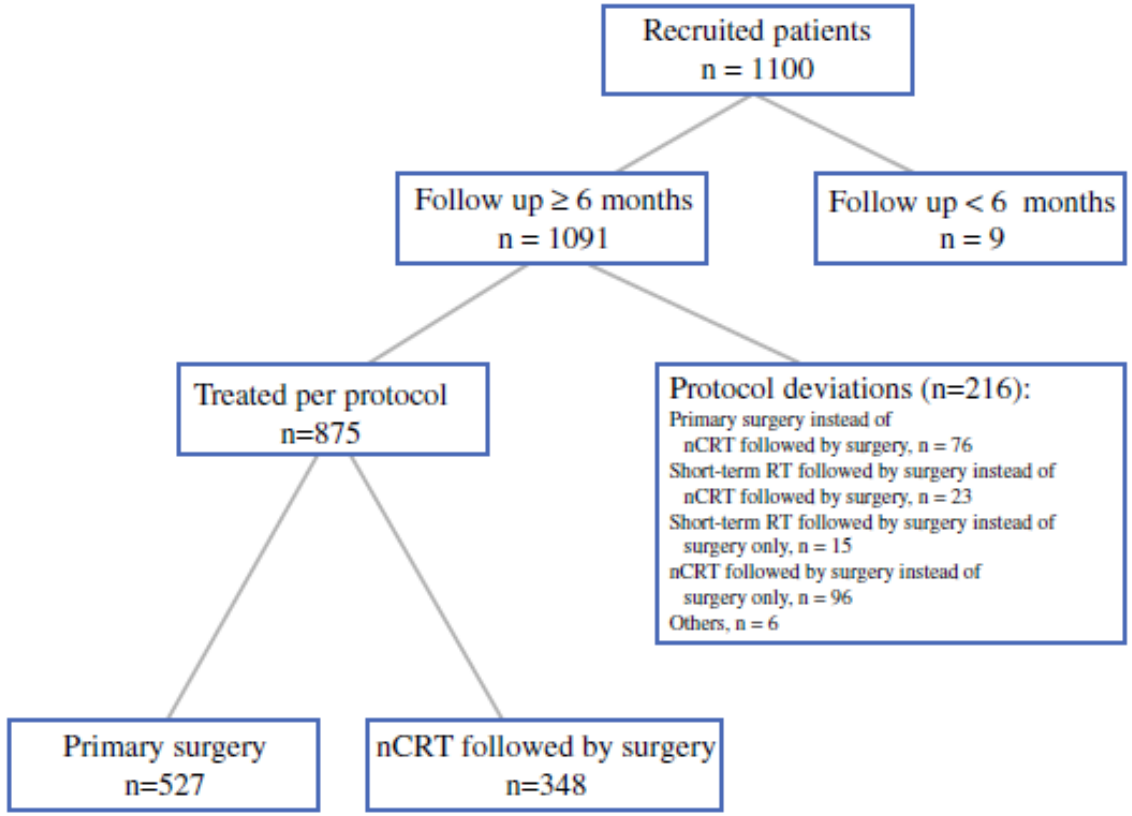
BJS 2018; **105**: 1519–1529

1021 pts 2007-2016
428 pts treated according to the study protocol (followed for at least 3 years et 2018)
254 (59,3%) had TME alone
174 (40,7%) received nCRT and TME

Table 7 Localization, clinical stage and raw local recurrence in 268 patients with clinical stage II or III of the lower and middle third of the rectum after a minimum of 3 years' follow-up

	Localization	Tumour stage cII	Tumour stage cIII	Local recurrence
Low risk (mrCRM–)				
Primary surgery ($n = 113$)	Lower third 11	2	9	1 after 4 months (cIII)
	Middle third 102	35	67	1 after 29 months (cII)
High risk (mrCRM+)				
Surgery after nCRT ($n = 123$)	Lower third 67	11	56	2 after 46 and 74 months (both cIII)
	Middle third 56	12	44	2 after 8 (cIII) and 56 months (cII)
High-risk mrCRM– (cT3 lower third)				
Surgery after nCRT ($n = 32$)	Lower third 32	15	17	1 after 17 months (cIII)

mrCRM–, uninvolved mesorectal fascia on MRI (distance greater than 1 mm); mrCRM+, involved mesorectal fascia on MRI (distance 1 mm or less). No local recurrence was observed in 13 patients with uncertain mrCRM status (surgery after neoadjuvant chemoradiotherapy (nCRT), 12; primary surgery, 1).



