



Λαπαροσκοπική προσπέλαση για τον καρκίνο του ορθού:

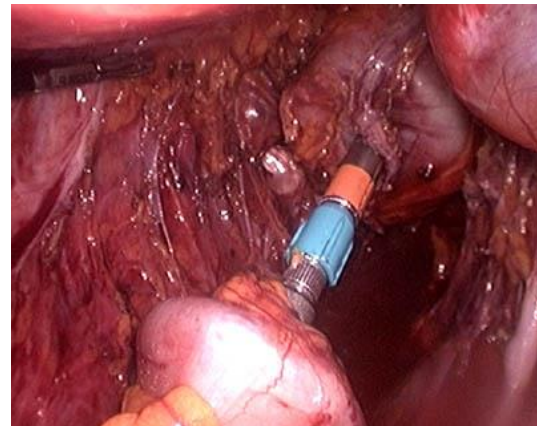
Σύγχρονες αντιλήψεις, πλεονεκτήματα και μειονεκτήματα
έναντι της «ανοικτής»

Δημήτρης Π. Κορκολής
Χειρουργός
Γ.Α.Ο.Ν.Α. «Άγιος Σάββας»

Λαπαροσκοπική Χειρουργική στον καρκίνο του ορθού



William Ernest Miles (1868-1947)



Πλεονεκτήματα

- Μικρότερη απώλεια αίματος
- Ταχύτερη ανάρρωση
- Λιγότερος μετεγχειρητικός πόνος
- Λιγότερες επιπλοκές από το χειρουργικό τραύμα
- Ταχύτερη επάνοδος της εντερικής λειτουργίας
- Καλύτερο αισθητικό αποτέλεσμα
- Γρηγορότερη έξοδος από το νοσοκομείο

Πλεονεκτήματα

- Ακριβέστερη παρασκευή των ιστών λόγω μεγέθυνσης
- Μικρότερος κίνδυνος ενδοκοιλιακών συμφύσεων
- Μειωμένη ανοσοκατασταλτική δράση στον ογκολογικό ασθενή
- Ταχύτερη έναρξη επικουρικής χημειοθεραπείας!!!
 - *25 days (50.1 days [laparoscopic] vs 75.2 days [open], $P < .0001$)*

Μειονεκτήματα

- Τεχνικά απαιτητική επέμβαση
- Μακρά καμπύλη εκμάθησης
- Παρατεταμένος χειρουργικός χρόνος
- Κόστος
- Ογκολογική ασφάλεια σε σχέση με ανοικτή TME???

Celentano V, et al. Int J Colorectal Dis 2017
Velazco JC, et al. Ann Surg 2016
Gyung MC, et al. Ann Coloproctol 2019

Τεχνικά Μειονεκτήματα

- Συγκέντρωση εργαλείων στη στενή πύελο
- Καπνός που εμποδίζει την όραση
- Δυσχερής χειρισμός του ορθού
- Αδυναμία αναγνώρισης του όγκου
- Τεχνικά δύσκολη διατομή του ορθού
- Άκαμπτα εργαλεία
- Πνευμοπεριτόναιο

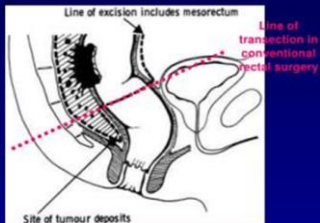
Κρίσιμα Σημεία στη Χειρουργική του Ορθού

- TME ως “the gold standard”
- CRM – Περιμετρικό όριο εκτομής >1mm
- Περιφερικό όριο εκτομής (fresh) >1cm
- Επαρκής λεμφαδενεκτομή ≥ 12 nodes
- ‘MRI-guided’ χρήση της PCRT
- Διαφύλαξη των αυτόνομων νευρικών πλεγμάτων
- Διατήρηση του σφικτηριακού μηχανισμού
- MDTs

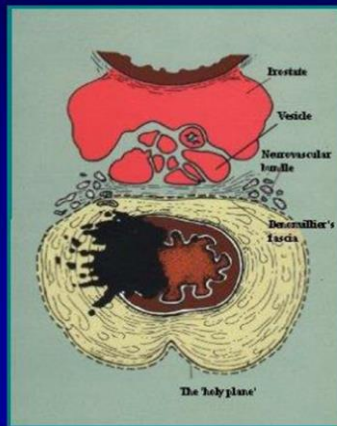
Ολική Εκτομή του Μεσοορθού

The mesorectum in rectal cancer: the clue to pelvic recurrence

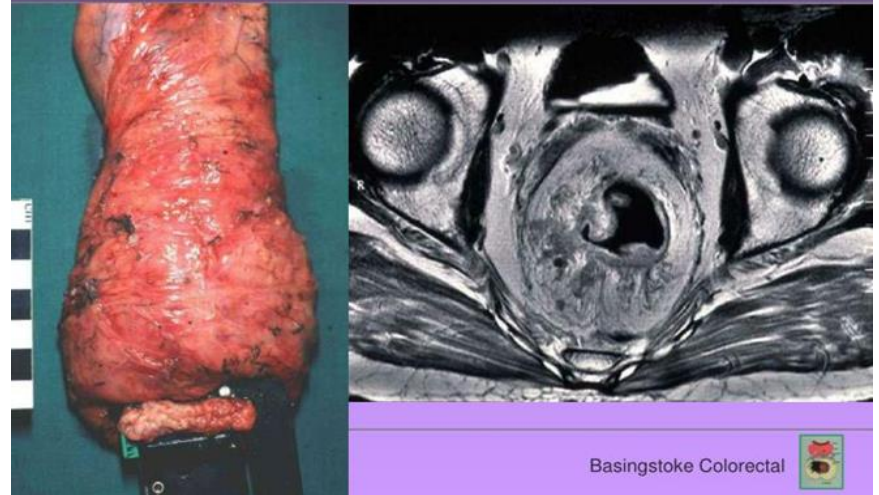
Heald et al. *Br J Surg* 1982; 69: 613-616.



