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Clínica Cirúrgica Avançada

MaterDei
Rede de Saúde

Tumores de reto cT3N1:
Porque indicar cirurgia upfront?

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DR. MATHEUS MEYER
COLOPROCTOLOGISTA | COLONOSCOPISTA

Decisão Multidisciplinar

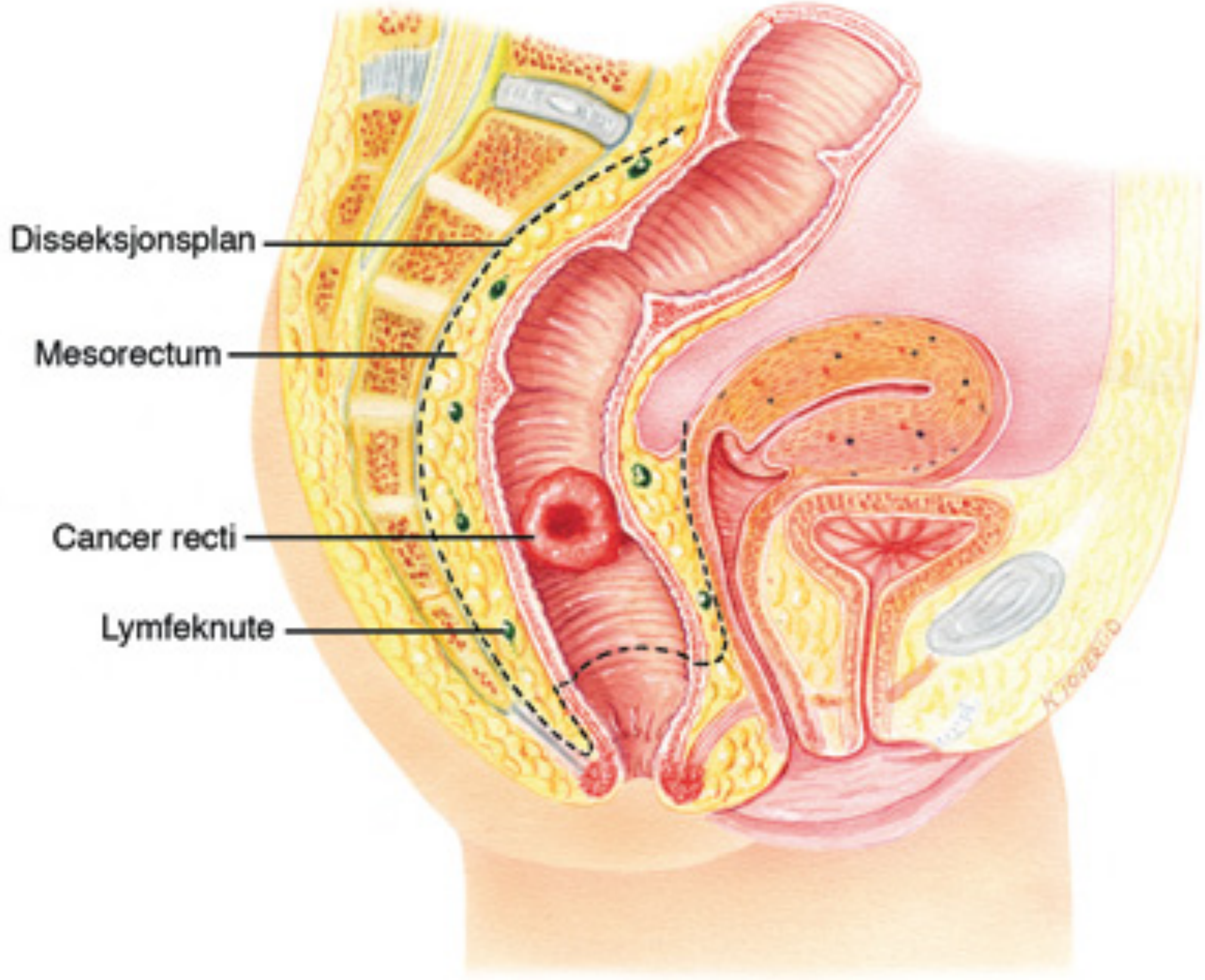
Coloproctologia

Oncologia

Radioterapia

Radiologia

Anatomia


Disseksjonsplan
Mesorectum
Cancer recti
Lymfeknute

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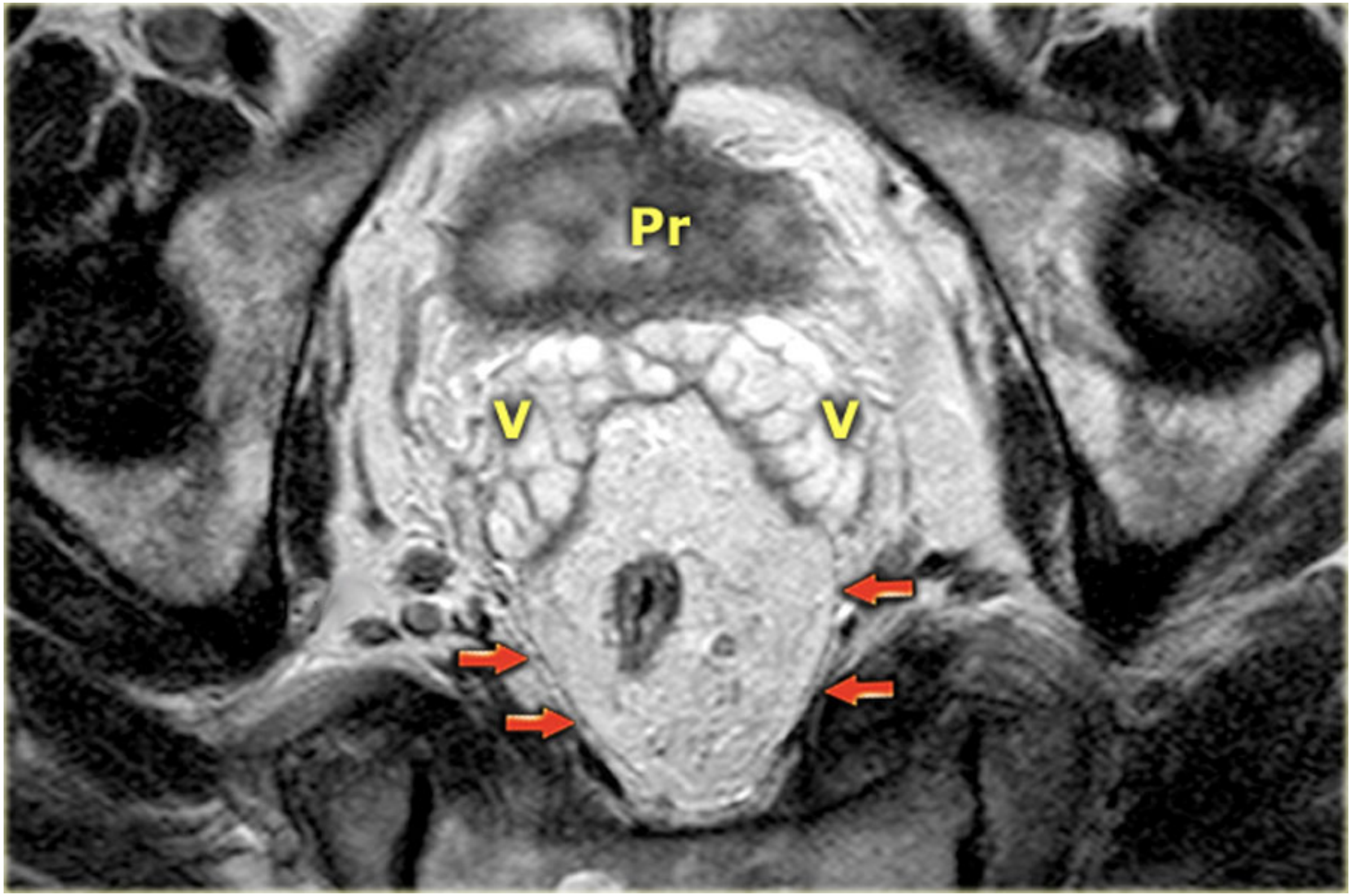
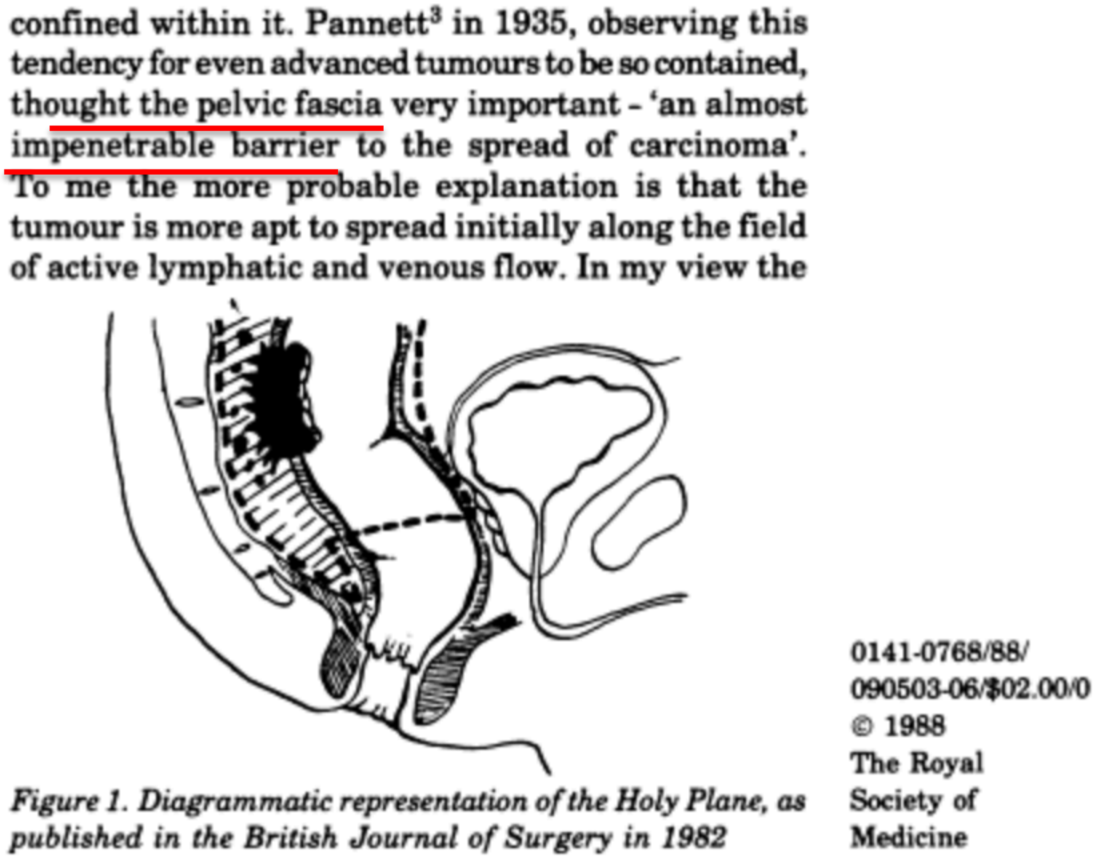
Anatomia



Anatomia



confined within it. Pannett[3] in 1935, observing this tendency for even advanced tumours to be so contained, thought the pelvic fascia very important – 'an almost impenetrable barrier to the spread of carcinoma'. To me the more probable explanation is that the tumour is more apt to spread initially along the field of active lymphatic and venous flow. In my view the