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The 3- and 5-year **local recurrence** rates were 1·3 and **2·7** per cent respectively, with no differences between the two treatment protocols. Patients with disease requiring nCRT had higher 3- and 5-year rates of **distant metastasis** (17·3 and **24·9** per cent respectively versus 8·9 and **14·4** per cent in patients who had TME alone; P = 0·005) and worse **disease-free survival** compared with that in patients who did not need nCRT (3- and 5-year rates 76·7 and **66·7** per cent, versus 84·9 and **76·0** per cent in the TME-alone group; P = 0·016).

surgical plane was mesorectal in 93% (90.8 in 2020)

Oncological outcome after MRI-based selection for neoadjuvant chemoradiotherapy in the OCUM Rectal Cancer Trial

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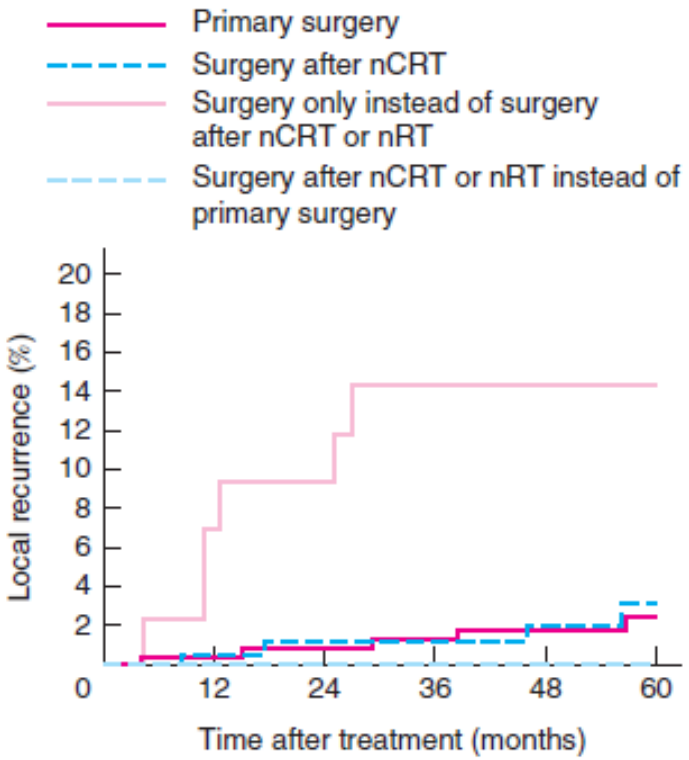
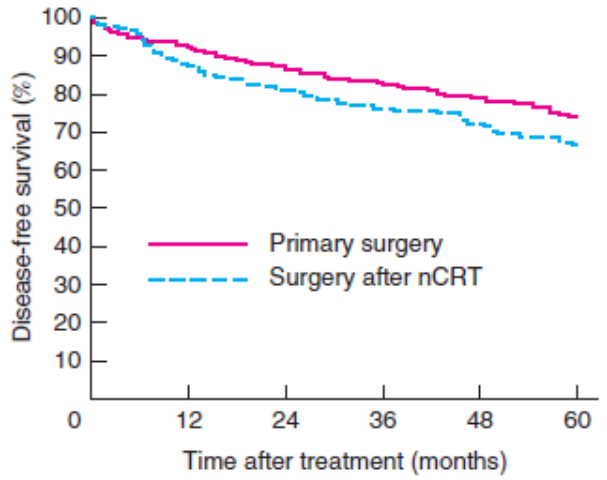


No. at risk

Primary surgery	254	239	229	218	177	127
Surgery after nCRT	174	163	156	139	118	83
Surgery only instead	44	40	36	31	26	20
nCRT or nRT instead	71	68	65	61	49	38