- Isolated tumour deposits can be found within the mesorectum up to 3-4 cm distal to the main tumour

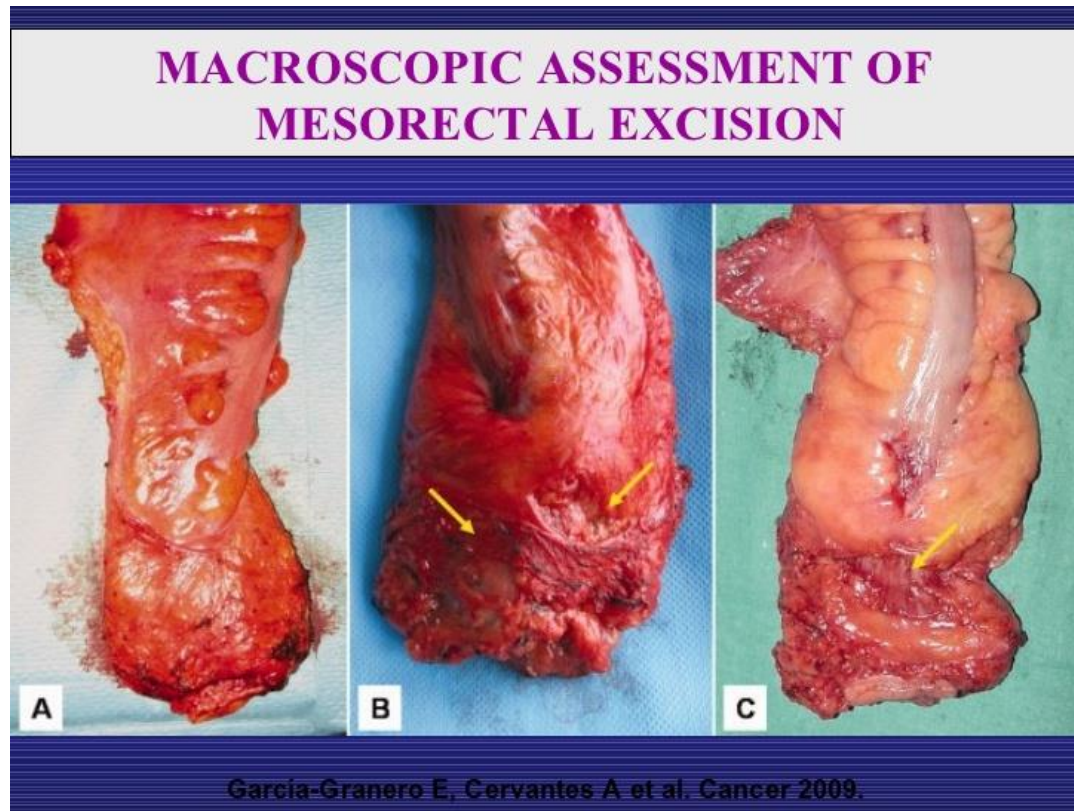


Surgical Technique



Heald RJ, et al. *Br J Surg* 1982

Αξιολόγηση Χειρουργικού Παρασκευάσματος



Complete

Near-complete

Incomplete

Nagtegaal ID, et al. J Clin Oncol 2002
Quirke P, et al. Lancet 1986



Risk - adjusted cumulative sum analysis:

- Change point for conversion Case 61
- Turning point for postop complications Case 79
- Operative time / Transfusion volumes stabilizes Cases 61-75
- Master learning curve for Lap TME Cases 60-80

Standardized Surgical Technique!!!

Major RCTs of laparoscopic vs open TME

Study	Type	n	Stages	Preoperative XRT	Location	Endpoint	Conclusion
CLASICC, ⁹ 2005	RCT	794	Colon and rectum Stage I-IV	Not reported	Not reported	Multiple	"...impaired short-term outcomes after laparoscopic-assisted anterior resection for cancer of the rectum do not yet justify its routine use."
CLASICC, ¹⁰ 2012						OS, DFS, LR	"Long-term results continue to support the use of laparoscopic surgery for both colonic and rectal cancer."
COREAN, ¹² 2014	RCT noninferiority 15% margin	340	Rectum (0-9 cm) Stage II-III	100%	0-3 cm 3-6 cm 6-9 cm	21% 39% 41% 3-y DFS	"...laparoscopic resection for locally advanced rectal cancer after preoperative chemoradiotherapy provides similar outcomes for disease-free survival as open resection, thus justifying its use."
COLOR II, ¹³ 2015	RCT noninferiority 5% margin	1044	Rectum (0-15 cm) Stage I-III	59%	0-5 cm 5-10 cm 10-15 cm	29% 39% 32% 3-y LR	"...laparoscopic surgery is as safe and effective as open surgery in patients with rectal cancers without invasion of adjacent tissues."
Z6051, ¹⁴ 2015	RCT noninferiority 6% margin	486	Rectum (0-12 cm) Stage II-III	100%	0-5 cm 5-10 cm 10-15 cm	51% 35% 14% Composite (neg DM, neg CRM, complete or near-complete TME)	"...the findings do not support the use of laparoscopic resection in these patients."
ALaCaRT, ¹⁵ 2015	RCT noninferiority 8% margin	475	Rectum (0-15 cm) Stage I-IV	50%	0-5 cm 5-10 cm 10-15 cm	35% 43% 22% Composite (neg DM, neg CRM, complete TME)	"...these findings do not provide sufficient evidence for the routine use of laparoscopic surgery."

Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial

Pierre J Guillou, Philip Quirke, Helen Thorpe, Joanne Walker, David G Jayne, Adrian M H Smith, Richard M Heath, Julia M Brown, for the MRC CLASICC trial group*

Lancet 2005

Randomized clinical trial

Five-year follow-up of the Medical Research Council CLASICC trial of laparoscopically assisted *versus* open surgery for colorectal cancer

D. G. Jayne¹, H. C. Thorpe³, J. Copeland³, P. Quirke², J. M. Brown³ and P. J. Guillou¹

Br J Surg 2010

Original article

Long-term follow-up of the Medical Research Council CLASICC trial of conventional *versus* laparoscopically assisted resection in colorectal cancer

B. L. Green¹, H. C. Marshall¹, F. Collinson¹, P. Quirke², P. Guillou³, D. G. Jayne³ and J. M. Brown¹

Br J Surg 2013

Both colon and rectal CA

No attempt to standardize surgical technique

Rectal CA (50%):

CRM+ Lap 12%
 Open 6% (p=0.19)

Conversion rate: 34%!!!

No difference in OS, DFS, and LR at 3yrs and 10yrs follow-up

Open versus laparoscopic surgery for mid-rectal or low-rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): survival outcomes of an open-label, non-inferiority, randomised controlled trial

Seung-Yong Jeong, Ji Won Park, Byung Ho Nam, Sohee Kim, Sung-Bum Kang, Seok-Byung Lim, Hyo Seong Choi, Duck-Woo Kim, Hee Jin Chang, Dae Yong Kim, Kyung Hae Jung, Tae-You Kim, Gyeong Hoon Kang, Eui Kyu Chie, Sun Young Kim, Dae Kyung Sohn, Dae-Hyun Kim, Jae-Sung Kim, Hye Seung Lee, Jee Hyun Kim, Jae Hwan Oh

RCT non-inferiority 15%

340 pts

3 institutions

Clinical stage II – III

Mid – to – Low (0 – 9cm) from anal verge

All PCRT

Conversion rate 1.2%

BMI 24

TME: 92% lap

88% open p=0.41

CRM+ 2.9% lap

4.1% open p=0.77

No diff in OS, DFS, and LR

A Randomized Trial of Laparoscopic versus Open Surgery for Rectal Cancer

H. Jaap Bonjer, M.D., Ph.D., Charlotte L. Deijen, M.D., Gabor A. Abis, M.D., Miguel A. Cuesta, M.D., Ph.D., Martijn H.G.M. van der Pas, M.D., Elly S.M. de Lange-de Klerk, M.D., Ph.D., Antonio M. Lacy, M.D., Ph.D., Willem A. Bemelman, M.D., Ph.D., John Andersson, M.D., Eva Angenete, M.D., Ph.D., Jacob Rosenberg, M.D., Ph.D., Alois Fuerst, M.D., Ph.D., and Eva Haglind, M.D., Ph.D., for the COLOR II Study Group*

N Engl J Med 2015

RCT non-inferiority 5%

1044 pts

30 centers in Europe/South Korea

Stage I – III within 15cm from anus

Conversion rate: 16%

33% of lap pStage I

32% 10 -15cm

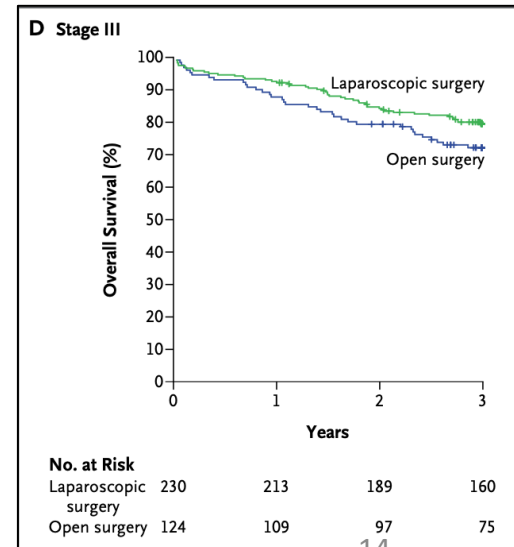
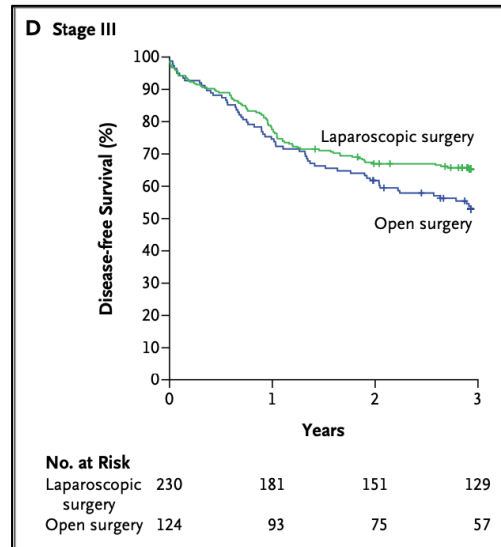
29% 0 – 5cm

