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Advances and Challenges in the Surgical Treatment of Locally Advanced Rectal Cancer

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I have no disclosures

OUTLINE

- List some recent advances in the management of rectal cancer
- Importance of surgical technique in rectal cancer surgery
- Evidence supporting the use of laparoscopy in rectal cancer
- Rationale and recent experience for the use of the robotic surgery in rectal cancer
- Discuss the principles of transanal TME

Advances in the management of LARC

- Clinical staging and risk stratification using MRI
  - Mesorectal fascia
  - Nodal staging
  - EMVI
- Neoadjuvant therapy:
  - SCRT vs. CMRT
  - Induction chemotherapy
- Pathology: understanding the cause of local recurrence
  - CRM positivity
  - Completeness of the mesorectal excision
- Surgery:
  - Sphincter saving procedures
  - Minimally invasive
  - Organ preservation (Local excision and Watch & Wait)

Surgical Technique Matters

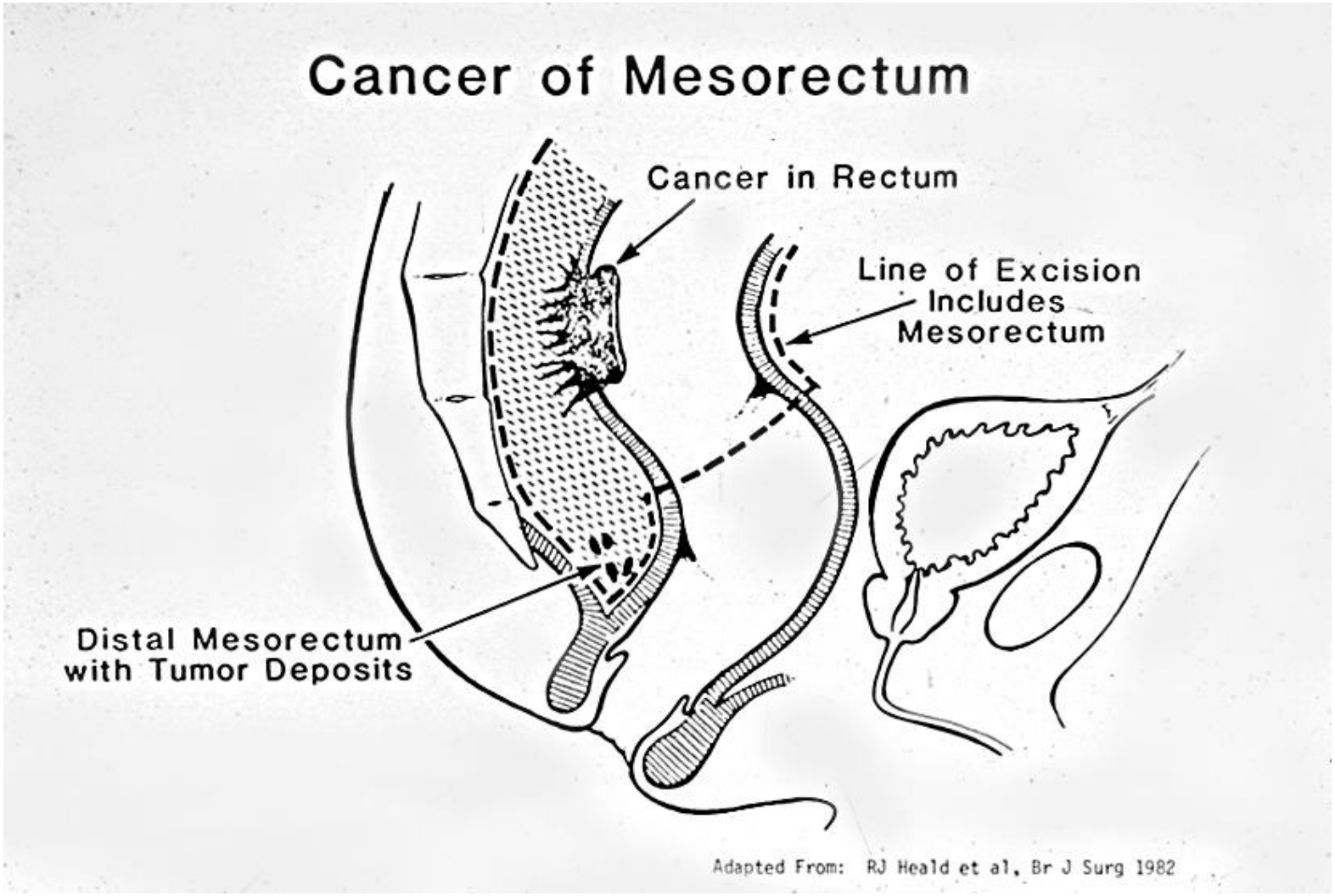
Local Recurrence After Radical Surgery For Rectal Cancer