Figure 1. Diagrammatic representation of the Holy Plane, as published in the British Journal of Surgery in 1982

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090503-06/$02.00/0
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Society of
Medicine

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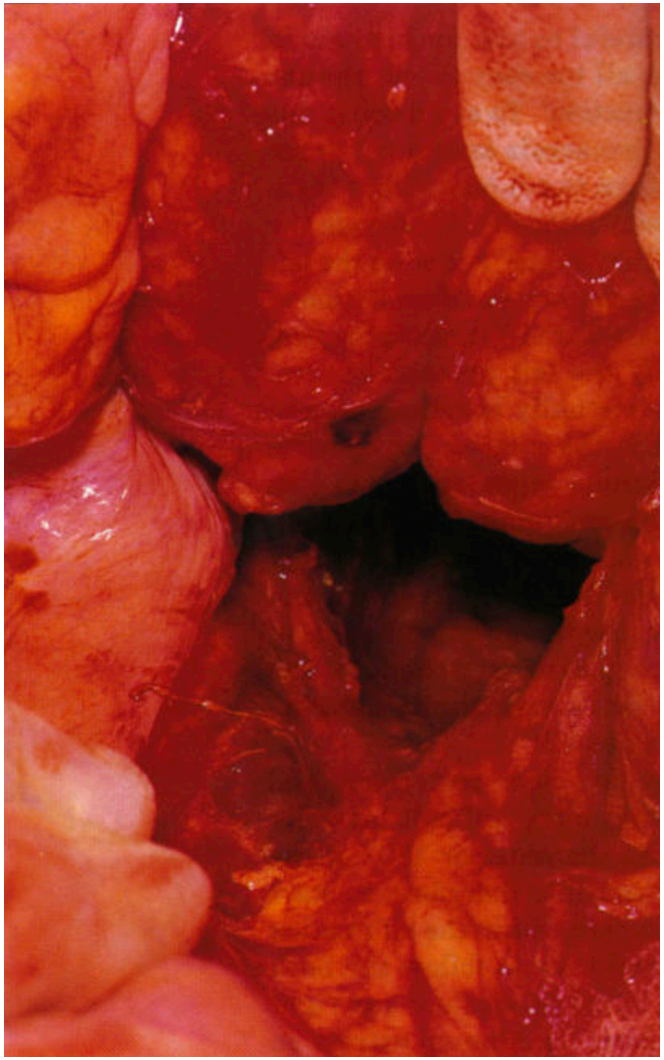
Plano cirúrgico

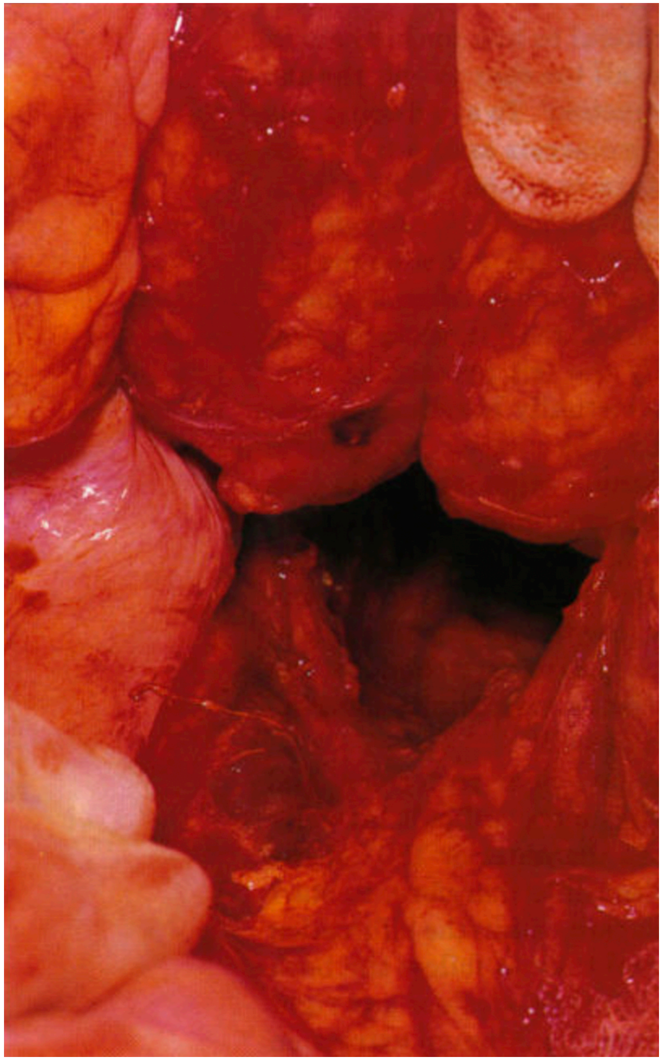
J R Soc Med. 1988 Sep; 81(9): 503–508.

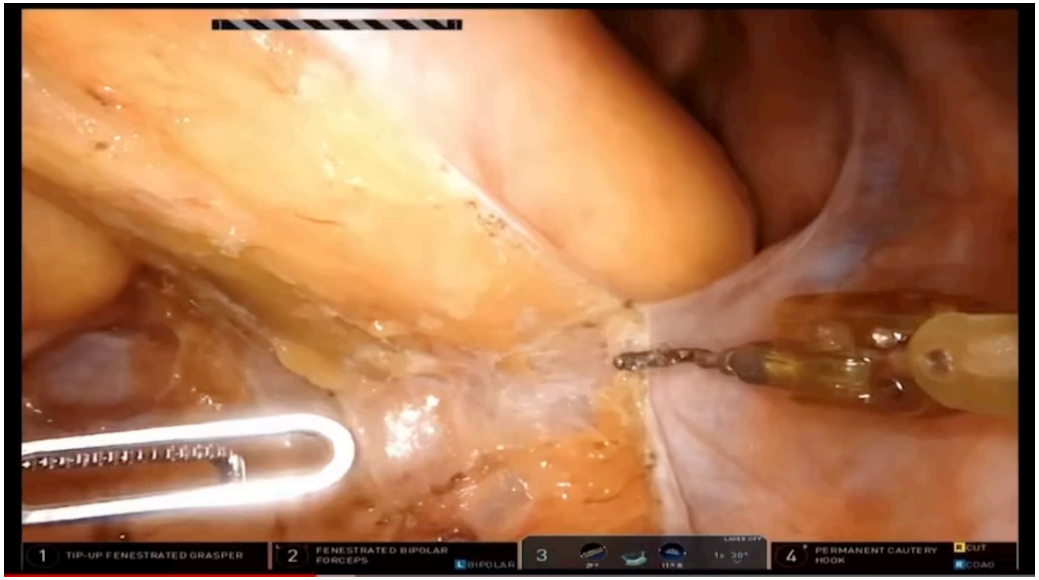
The 'Holy Plane' of rectal surgery.

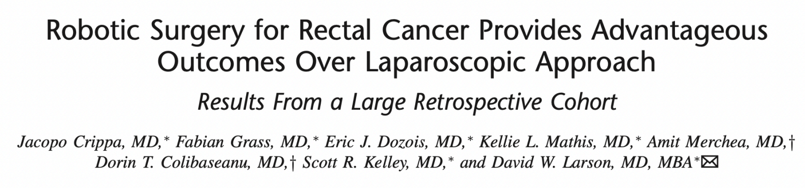
R J Heald



Plano cirúrgico




1 TIP-UP FENESTRATED GRASPER
2 FENESTRATED BIPOLAR FORCEPS
L BIPOLAR
3
1x 30°
4 PERMANENT CAUTERY HOOK
R CUT
R COAG



Robotic Surgery for Rectal Cancer Provides Advantageous Outcomes Over Laparoscopic Approach

Results From a Large Retrospective Cohort

Jacopo Crippa, MD, Fabian Grass, MD,* Eric J. Dozois, MD,* Kellie L. Mathis, MD,* Amit Merchea, MD,† Dorin T. Colibaseanu, MD,† Scott R. Kelley, MD,* and David W. Larson, MD, MBA*✉*

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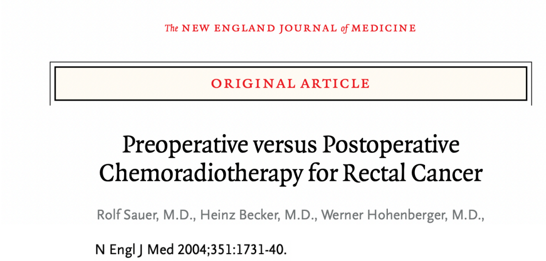


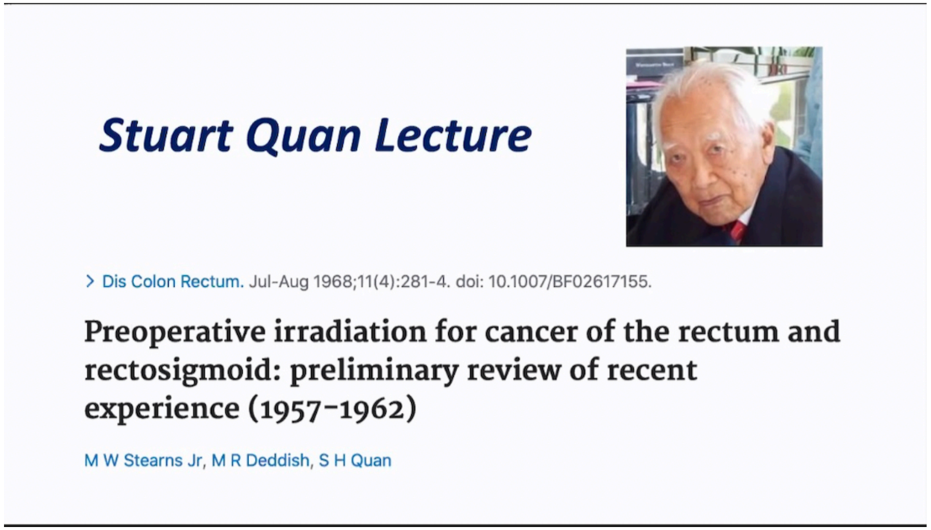
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Preoperative versus Postoperative Chemoradiotherapy for Rectal Cancer

Rolf Sauer, M.D., Heinz Becker, M.D., Werner Hohenberger, M.D.,

N Engl J Med 2004;351:1731-40.