59% only PCRT

No diff in TME, 3yr OS, DFS

Table 2. Involved Circumferential Resection Margin and Locoregional Recurrence.

Type of Lesion and Surgery	Involved Circumferential Resection Margin*		Locoregional Recurrence in Intention-to-Treat Population		Locoregional Recurrence in As-Treated Population	
	Patients with Finding†	Between-Group Difference‡ percentage points (95% CI)	Rate	Between-Group Difference‡ percentage points (90% CI)	Rate	Between-Group Difference‡ percentage points (90% CI)
			no./total no. (%)	%	%	%
All lesions						
Laparoscopic surgery	56/588 (10)	-0.5 (-4.9 to 3.5)	5.0	0.0 (-2.6 to 2.6)	4.3	-2.0 (-4.7 to 0.7)
Open surgery	30/300 (10)		5.0		6.3	
Upper rectal lesion						
Laparoscopic surgery	18/196 (9)	-0.1 (-8.2 to 6.4)	3.5	0.6 (-2.9 to 4.1)	3.0	-0.9 (-4.6 to 2.8)
Open surgery	9/97 (9)		2.9		3.9	
Middle rectal lesion						
Laparoscopic surgery	22/228 (10)	6.2 (0.1 to 11.2)	6.5	4.1 (0.7 to 7.5)	5.7	1.6 (-2.3 to 5.5)
Open surgery	4/115 (3)		2.4		4.1	
Lower rectal lesion						
Laparoscopic surgery	15/164 (9)	-12.4 (-23.2 to -3.0)	4.4	-7.3 (-13.9 to -0.7)	3.8	-8.9 (-15.6 to -2.2)
Open surgery	17/79 (22)		11.7		12.7	



Original Investigation

Effect of Laparoscopic-Assisted Resection vs Open Resection of Stage II or III Rectal Cancer on Pathologic Outcomes

The ACOSOG Z6051 Randomized Clinical Trial

James Fleshman, MD; Megan Branda, MS; Daniel J. Sargent, PhD; Anne Marie Boller, MD; Virgilio George, MD; Maher Abbas, MD; Walter R. Peters Jr, MD; Dipen Maun, MD; George Chang, MD; Alan Herline, MD; Alessandro Fichera, MD; Matthew Mutch, MD; Steven Wexner, MD; Mark Whiteford, MD; John Marks, MD; Elisa Birnbaum, MD; David Margolin, MD; David Larson, MD; Peter Marcello, MD; Mitchell Posner, MD; Thomas Read, MD; John Monson, MD; Sherry M. Wren, MD; Peter W. T. Pisters, MD; Heidi Nelson, MD

JAMA 2015

RCT non-inferiority 5%
35 centers in US and Canada
Stage II-III within 12 cm
40 Surgeons with OP report and video
PCRT 100%
More than half in low rectum
Hand-assisted/ robotic: 17% / 14%

Conversion rate: 11.3%

Leak: 2.2%

Composite pathologic endpoint:

- a. DM
- b. CRM
- c. Complete/near complete TME

Table 2. Surgical Success Outcomes

	Laparoscopic Resection (n = 240)	Open Resection (n = 222)	Difference (95% CI)	P Value
Composite Outcome, No. (%)				
Total mesorectal excision complete				
CRM ≤1 mm, DM(+)	1 (0.4)	0		
CRM ≤1 mm, DM(-)	16 (6.7)	14 (6.3)		
CRM >1 mm, DM(+)	2 (0.8)	3 (1.4)		
CRM >1 mm, DM(-)	156 (65.0)	164 (73.9)		
Total mesorectal excision nearly complete				
CRM ≤1 mm, DM(+)	0	1 (0.5)		
CRM ≤1 mm, DM(-)	6 (2.5)	0		
CRM >1 mm, DM(-)	40 (16.7)	29 (13.1)		
Total mesorectal excision incomplete				
CRM ≤1 mm, DM(-)	6 (2.5)	2 (0.9)		
CRM >1 mm, DM(+)	1 (0.4)	0		
CRM >1 mm, DM(-)	12 (5.0)	9 (4.1)		
Percentage (95% CI)^a				
CRM >1 mm or distance = NA	87.9 (83.8 to 92.0)	92.3 (88.8 to 95.8)	-4.4 (-9.8 to 0.98)	.11 ^b
Distal margin negative	98.3 (96.7 to 99.95)	98.2 (96.5 to 99.95)	-0.1 (-2.3 to 2.5)	.91 ^b
Complete or nearly complete total mesorectal excision	92.1 (88.7 to 95.5)	95.1 (92.2 to 97.9)	-3.0 (-7.4 to 1.5)	.20 ^b
Successful resection^d				
Modified intent to treat	81.7 (76.8 to 86.6)	86.9 (82.5 to 91.4)	-5.3 (-10.8 to ∞) ^c	.41
Per protocol ^e	81.7 (76.5 to 86.9)	86.9 (82.5 to 91.4)	-5.3 (-11.0 to ∞) ^c	.41