No. at risk

Primary surgery	254	233	219	205	165	116
Surgery after nCRT	174	151	140	126	106	77

Effect of the plane of surgery achieved on local recurrence in patients with operable rectal cancer: a prospective study using data from the MRC CR07 and NCIC-CTG CO16 randomised clinical trial

*Phil Quirke, Robert Steele, John Monson, Robert Grieve, Subhash Khanna, Jean Couture, Chris O'Callaghan, Arthur Sun Myint, Eric Bessell, Lindsay C Thompson, Mahesh Parmar, Richard J Stephens, David Sebag-Montefiore, on behalf of the MRC CR07/NCIC-CTG CO16 trial investigators and the NCRI colorectal cancer study group**

Lancet 2009; 373: 821–28

plane of surgery

- mesorectal in 604 (52%)
- intermediate intramesorectal in 398 (34%)
- muscularis propria plane in 154 (13%)

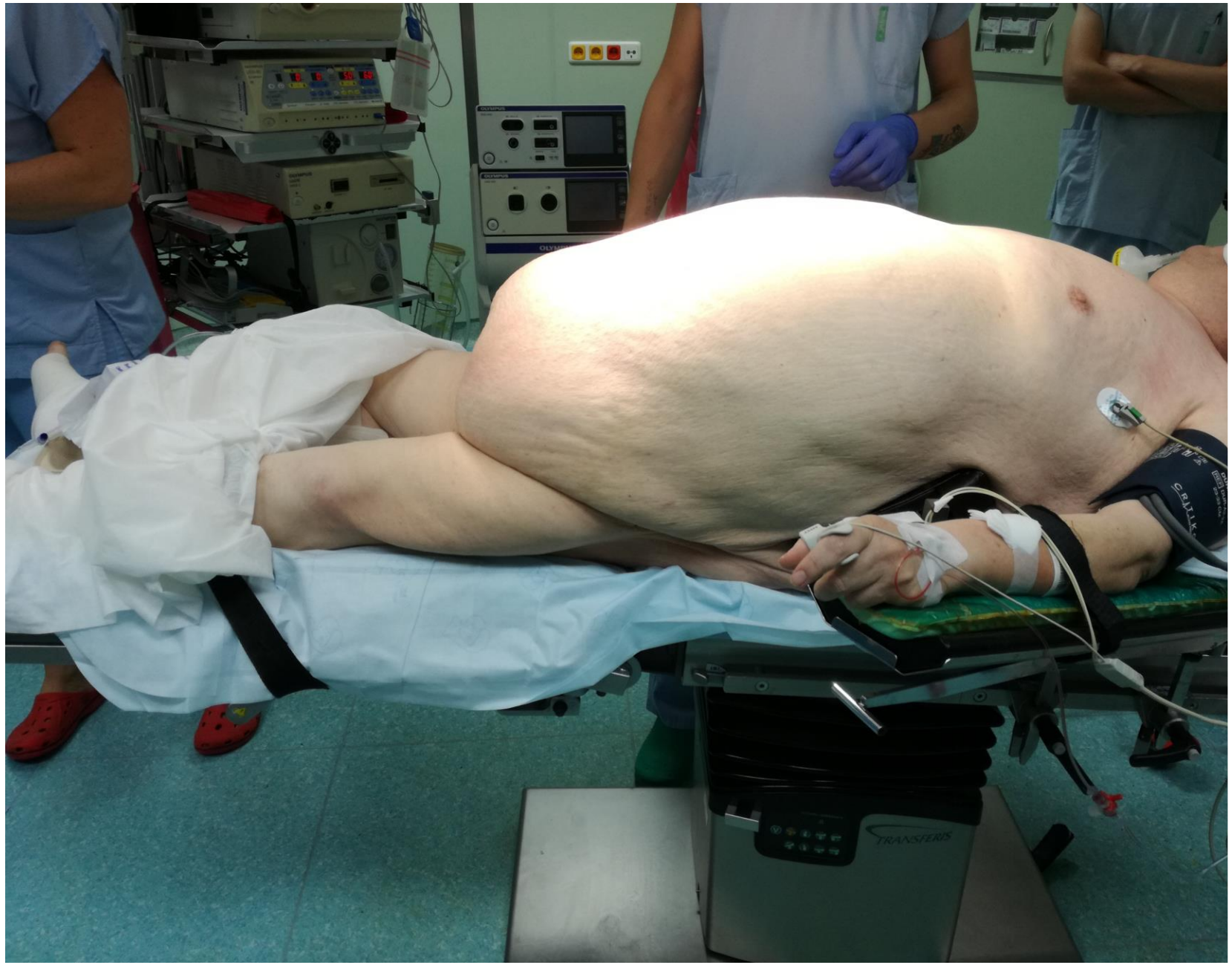
Ann Surg Oncol (2020) 27:417–427
https://doi.org/10.1245/s10434-019-07696-y