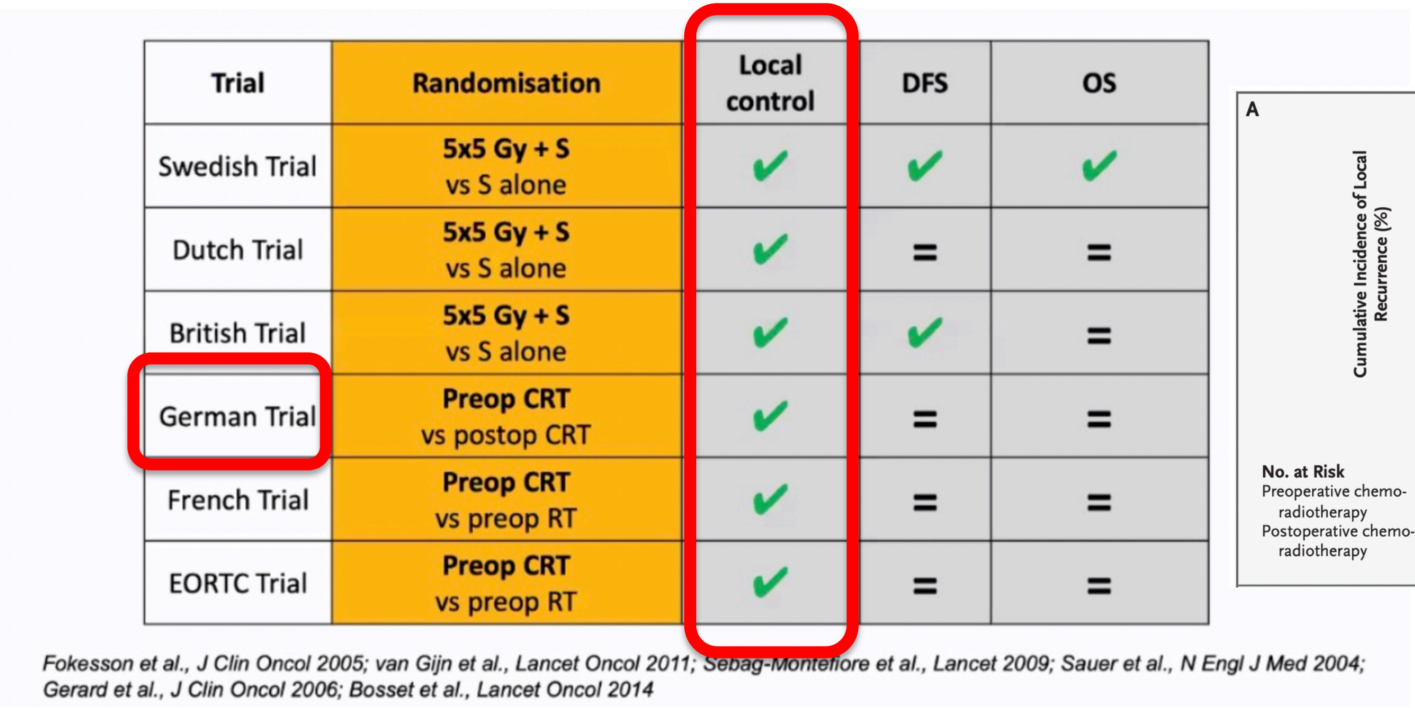


Stuart Quan Lecture

> Dis Colon Rectum. Jul-Aug 1968;11(4):281-4. doi: 10.1007/BF02617155.

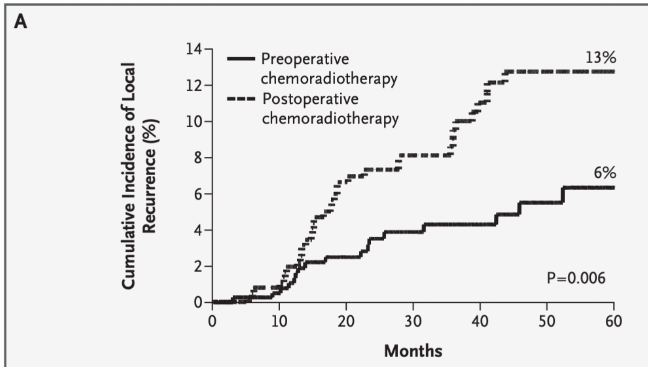
Preoperative irradiation for cancer of the rectum and rectosigmoid: preliminary review of recent experience (1957-1962)

M W Stearns Jr, M R Deddish, S H Quan



Trial	Randomisation	Local control	DFS	OS
Swedish Trial	5x5 Gy + S vs S alone	✓	✓	✓
Dutch Trial	5x5 Gy + S vs S alone	✓	=	=
British Trial	5x5 Gy + S vs S alone	✓	✓	=
German Trial	Preop CRT vs postop CRT	✓	=	=
French Trial	Preop CRT vs preop RT	✓	=	=
EORTC Trial	Preop CRT vs preop RT	✓	=	=

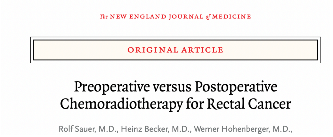
Fokesson et al., J Clin Oncol 2005; van Gijn et al., Lancet Oncol 2011; Sebag-Montefiore et al., Lancet 2009; Sauer et al., N Engl J Med 2004; Gerard et al., J Clin Oncol 2006; Bosset et al., Lancet Oncol 2014



No. at Risk	0	10	20	30	40	50	60
Preoperative chemoradiotherapy	397	368	312	250	190	133	97
Postoperative chemoradiotherapy	384	351	299	240	184	135	85

ESTUDOS DOS ANOS 2000

- Incluiam todos os tumores de reto (mesmo reto alto)
- Estadiamento era realizado com EUS e não RNM
- A Cirurgia no plano do mesorreto não era tão consolidada como é hoje



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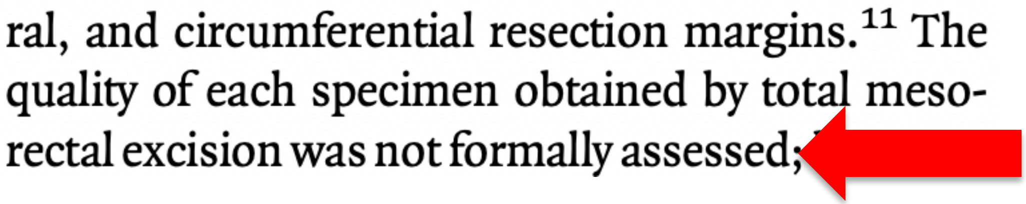
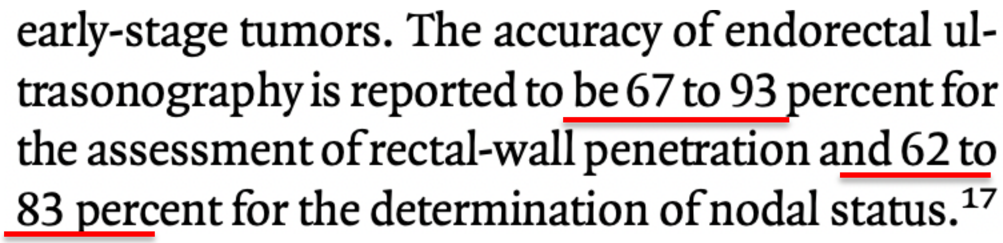


ral, and circumferential resection margins.[11] The quality of each specimen obtained by total mesorectal excision was not formally assessed;



early-stage tumors. The accuracy of endorectal ultrasonography is reported to be 67 to 93 percent for the assessment of rectal-wall penetration and 62 to 83 percent for the determination of nodal status.[17]

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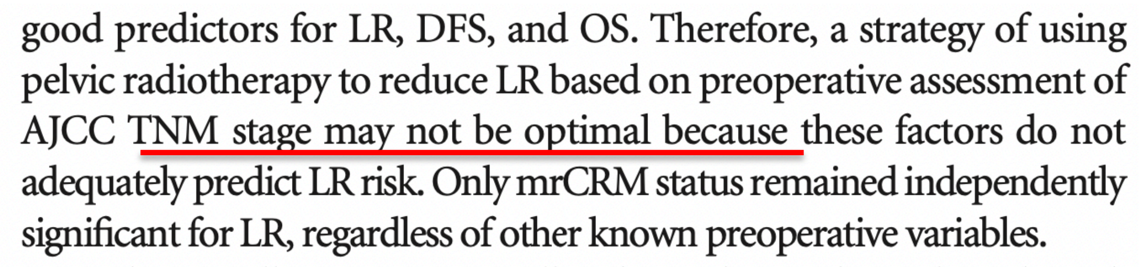
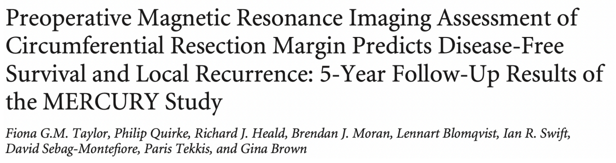
ESTADIAMENTO

- RNM é superior ao EUS
- TNM apenas, não é mais o suficiente
    - Margem circunferencial (CRM) – subdivisão do T3
    - Proximidade da margem anal
    - Invasão vascular extramural (EMVI)



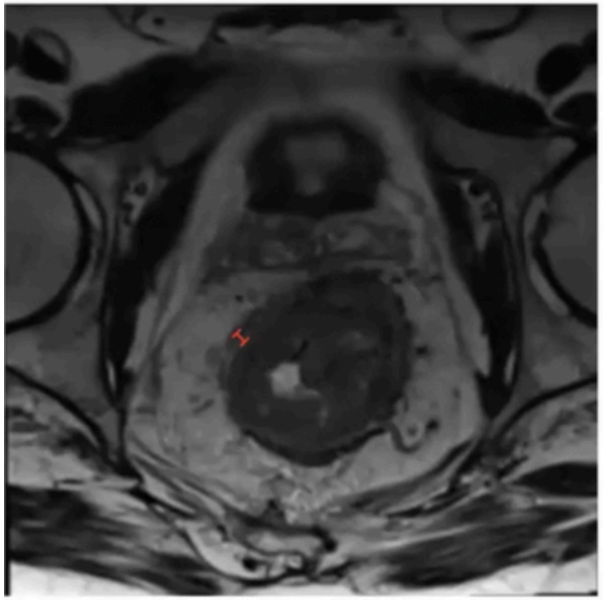
good predictors for LR, DFS, and OS. Therefore, a strategy of using pelvic radiotherapy to reduce LR based on preoperative assessment of AJCC TNM stage may not be optimal because these factors do not adequately predict LR risk. Only mrCRM status remained independently significant for LR, regardless of other known preoperative variables.



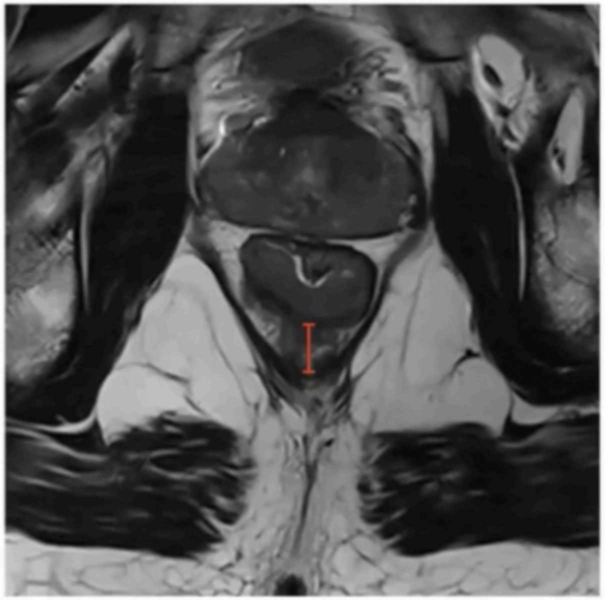
Preoperative Magnetic Resonance Imaging Assessment of Circumferential Resection Margin Predicts Disease-Free Survival and Local Recurrence: 5-Year Follow-Up Results of the MERCURY Study

Fiona G.M. Taylor, Philip Quirke, Richard J. Heald, Brendan J. Moran, Lennart Blomqvist, Ian R. Swift, David Sebag-Montefiore, Paris Tekkis, and Gina Brown

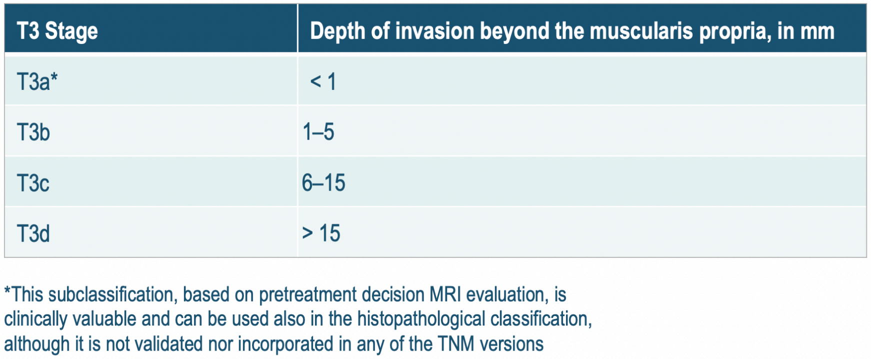
T



T3 a/b

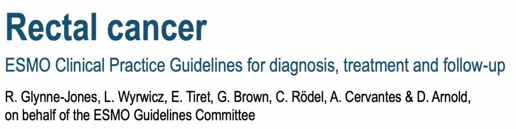


T3 c/d



T3 Stage	Depth of invasion beyond the muscularis propria, in mm
T3a*	< 1
T3b	1–5
T3c	6–15
T3d	> 15

*This subclassification, based on pretreatment decision MRI evaluation, is clinically valuable and can be used also in the histopathological classification, although it is not validated nor incorporated in any of the TNM versions



Rectal cancer

ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up

R. Glynne-Jones, L. Wyrwicz, E. Tiret, G. Brown, C. Rödel, A. Cervantes & D. Arnold,
on behalf of the ESMO Guidelines Committee

POR QUÊ OMITIR A RT?