Original Investigation

Effect of Laparoscopic-Assisted Resection vs Open Resection on Pathological Outcomes in Rectal Cancer

The ALaCaRT Randomized Clinical Trial

Andrew R. L. Stevenson, MB BS, FRACS; Michael J. Solomon, MB BCh, MSc, FRCSI, FRACS;
John W. Lumley, MBBS, FRACS; Peter Hewett, MB BS, FRACS; Andrew D. Clouston, MB BS, PhD, FRCPA;
Val J. GebSKI, MStat; Lucy Davies, MSc; Kate Wilson, BA, MPH; Wendy Hague, MB BS, PhD, MBA;
John Simes, BSc (Med), MB BS, SM, FRACP, MD; for the ALaCaRT Investigators

JAMA 2015

RCT non-inferiority 8%
24 centers in Australia/New Zealand
26 accredited surgeons
Stage I-IV within 15cm
35% of tumors 0-5cm from anus
Only 50% had PCRT

Conversion rate: 9%

Composite pathologic endpoint:

- DM
- CRM
- Complete TME

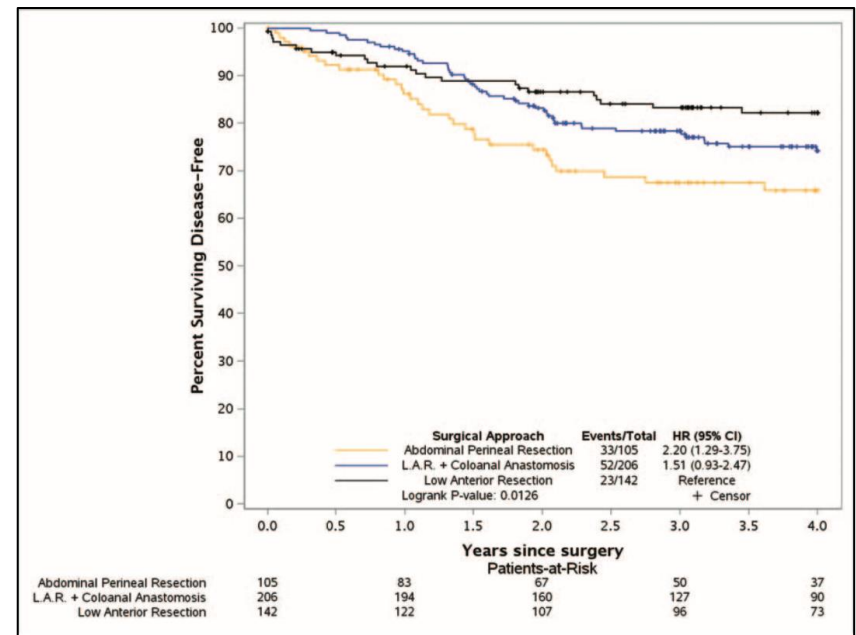
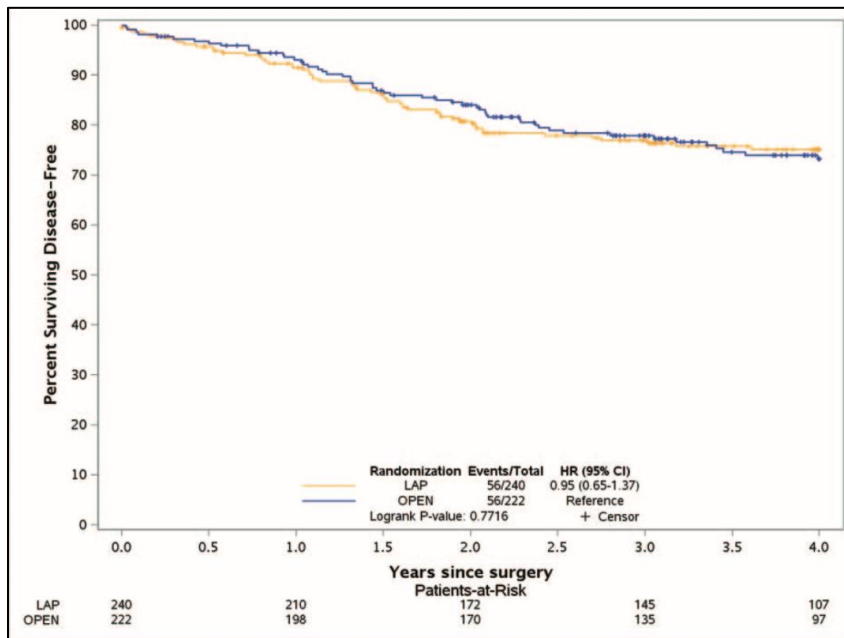
Table 2. Pathological Assessment of Patients in the ALaCaRT Trial