Annals of SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – COLORECTAL CANCER

MRI-Based Use of Neoadjuvant Chemoradiotherapy in Rectal Carcinoma: Surgical Quality and Histopathological Outcome of the OCUM Trial

	Primary surgery [n = 527]	nCRT followed by surgery [n = 348]
Mesorectal plane	496 (94.1)	299 (85.9)
Intramesorectal plane	30 (5.7)	40 (11.5)
Muscularis propria plane	1 (0.2)	9 (2.6)


OLYMPUS
TRANSFERIS

CLINICAL PRACTICE GUIDELINES

Personalised medicine

Summary of recommendations
There are no molecular markers to guide treatment approaches or to predict response to RT or CRT
Rectal cancers with distant metastases should be studied for *RAS* and *BRAF* mutational status and the other requirements addressed in the ESMO consensus guidelines on metastatic colorectal cancer

ESMO

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Děkuji za pozornost!

Does A Longer Waiting Period After Neoadjuvant Radio-chemotherapy Improve the Oncological Prognosis of Rectal Cancer?

Three Years' Follow-up Results of the Greccar-6 Randomized Multicenter Trial

Annals of Surgery Volume 270, Number 5, November 2019

Patients with cT3/T4 or TxNþ tumors of the mid or lower rectum who had received RCT (45–50 Gy with 5- fluorouracil or capecitabine) were included and randomized into a 7- or 11-week waiting period. Primary endpoint was the pCR rate. Secondary endpoints were 3-year overall (OS), disease-free survival (DFS), and recurrence rates.

Does A Longer Waiting Period After Neoadjuvant Radio-chemotherapy Improve the Oncological Prognosis of Rectal Cancer?

reccar-6 Randomized Multicenter Trial

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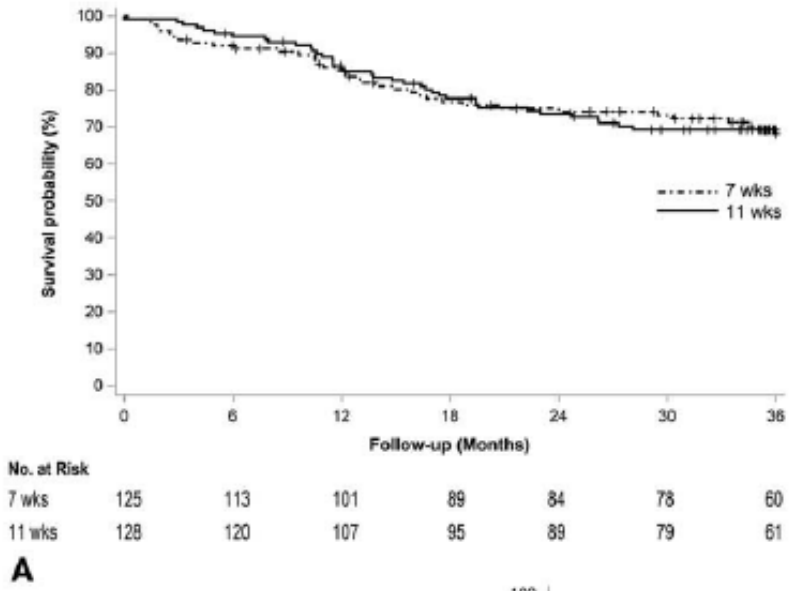