- Toxicidade
- O grande objetivo da RT é atingir CRM livre
- CRM é o grande preditor de recorrência local
- É preciso RT para diminuir a recidiva local nos T3N1 com margem segura a RNM?
- Supertratamento?

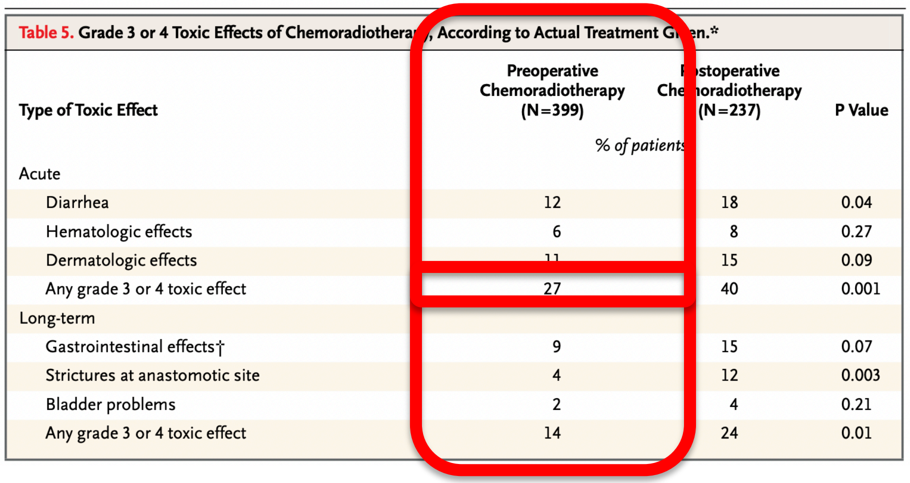
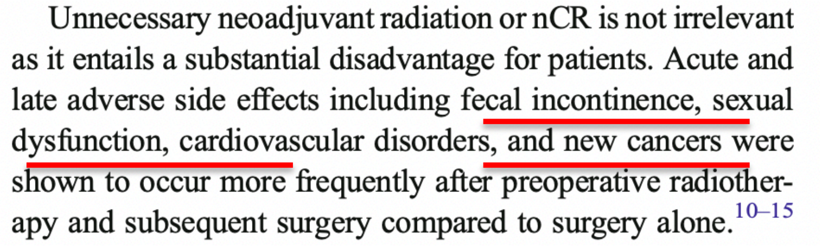


Table 5. Grade 3 or 4 Toxic Effects of Chemoradiothera, According to Actual Treatment Gi en.*

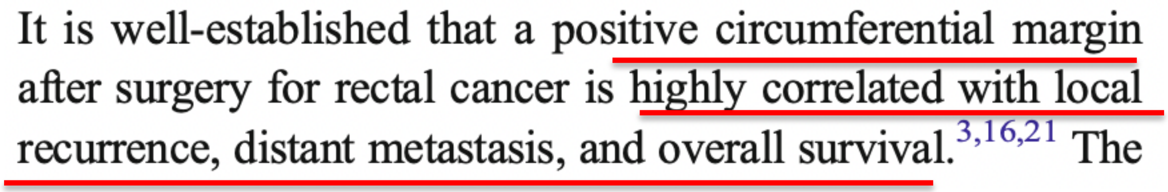
Type of Toxic Effect	Preoperative Chemoradiotherapy (N=399)	stoperative Che oradiotherapy (N=237)	P Value
	% of patients		
Acute			
Diarrhea	12	18	0.04
Hematologic effects	6	8	0.27
Dermatologic effects	11	15	0.09
Any grade 3 or 4 toxic effect	27	40	0.001
Long-term			
Gastrointestinal effects†	9	15	0.07
Strictures at anastomotic site	4	12	0.003
Bladder problems	2	4	0.21
Any grade 3 or 4 toxic effect	14	24	0.01



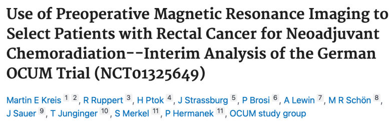
Unnecessary neoadjuvant radiation or nCR is not irrelevant as it entails a substantial disadvantage for patients. Acute and late adverse side effects including fecal incontinence, sexual dysfunction, cardiovascular disorders, and new cancers were shown to occur more frequently after preoperative radiotherapy and subsequent surgery compared to surgery alone.[10–15]

CRM

- CRM é também preditor de:
  - Doença a distância
  - Sobrevida global



It is well-established that a positive circumferential margin after surgery for rectal cancer is highly correlated with local recurrence, distant metastasis, and overall survival.[3,16,21] The



Use of Preoperative Magnetic Resonance Imaging to Select Patients with Rectal Cancer for Neoadjuvant Chemoradiation--Interim Analysis of the German OCUM Trial (NCT01325649)

Martin E Kreis [1,2], R Ruppert [3], H Ptok [4], J Strassburg [5], P Brosi [6], A Lewin [7], M R Schön [8], J Sauer [9], T Junginger [10], S Merkel [11], P Hermanek [11], OCUM study group

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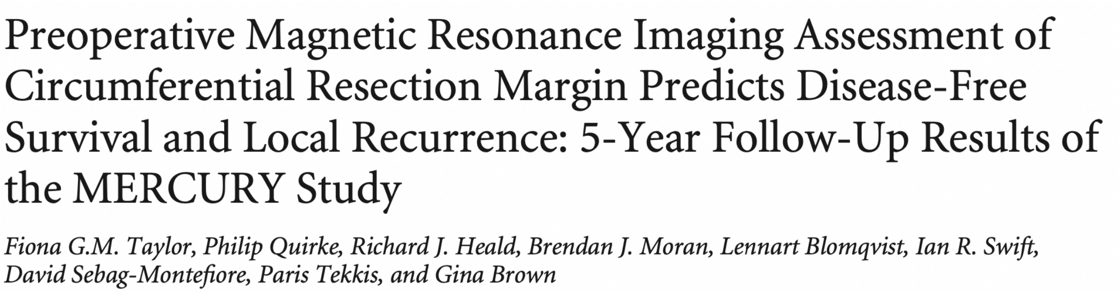
Fundamentos teóricos

- Mercury
- Quicksilver
- Occum



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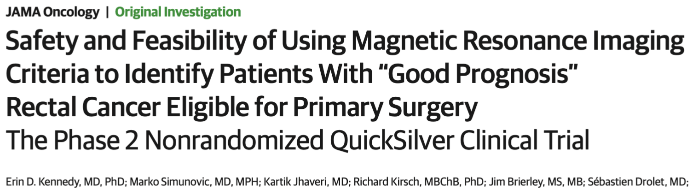
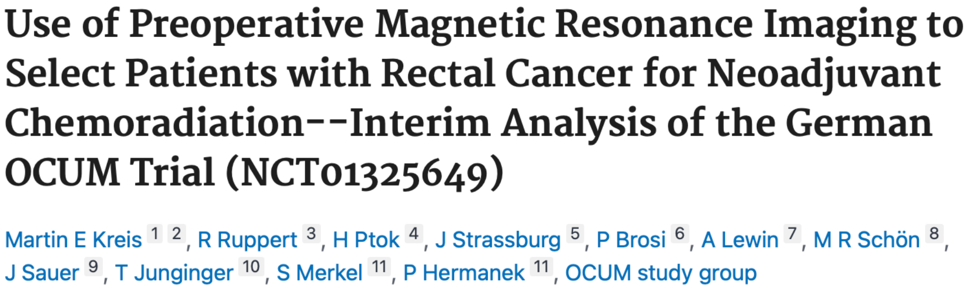


JAMA Oncology | Original Investigation

Safety and Feasibility of Using Magnetic Resonance Imaging Criteria to Identify Patients With "Good Prognosis" Rectal Cancer Eligible for Primary Surgery
The Phase 2 Nonrandomized QuickSilver Clinical Trial

Erin D. Kennedy, MD, PhD; Marko Simunovic, MD, MPH; Kartik Jhaveri, MD; Richard Kirsch, MBChB, PhD; Jim Brierley, MS, MB; Sébastien Drolet, MD;



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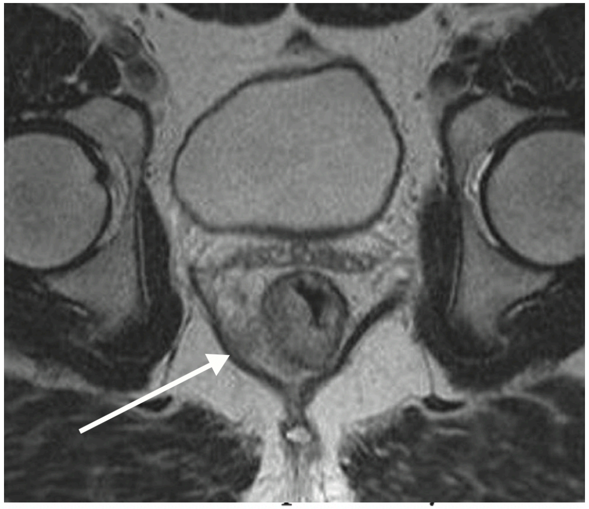
Fundamentos teóricos

- Mercury
  - Melhor seleção do tratamento
  - RNM como prognóstico baseado na definição da CRM
  - Se a pCRM é -, praticamente elimina o risco de recidiva local.
  - mrCRM segura >>> 1mm da fáscia