	Laparoscopic Rectal Resection (n = 238)	Open Laparotomy and Rectal Resection (n = 235)	Risk Difference, % (95% CI)	P Value
Primary Outcome				
No. (%) with negative circumferential and distal margins and complete total mesorectal excision	194 (82)	208 (89)	-7.0 (-12.4 to ∞)	.38 ^a
Primary Outcome Components				
Circumferential resection margin, median (IQR), mm	10 (6-20) ^b	12 (6-20) ^c		.43 ^d
No. (%) with negative margin (≥1 mm)	222 (93)	228 (97)	-3.7 (-7.6 to 0.1)	.06
Distal resection margin, median (IQR), mm	26 (15-45) ^b	30 (16-40) ^c		.50 ^d
No. (%) with negative margin (≥1 mm)	236 (99)	234 (99)	-0.4 (-1.8 to 1.0)	.67
Total mesorectal excision, No. (%)				
Complete	206 (87)	216 (92)	-5.4 (-10.9 to 0.2)	
Nearly complete	24 (10)	17 (7)	2.8 (-2.2 to 7.9)	.06
Incomplete	8 (3)	2 (1)	2.5 (-0.06 to 5.1)	

Disease-free Survival and Local Recurrence for Laparoscopic Resection Compared With Open Resection of Stage II to III Rectal Cancer

Follow-up Results of the ACOSOG Z6051 Randomized Controlled Trial

Ann Surg 2019



“Factors that negatively impact DFS after resection of rectal cancer include operation (APR), low position of the tumor, rectal perforation during the resection, and unsuccessful operation based on circumferential radial margin positivity.”

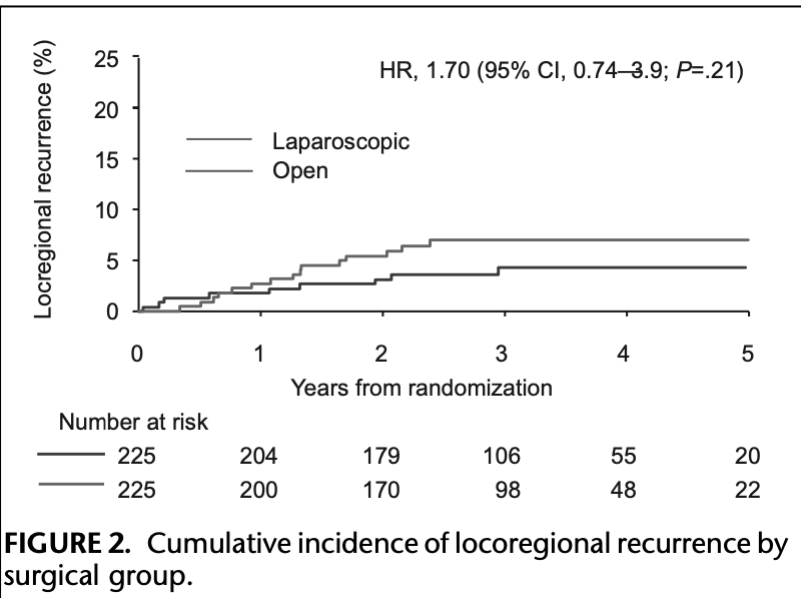
Disease-free Survival and Local Recurrence After Laparoscopic-assisted Resection or Open Resection for Rectal Cancer

The Australasian Laparoscopic Cancer of the Rectum Randomized Clinical Trial

Ann Surg 2019

TABLE 2. Summary Outcomes: Events During Follow-up and Difference in Disease-free Survival and Overall Survival Actuarial Rates at 2 years

Characteristic	Laparoscopic Surgery (n = 225)	Open Surgery (n = 225)	Difference at 2 yrs	95% CI for Difference
Follow-up (IQR), yrs	3.2 (3.0–4.1)	3.3 (3.0–4.2)		
Recurrences	53 (24)	42 (19)	-2.0%*	-9.3% to 5.4%
Locoregional	15	9		
Distant	44	39		
Deaths	27 (12)	26 (12)	0.9%	-3.6% to 5.4%
Rectal cancer	18	14		
Treatment	1	0		
Other	8	12		



“... caution is still needed in recommending laparoscopic procedures and, laparoscopic resection could not be advocated as routine standard treatment...”

Laparoscopy for rectal cancer is oncologically adequate: a systematic review and meta-analysis of the literature

**Alberto Arezzo · Roberto Passera · Alessandro Salvai ·
Simone Arolfo · Marco Ettore Allaix ·
Guido Schwarzer · Mario Morino**

8 RCTs – 19 Non RCTs
2000 – 2013
10861 pts

No significant difference in:

- a. TME
- b. CRM
- c. DM
- d. LNs
- e. DFS
- f. 5-year Local Recurrence rate

Pathologic Outcomes of Laparoscopic vs Open Mesorectal Excision for Rectal Cancer

A Systematic Review and Meta-analysis

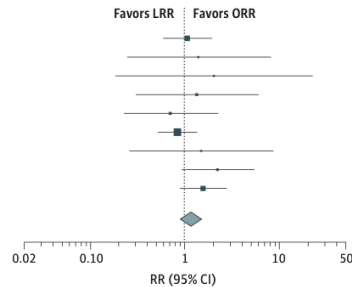
Aleix Martínez-Pérez, MD; Maria Clotilde Carra, PhD; Francesco Brunetti, MD; Nicola de'Angelis, MD, PhD