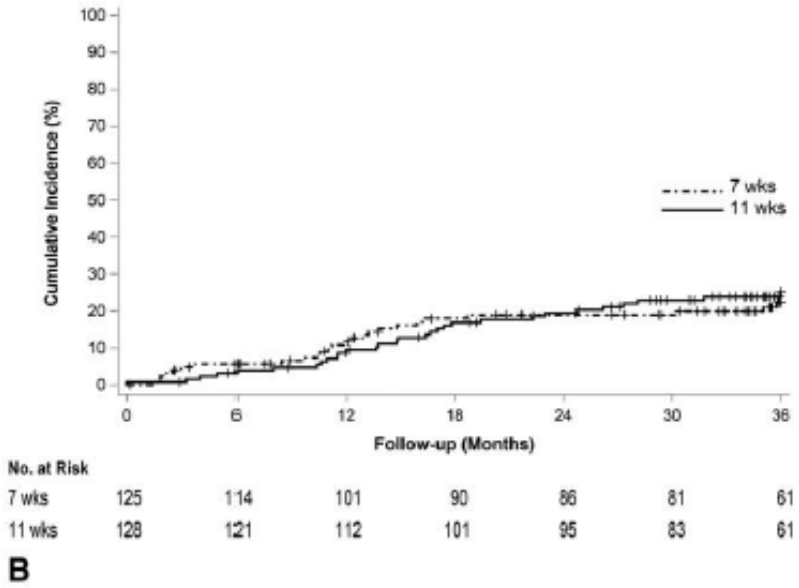

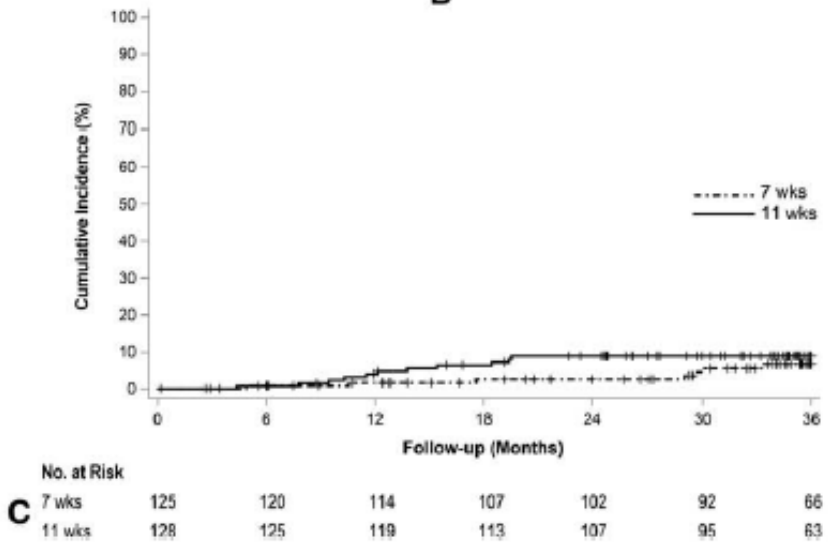

FIGURE 2. Survival curves according to the waiting period after radiochemotherapy (A) DFS (log-rank = 0.9409). (B) Metastatic recurrences (log-rank = 0.7432). (C) Local recurrences (log-rank = 0.3944).

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Three Years' Follow-up Results of the Greccar-6 Randomized Multicenter Trial