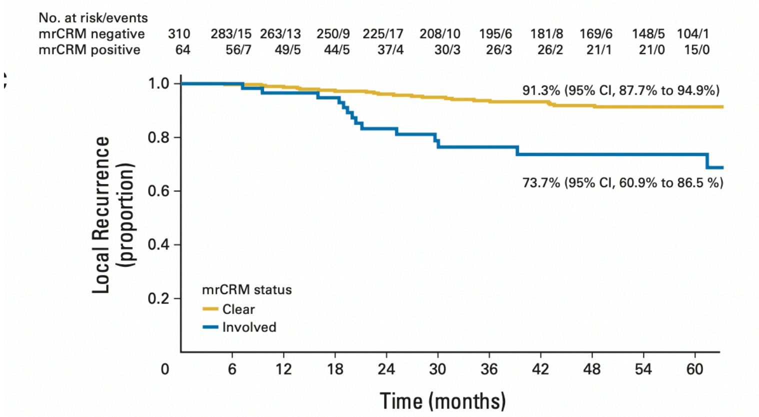


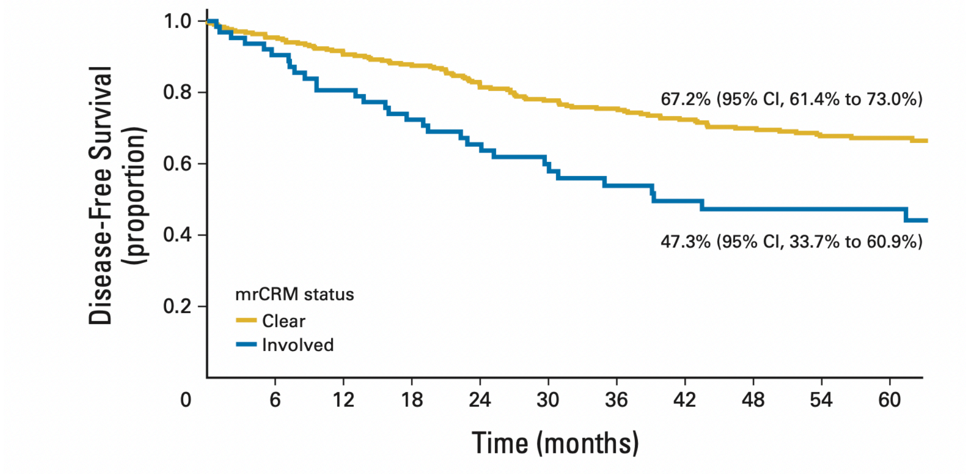
its, and lymph nodes.[5,6] If complete removal of the tumor with a clear CRM is achieved, this should largely eliminate the risk of LR.

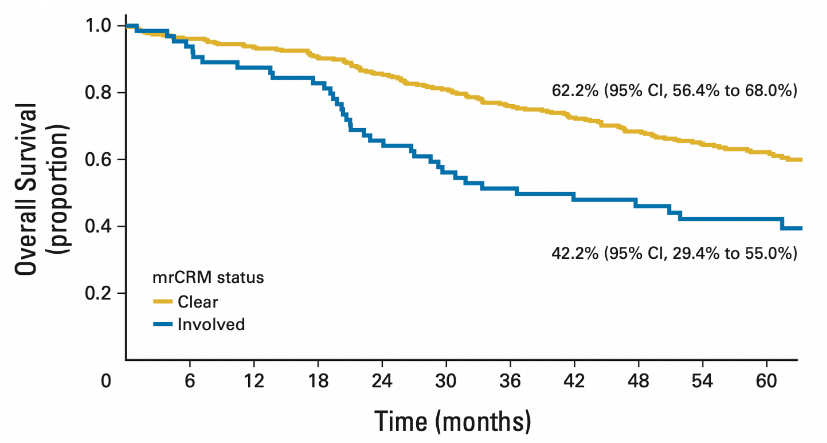
Predicted clear mrCRM was defined if the distance from tumor to the mesorectal fascia was greater than 1 mm. For lower-third rectal tumors, mrCRM involvement was defined as tumor ≤ 1 mm from the levator muscle. If tumor

Fundamentos teóricos

- Mercury
  - Tumores mais baixos que 5cm contribuíram para LR apesar da CRT

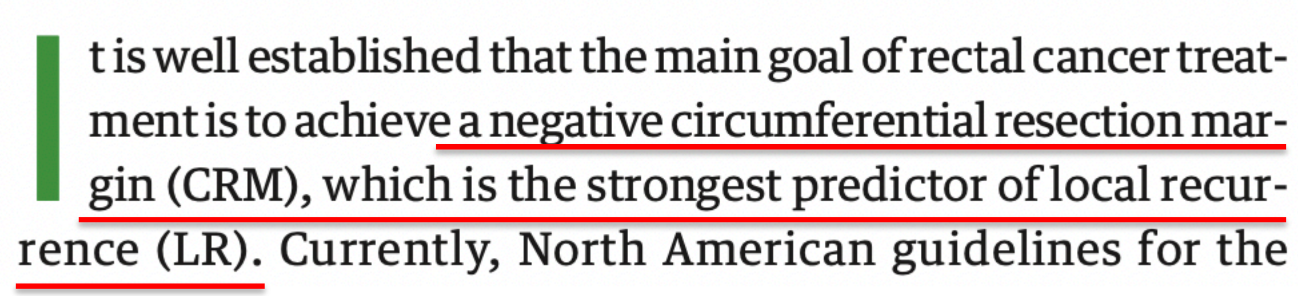




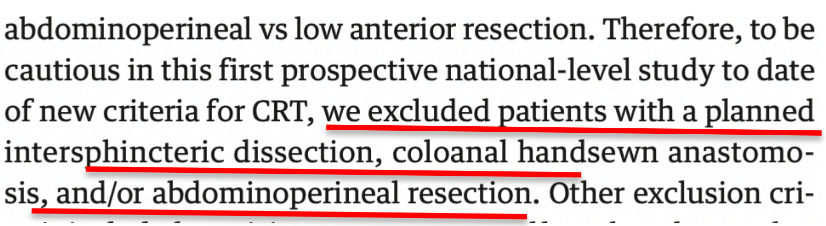


Fundamentos teóricos

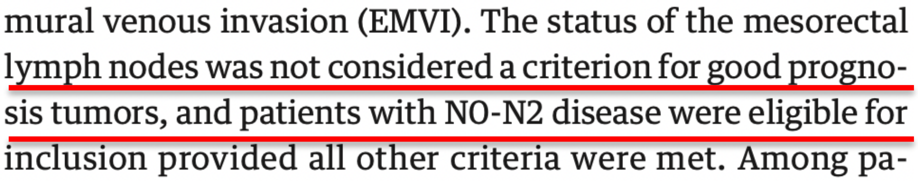
- Quicksilver
    - Objetivo: melhor seleção dos pacientes para QRT
    - Foco do tratamento do reto>>> CRM negativa
    - Linfonodos não foram considerados critérios prognósticos
    - Excluídas lesões muito baixas



It is well established that the main goal of rectal cancer treatment is to achieve a negative circumferential resection margin (CRM), which is the strongest predictor of local recurrence (LR). Currently, North American guidelines for the



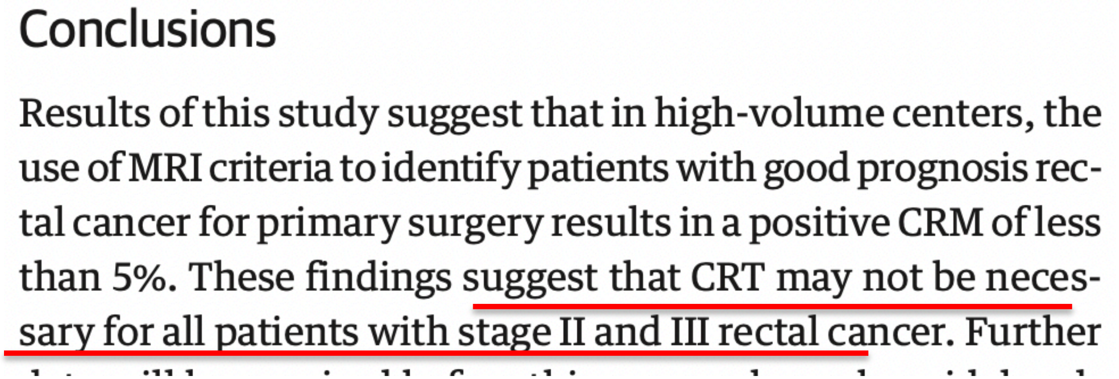
abdominoperineal vs low anterior resection. Therefore, to be cautious in this first prospective national-level study to date of new criteria for CRT, we excluded patients with a planned intersphincteric dissection, coloanal handsewn anastomosis, and/or abdominoperineal resection. Other exclusion cri-



mural venous invasion (EMVI). The status of the mesorectal lymph nodes was not considered a criterion for good prognosis tumors, and patients with N0-N2 disease were eligible for inclusion provided all other criteria were met. Among pa-

Fundamentos teóricos

- Quicksilver
  - Mesorreto de qualidade em 98% dos casos
  - 29% n+
  - Concordância de N na RNM x patologia: 68%
    - 12% subestadiados
    - 20% superestadiados
  - CRM+: 4,9%
  - > QRT pode não ser necessária para todos Est II e III

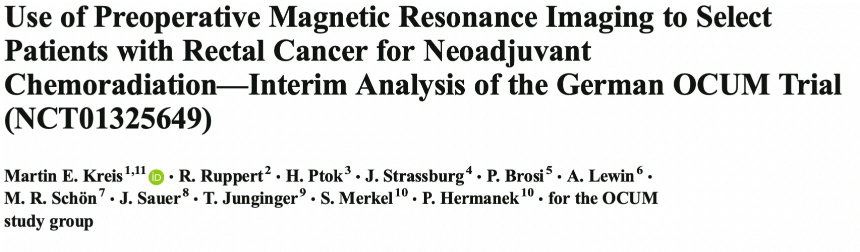


Conclusions

Results of this study suggest that in high-volume centers, the use of MRI criteria to identify patients with good prognosis rectal cancer for primary surgery results in a positive CRM of less than 5%. These findings suggest that CRT may not be necessary for all patients with stage II and III rectal cancer. Further

Fundamentos teóricos

- OCUM
  - 98,5% VPN para CRM-



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Martin E. Kreis[1,11] · R. Ruppert[2] · H. Ptok[3] · J. Strassburg[4] · P. Brosi[5] · A. Lewin[6] · M. R. Schön[7] · J. Sauer[8] · T. Junginger[9] · S. Merkel[10] · P. Hermanek[10] · for the OCUM study group