Figure 2. Forest Plots of the Primary Outcomes

A Circumferential resection margin involvement

Source	LRR		ORR		RR (95% CI)
	No. of Events	Participants	No. of Events	Participants	
Guillou et al, ¹⁵ 2005	30	193	14	97	1.08 (0.60-1.93)
Ng et al, ³⁵ 2008	3	51	2	48	1.41 (0.25-8.09)
Ng et al, ³³ 2009	2	76	1	77	2.03 (0.19-21.88)
Luján et al, ³⁴ 2009	4	101	3	103	1.36 (0.31-5.92)
Kang et al, ¹⁴ 2010	5	170	7	170	0.71 (0.23-2.21)
van der Pas et al, ¹³ 2013	43	588	26	300	0.84 (0.53-1.35)
Ng et al, ³⁰ 2014	3	40	2	40	1.50 (0.26-8.50)
Stevenson et al, ²¹ 2015	16	238	7	235	2.26 (0.95-5.39)
Fleshman et al, ²⁰ 2015	29	240	17	222	1.58 (0.89-2.79)
Total	135	1697	79	1292	1.17 (0.89-1.53)

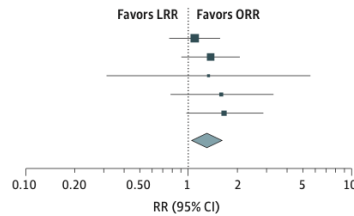
Heterogeneity $\tau^2=0.00$, $\chi^2_8=6.32$ ($P=.61$), $I^2=0\%$
 Test for overall effect: $Z=1.13$ ($P=.26$)



B Noncomplete mesorectal excision

Source	LRR		ORR		RR (95% CI)
	No. of Events	Participants	No. of Events	Participants	
Kang et al, ¹⁴ 2010	47	170	43	170	1.09 (0.77-1.56)
van der Pas et al, ¹³ 2013	77	666	28	331	1.37 (0.91-2.06)
Ng et al, ³⁰ 2014	4	40	3	40	1.33 (0.32-5.58)
Fleshman et al, ²⁰ 2015	19	240	11	222	1.60 (0.78-3.28)
Stevenson et al, ²¹ 2015	32	238	19	235	1.66 (0.97-2.85)
Total	179	1354	104	998	1.31 (1.05-1.64)

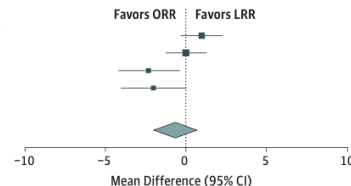
Heterogeneity $\tau^2=0.00$, $\chi^2_4=2.11$ ($P=.71$), $I^2=0\%$
 Test for overall effect: $Z=2.36$ ($P=.02$)



B Distance to radial margin

Source	Distance, mm						Mean Difference (95% CI)
	LRR			ORR			
	Mean	(SD)	Total	Mean	(SD)	Total	
Kang et al, ¹⁴ 2010	9	(5.92)	170	8	(5.92)	170	1.00 (-0.26 to 2.26)
van der Pas et al, ¹³ 2013	10	(9.62)	588	10	(8.14)	300	0.00 (-1.21 to 1.21)
Fleshman et al, ²⁰ 2015	10.5	(9.2)	240	12.8	(11.2)	222	-2.30 (-4.18 to -0.42)
Stevenson et al, ²¹ 2015	10	(10.37)	211	12	(10.37)	201	-2.00 (-4.00 to 0.00)
Total			1209			893	-0.67 (-2.16 to 0.83)

Heterogeneity $\tau^2=1.69$, $\chi^2_3=11.46$ ($P=.009$), $I^2=74\%$
 Test for overall effect: $Z=0.87$ ($P=.38$)



Key Points

Question What are the pathologic outcomes of laparoscopic rectal resection compared with open rectal resection for rectal cancer?

Finding Based on this systematic review and meta-analysis of 14 randomized clinical trials, the risk of achieving a noncomplete (incomplete or nearly complete) mesorectal excision is significantly higher in patients undergoing laparoscopic compared with open rectal resections.

Meaning These pathologic findings challenge the oncologic safety of laparoscopy for the treatment of rectal cancer.

Noncomplete (incomp/nearcomp) TME

lap	13.2%	
open	10.4%	p=0.02

Surgical resection for rectal cancer. Is laparoscopic surgery as successful as open approach? A systematic review with meta-analysis

Marco Milone^{1*}, Michele Manigrasso¹, Morena Burati¹, Nunzio Velotti¹, Francesco Milone¹, Giovanni Domenico De Palma²

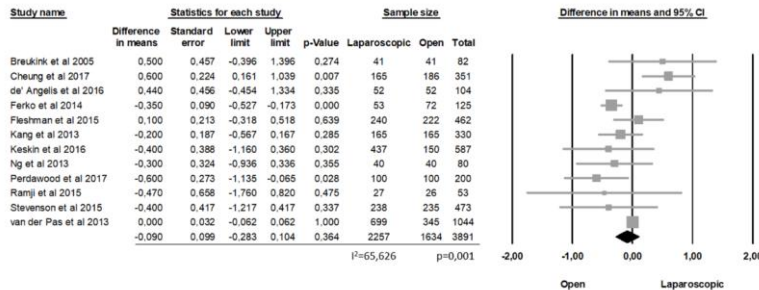


Fig 1. Distance from distal margin of the specimen (DRM).