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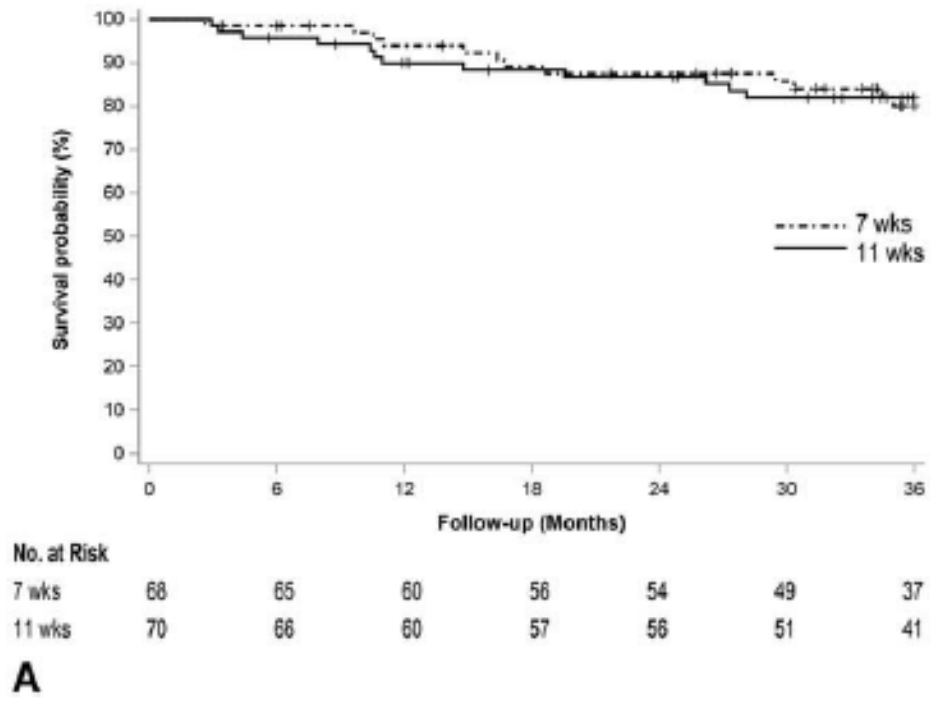

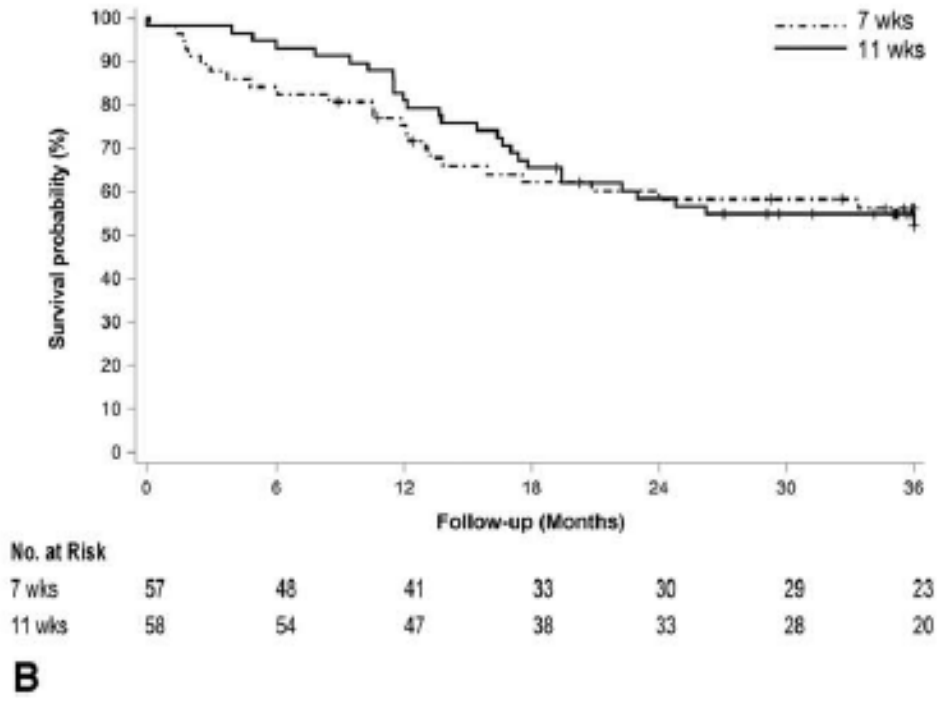

FIGURE 3. Disease-free survival according to the randomization group of: (A) good responders (ypT0-Tis-T1-T2) (log-rank = 0.9509); (b) bad responders (ypT3-T4) (log-rank = 0.9726).