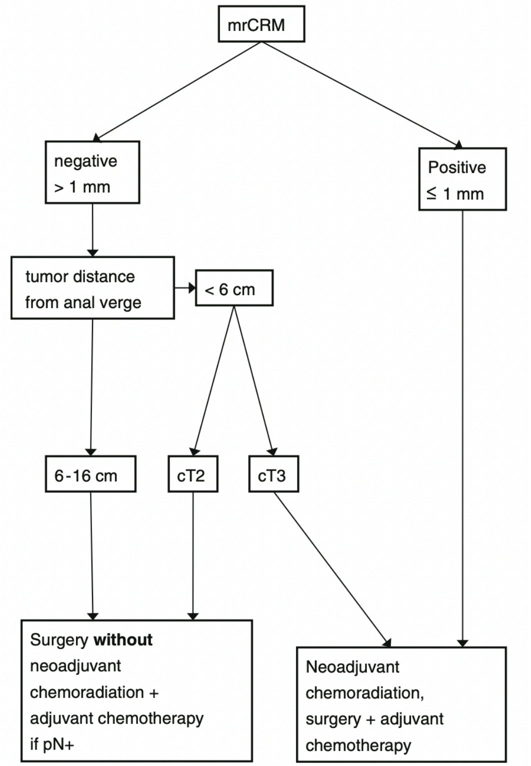
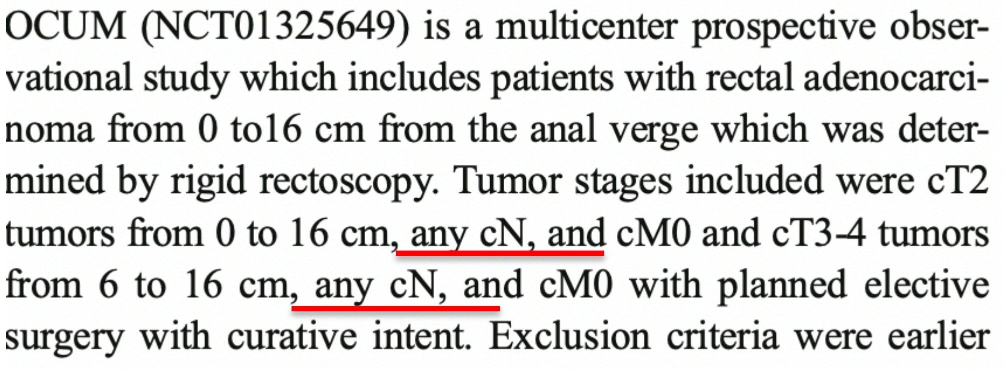

mrCRM
negative
> 1 mm
Positive
≤ 1 mm
tumor distance
from anal verge
< 6 cm
6-16 cm
cT2
cT3
Surgery **without**
neoadjuvant
chemoradiation +
adjuvant chemotherapy
if pN+
Neoadjuvant
chemoradiation,
surgery + adjuvant
chemotherapy

Fig. 2 OCUM—treatment algorithm



OCUM (NCT01325649) is a multicenter prospective observational study which includes patients with rectal adenocarcinoma from 0 to16 cm from the anal verge which was determined by rigid rectoscopy. Tumor stages included were cT2 tumors from 0 to 16 cm, any cN, and cM0 and cT3-4 tumors from 6 to 16 cm, any cN, and cM0 with planned elective surgery with curative intent. Exclusion criteria were earlier

Fundamentos teóricos

- OCUM
    - 60% cirurgia “upfront”
        - 98,3% CRM -
    - 40% QRT neoajduvante
        - 77% mrCRM+
        - 9,1% pCRM+
    - Boa qualidade de mesorreto: 92%

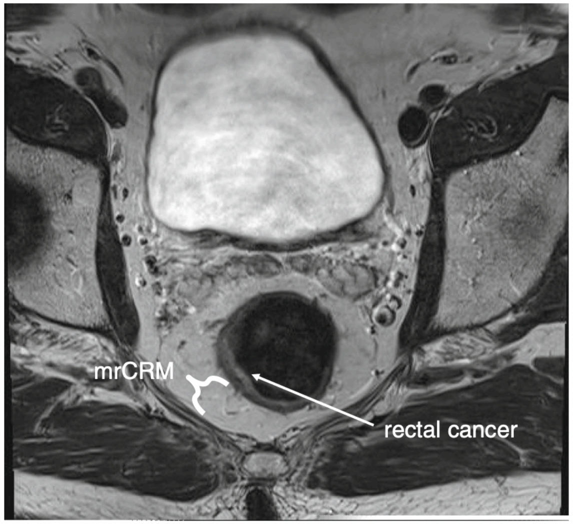


Fig. 1 Magnetic resonance imaging to determine circumferential margin between rectal cancer and mesorectal plane (mrCRM)

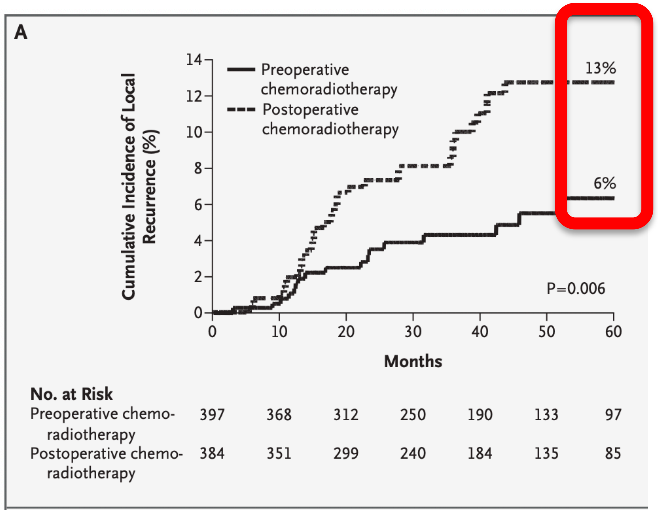
Fundamentos teóricos

- OCUM
  - Grande conversão de mrCRM+ para pCRM – com a radioterapia. Apenas 10% permaneceu pCRM+
  - QRT é ótima ferramenta para regressão tumoral nos casos de mrCRM+ e é ainda indispensável nesses pacientes
  - A indicação de QRT cai de 80 para 40% *quando se usa RNM*

Fundamentos teóricos

- Mercury
  - CRM +: 3%
  - LR: 3,3%
- Quicksilver
  - CRM+: 5%
- Occum
  - CRM+: 2%
  - LR: 2%

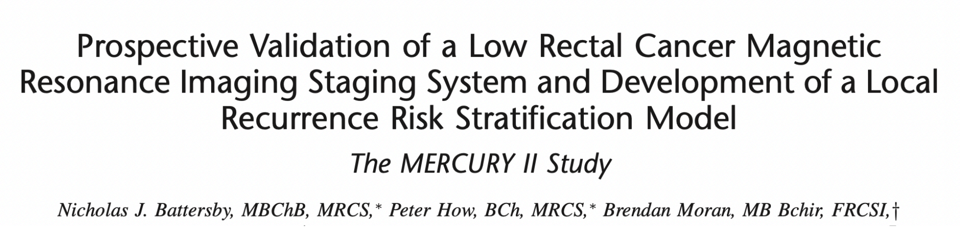
German Trial, 2004



AO INVÉS DE QRT PARA TODOS ESTADIOS II E III, A MELHOR SELEÇÃO DOS PACIENTES BASEADA NA CRM PODE LEVAR A EXCELENTES RESULTADOS ONCOLÓGICOS

Recidiva local: 2-3,3%
Margem Circunferencial positiva: 1,3-7,2%

Fundamentos teóricos



Prospective Validation of a Low Rectal Cancer Magnetic Resonance Imaging Staging System and Development of a Local Recurrence Risk Stratification Model

The MERCURY II Study

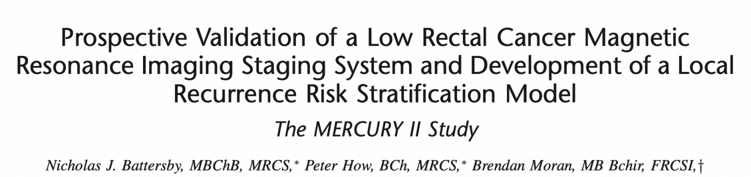
Nicholas J. Battersby, MBChB, MRCS, Peter How, BCh, MRCS,* Brendan Moran, MB Bchir, FRCSI,†*

- Mercury II
  - Tumores abaixo de 6cm
  - Motivos do estudo
    - Em geral tem maior taxa de pCRM+ (20-36%)
    - Decisão entre amputação e anastomose inconsistente
    - Aprimorar a seleção e conduta com uso da RNM

Quíron
Clínica Cirúrgica Avançada

Fundamentos teóricos

- Mercury II



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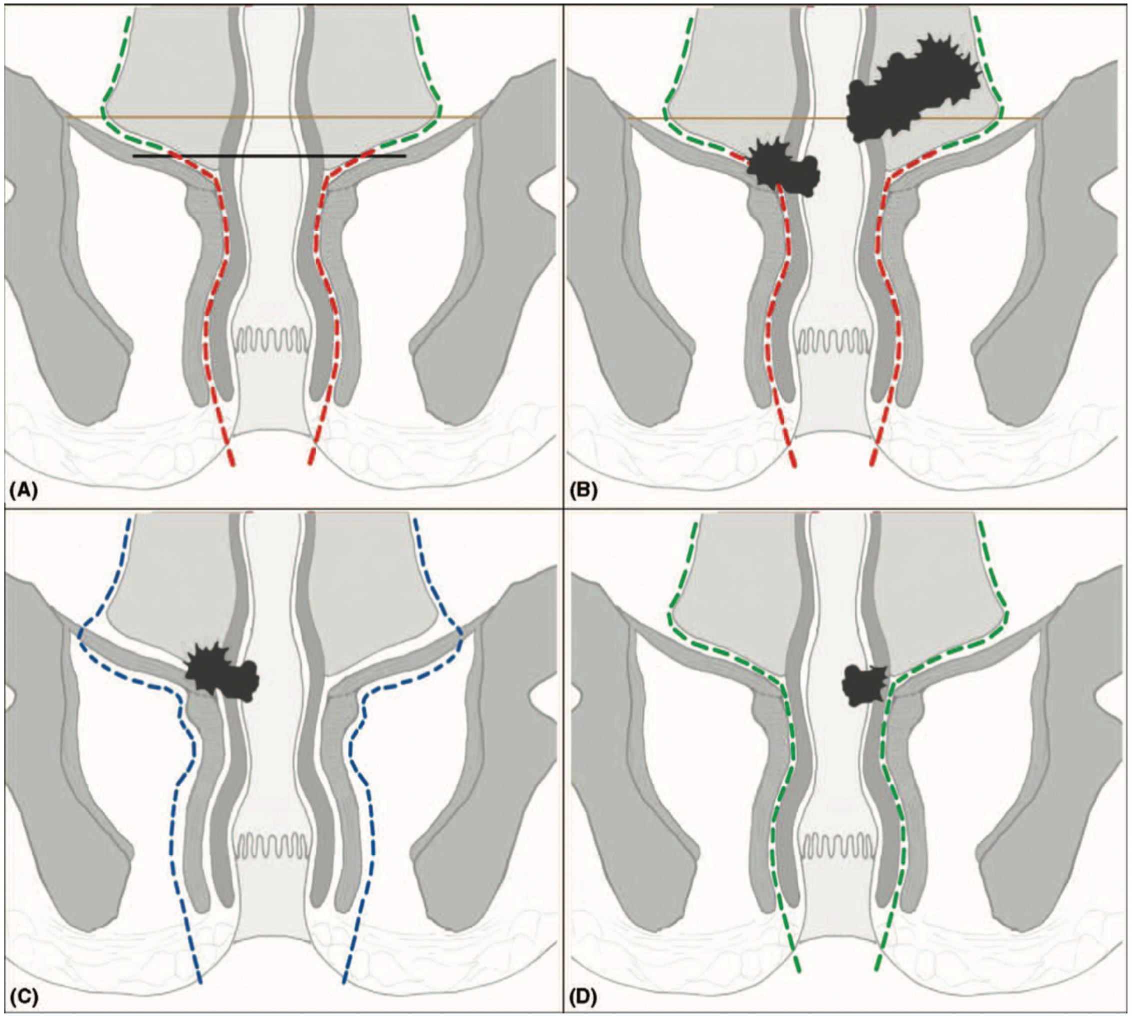
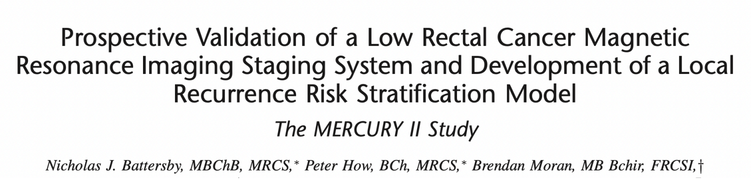


Fundamentos teóricos



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- Mercury II
  - pCRM+: 9%
  - 44% “safe”RNM > cirurgia “upfront” > 98%pCRM-

  - 81% dos “unsafe”receberam QRT
    - 29% responderam bem, destes, nenhum pCRM+
    - 24% tiveram a cirurgia num plano menos radical
    - 25% pCRM+ > oferecer QRT ou amputação parece não ser o suficiente para este grupo > TNT???