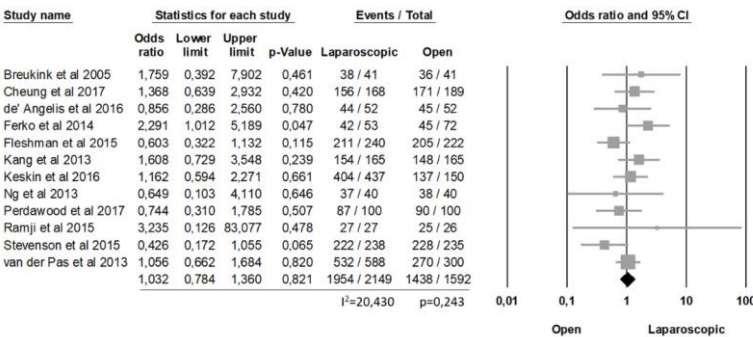


Fig 2. Clear CRM.

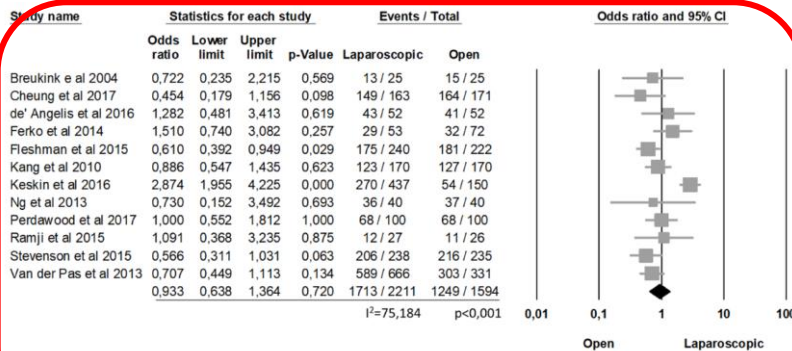


Fig 3. Complete TME.

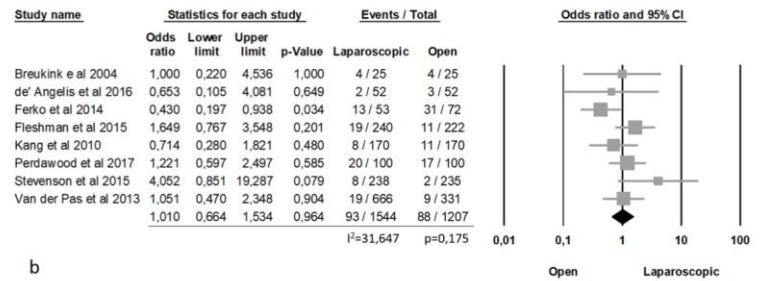
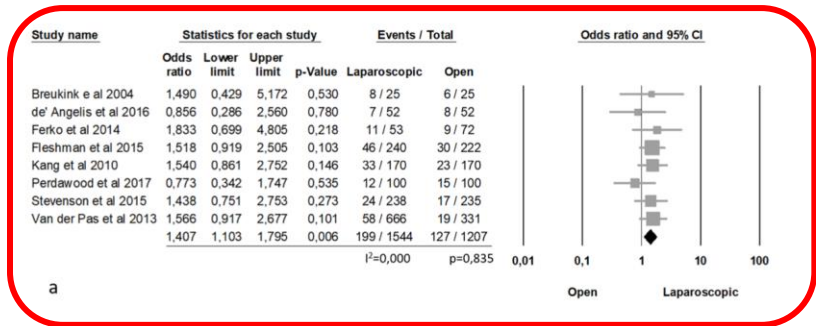


Fig 4. a) nearly complete TME; b) incomplete TME.

"...mesorectal shearing caused by traction with rigid instruments in the narrow pelvic cavity during laparoscopic TME..."



Rectal Cancer

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- ▶ **Some studies have shown that laparoscopy is associated with similar short- and long-term outcomes when compared to open surgery,³ whereas other studies have shown that laparoscopy is associated with higher rates of circumferential margin positivity and incomplete TME.^{4,5} Therefore, minimally invasive resection may be considered based on the following principles:**

- ◇ **The surgeon should have experience performing minimally invasive proctectomy with TME.**
- ◇ **It is not indicated for locally advanced disease with a threatened or high-risk circumferential margin based on staging. For these high-risk tumors, open surgery is preferred.**
- ◇ **It is not generally indicated for acute bowel obstruction or perforation from cancer.**
- ◇ **Thorough abdominal exploration is required.**

Συμπεράσματα

- Lap TME μπορεί να γίνει με ασφάλεια
- Χειρουργική εμπειρία και εξειδίκευση
- Τυποποιημένη τεχνική
- Καλύτερα βραχυπρόθεσμα αποτελέσματα
- Ικανοποιητική έκβαση σε όγκους άνω/μέσου 3μορίου
- CA κάτω 3μορίου???
- Μακροπρόθεσμες Επιβιώσεις...
- Μετα – Αναλύσεις...
- Εξατομικευμένη προσέγγιση!