  - Tumores ultrabaixos (<4cm) tiveram mais CRM+
  - Tumores anteriores tiveram mais CRM+
  - EMVI foi mais presente nos CRM+ (regressão inadequada?)

Qual T3N1 temos que estar ALERTAS?

- Tumores extra baixos e próximos aos esfíncteres
    - QRT neoadjuvante pode preservar o esfíncter
- A qualidade e margem do mesorreto não podem ser bem asseguradas
- Atenção aos tumores anteriores e ao EMVI
- Quando se planeja preservação de órgão

- Não se esquecer que apesar das baixas taxas de recorrência local, a recorrência sistêmica ainda é alta, cerca de 30%.

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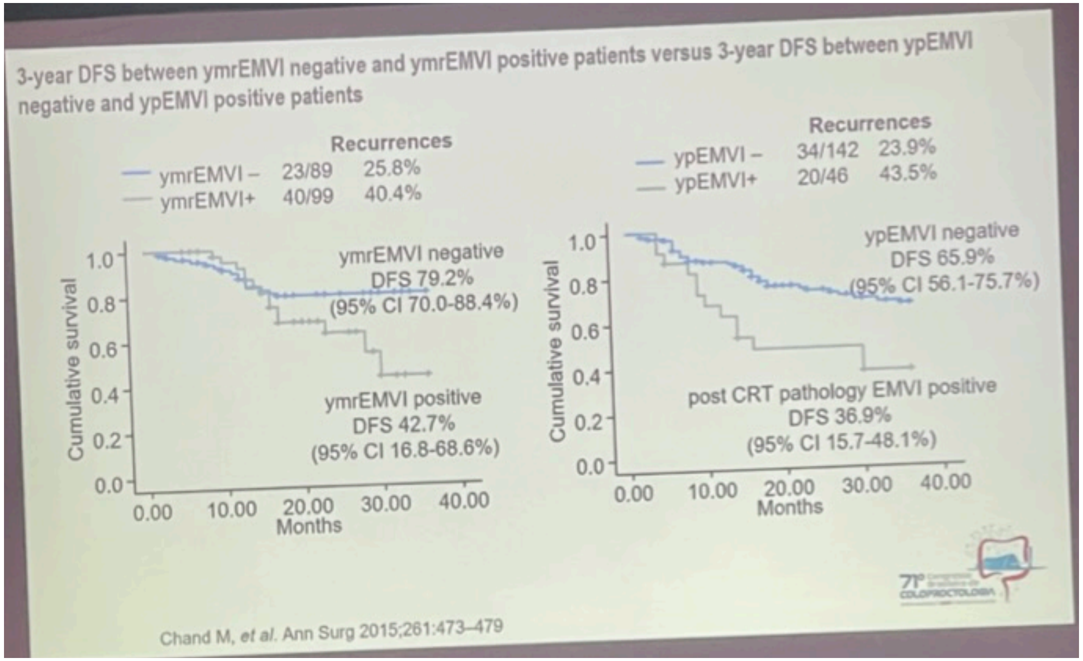
EMVI

- Dados em resumo
  - Negativar o EMVI e TD com CRT aumenta sobrevida
  - Qual maneira ideal de se negativar (TNT?CRT?QT?)
  - Linfonodos aumentados mas EMVI/TD negativos, o prognóstico é favorável



3-year DFS between ymrEMVI negative and ymrEMVI positive patients versus 3-year DFS between ypEMVI negative and ypEMVI positive patients

	Recurrences	
ymrEMVI –	23/89	25.8%
ymrEMVI+	40/99	40.4%

ymrEMVI negative
DFS 79.2%
(95% CI 70.0-88.4%)

ymrEMVI positive
DFS 42.7%
(95% CI 16.8-68.6%)

	Recurrences	
ypEMVI –	34/142	23.9%
ypEMVI+	20/46	43.5%

ypEMVI negative
DFS 65.9%
(95% CI 56.1-75.7%)

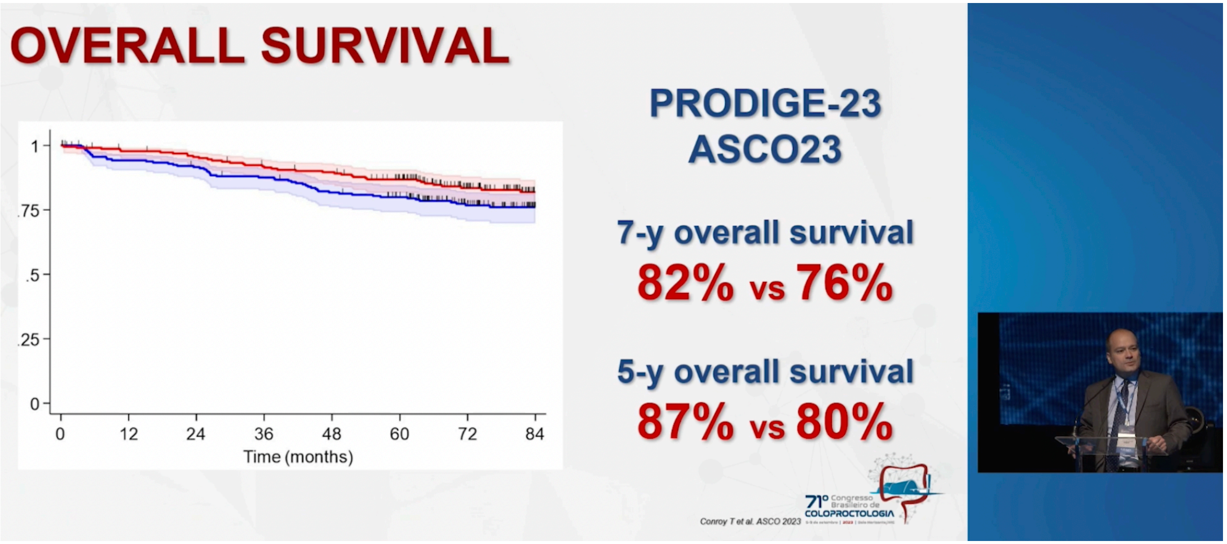
post CRT pathology EMVI positive
DFS 36.9%
(95% CI 15.7-48.1%)

Cumulative survival
1.0
0.8
0.6
0.4
0.2
0.0
0.00
10.00
20.00
30.00
40.00
Months
Cumulative survival
1.0
0.8
0.6
0.4
0.2
0.0
0.00
10.00
20.00
30.00
40.00
Months
71º

Chand M, et al. Ann Surg 2015;261:473–479

TNT

- Dados em resumo
  - Pode ser feito QT de indução ou consolidação
  - Foco que se deu foi no aumento de sobrevida
  - Maior toxicidade
  - Rapido teve recidiva local elevada sem mudar a OS
  - Se tornou padrão?



OVERALL SURVIVAL

PRODIGE-23
ASCO23

7-y overall survival
82% vs 76%

5-y overall survival
87% vs 80%

Conroy T et al. ASCO 2023

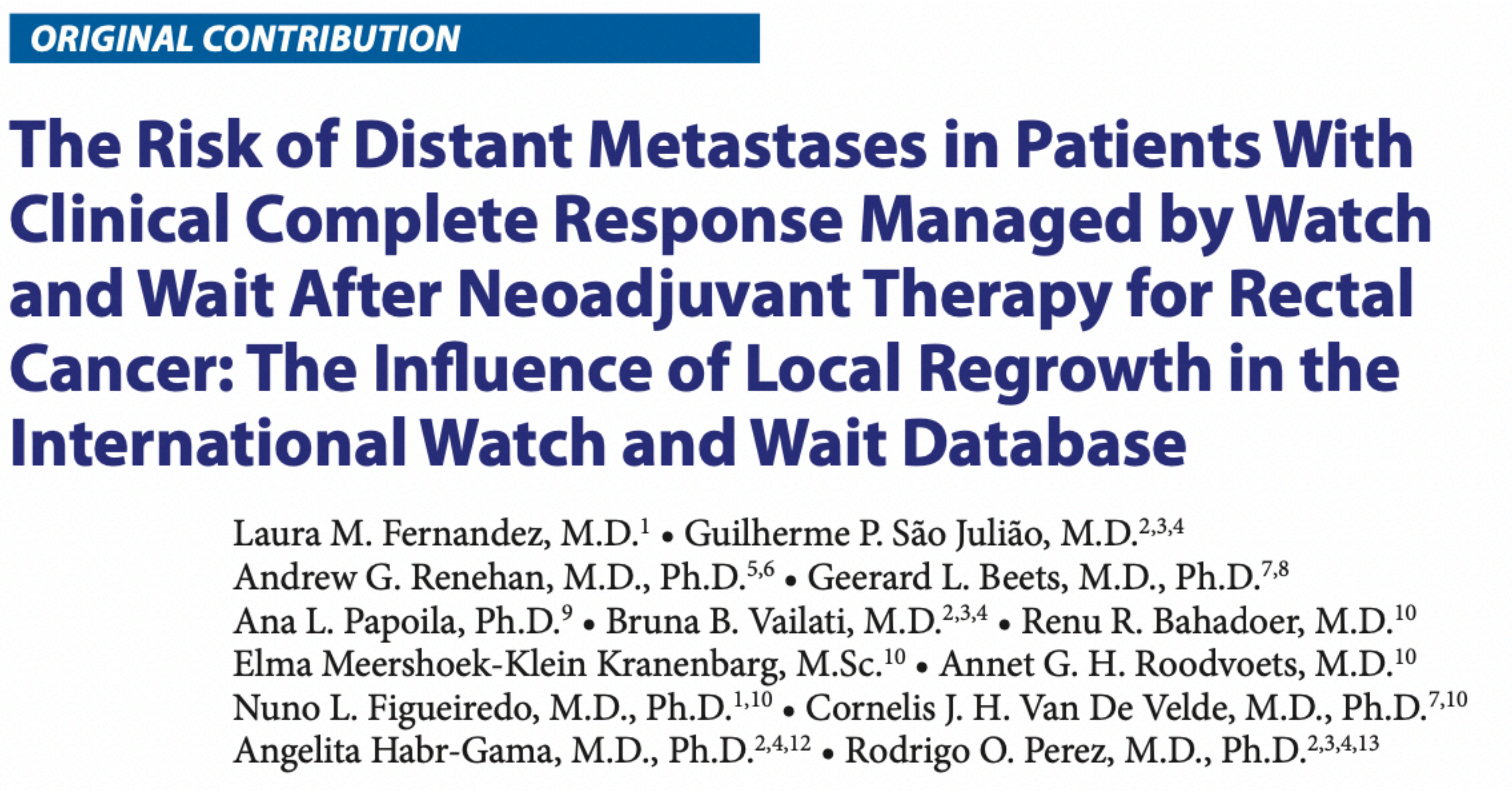
71º Congresso Brasileiro de COLOPROCTOLOGIA

WW

- Dados em resumo
  - Se o objetivo é preservar órgão, tem que ser TNT.
  - A intenção de preservar órgão é válida para tumores que seriam amputados, anastomoses manuais com continência prejudicada, paciente clinicamente ruins para cirurgia.
  - Partilhar com o paciente os dados

WW

- Dados Preocupantes



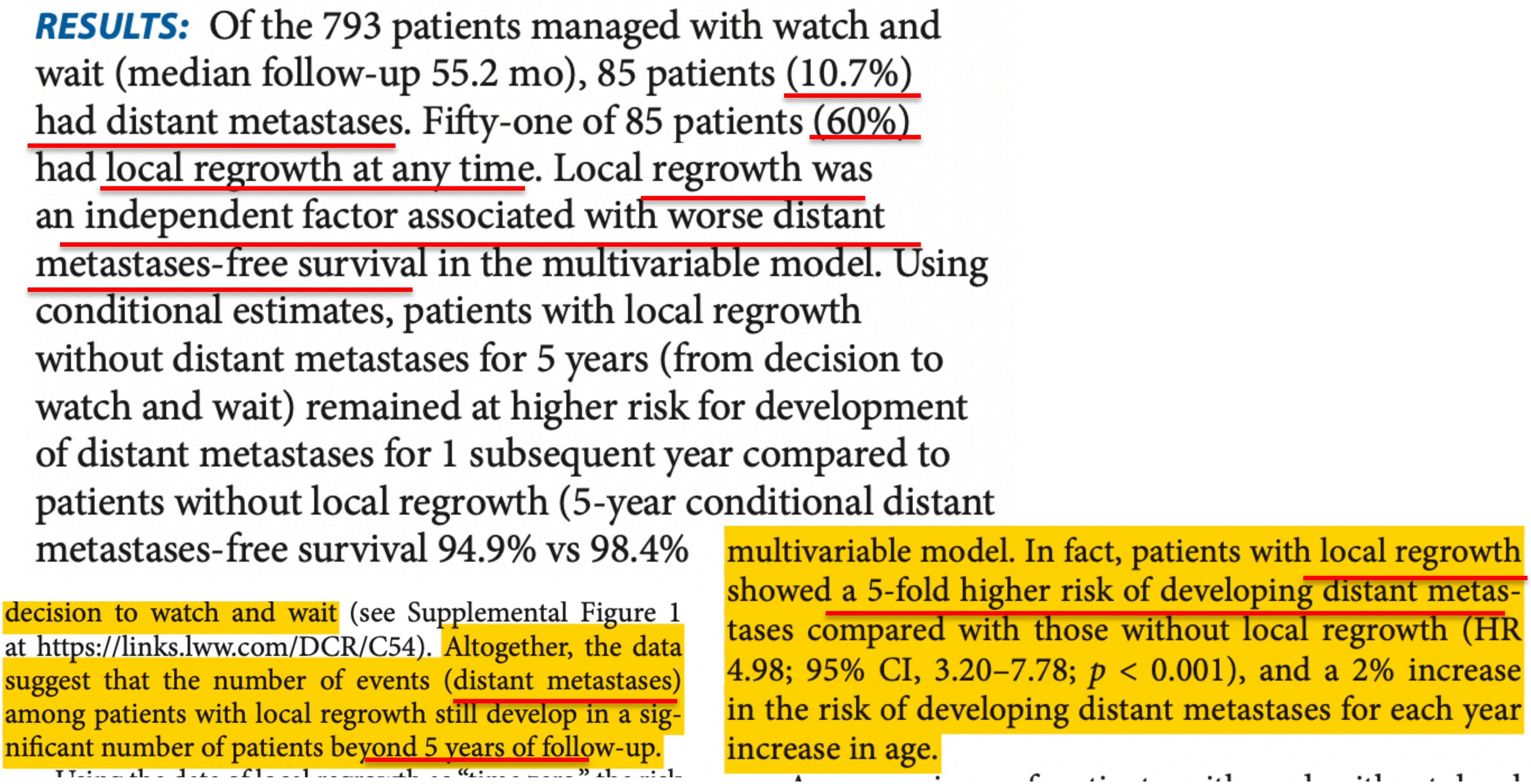
ORIGINAL CONTRIBUTION

The Risk of Distant Metastases in Patients With Clinical Complete Response Managed by Watch and Wait After Neoadjuvant Therapy for Rectal Cancer: The Influence of Local Regrowth in the International Watch and Wait Database

Laura M. Fernandez, M.D.[1] • Guilherme P. São Julião, M.D.[2,3,4]
Andrew G. Renehan, M.D., Ph.D.[5,6] • Geerard L. Beets, M.D., Ph.D.[7,8]
Ana L. Papoila, Ph.D.[9] • Bruna B. Vailati, M.D.[2,3,4] • Renu R. Bahadoer, M.D.[10]
Elma Meershoek-Klein Kranenbarg, M.Sc.[10] • Annet G. H. Roodvoets, M.D.[10]
Nuno L. Figueiredo, M.D., Ph.D.[1,10] • Cornelis J. H. Van De Velde, M.D., Ph.D.[7,10]
Angelita Habr-Gama, M.D., Ph.D.[2,4,12] • Rodrigo O. Perez, M.D., Ph.D.[2,3,4,13]

WW

- Dados Preocupantes



RESULTS: Of the 793 patients managed with watch and wait (median follow-up 55.2 mo), 85 patients (10.7%) had distant metastases. Fifty-one of 85 patients (60%) had local regrowth at any time. Local regrowth was an independent factor associated with worse distant metastases-free survival in the multivariable model. Using conditional estimates, patients with local regrowth without distant metastases for 5 years (from decision to watch and wait) remained at higher risk for development of distant metastases for 1 subsequent year compared to patients without local regrowth (5-year conditional distant metastases-free survival 94.9% vs 98.4%

decision to watch and wait (see Supplemental Figure 1 at https://links.lww.com/DCR/C54). Altogether, the data suggest that the number of events (distant metastases) among patients with local regrowth still develop in a significant number of patients beyond 5 years of follow-up.

multivariable model. In fact, patients with local regrowth showed a 5-fold higher risk of developing distant metastases compared with those without local regrowth (HR 4.98; 95% CI, 3.20–7.78; $p < 0.001$), and a 2% increase in the risk of developing distant metastases for each year increase in age.

THE GOOD
THE BAD
THE UGLY

Médio/alto
T3a-b
N0
CRM-
EMVI/TD -

Baixo
T3a-b, N+
CRM-
EMVI/TD -

T3c-d/T4
EMVI/TD +
CRM+
WW

Lennart Blomqvist & Bengt Glimelius (2008) The 'good', the 'bad', and the 'ugly' rectal cancers, Acta Oncologica, 47:1, 5-8.
G. P. São Julião, A. Habr-Gama, B. B. Vailati, R. O. Perez (2017). The good, the bad and the ugly: rectal cancers in the twenty-first century. Tech Coloproctol.

THE GOOD
THE BAD
THE UGLY

Médio/alto
T3a-b
N0
CRM-
EMVI/TD -

Cirurgia

Baixo
T3a-b, N+
CRM-
EMVI/TD -

CRT

T3c-d/T4
EMVI/TD +
CRM+
WW

TNT

Le lius (2008) The 'good', the 'bad' and the 'ugly' rectal cancers, Acta Oncologica, 47:1, 5-8.
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THE GOOD
THE BAD
THE UGLY

Médio/alto
T3a-b
N0
CRM-
EMVI/TD -

Baixo
T3a-b, N+
CRM-
EMVI/TD -

T3c-d/T4
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CRT

TNT

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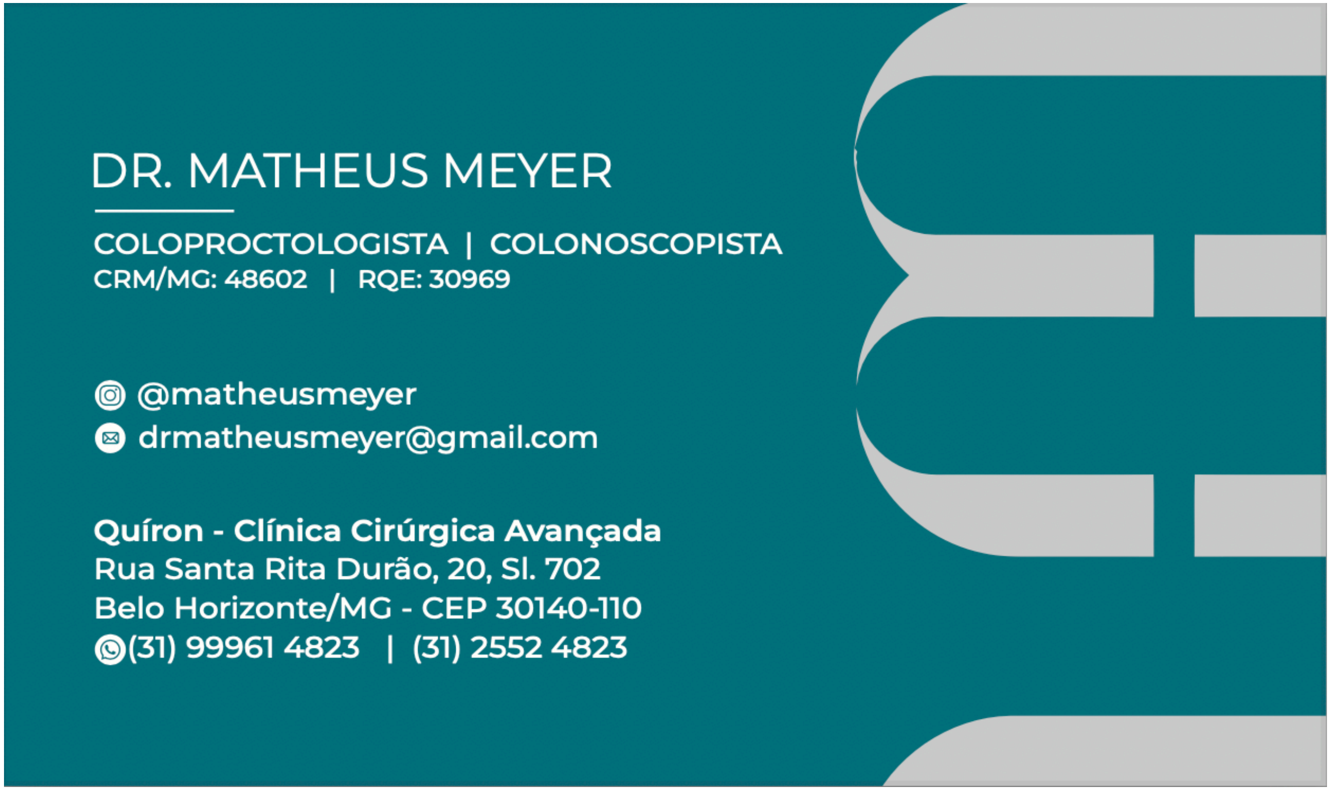
CONCLUSÃO

- O tratamento do câncer de reto é um grande desafio
- Não podemos tratar todos os tumores de reto do mesmo jeito, pois eles são diferentes entre si
- Evidências e estudos muito dinâmicos nos últimos anos
- Fundamental a participação do especialista
- Multidisciplinaridade e decisão em conjunto com o paciente são o grande pilar do tratamento

OBRIGADO



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