Variation Between Surgeons

Philips et al, 1984	5 - 20%
McArdle et al, 1991	0 - 21%
Holm et al, 1997	0 - 41%

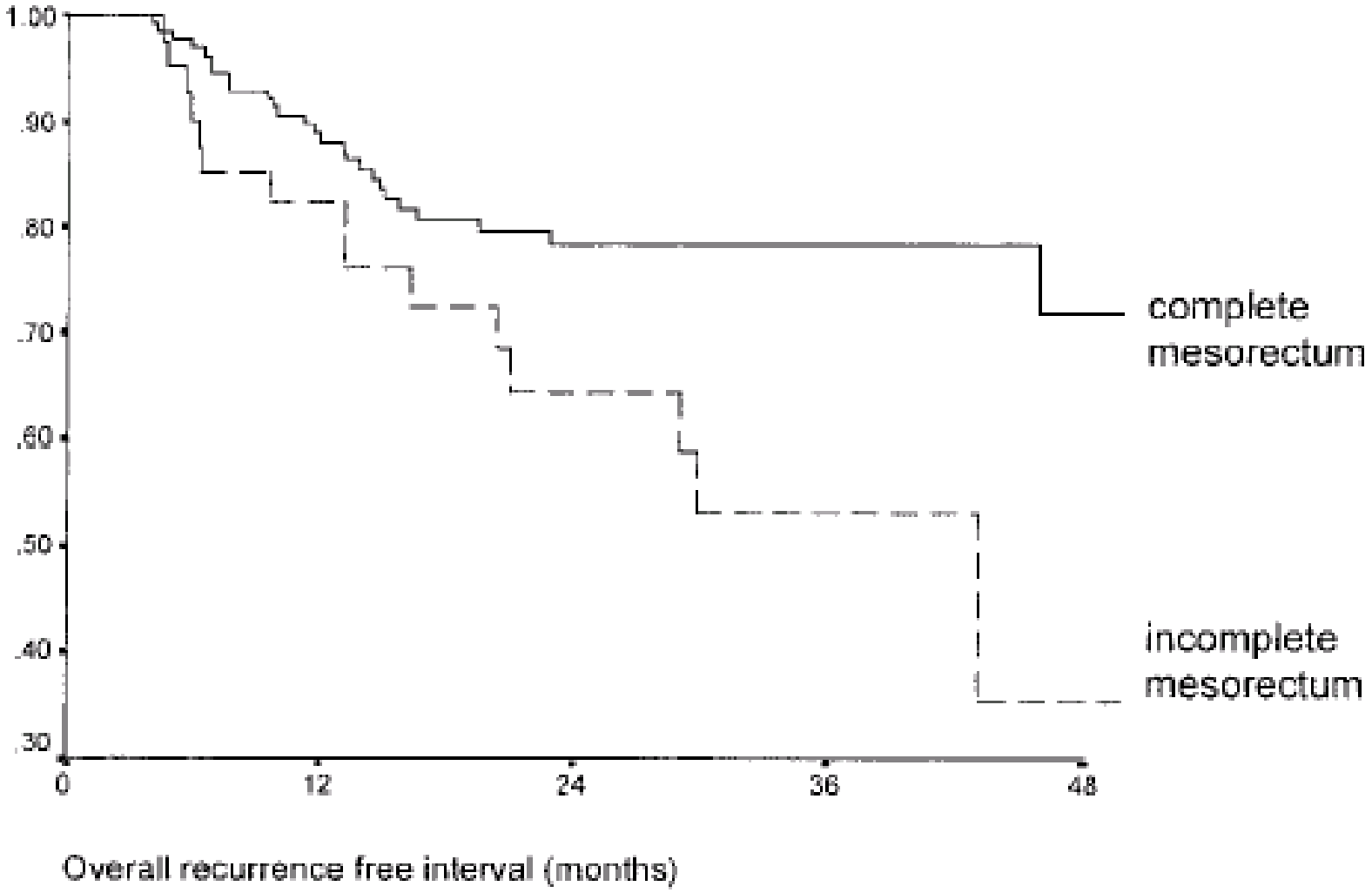
Distal Mesorectal Spread

Total Mesorectal Excision

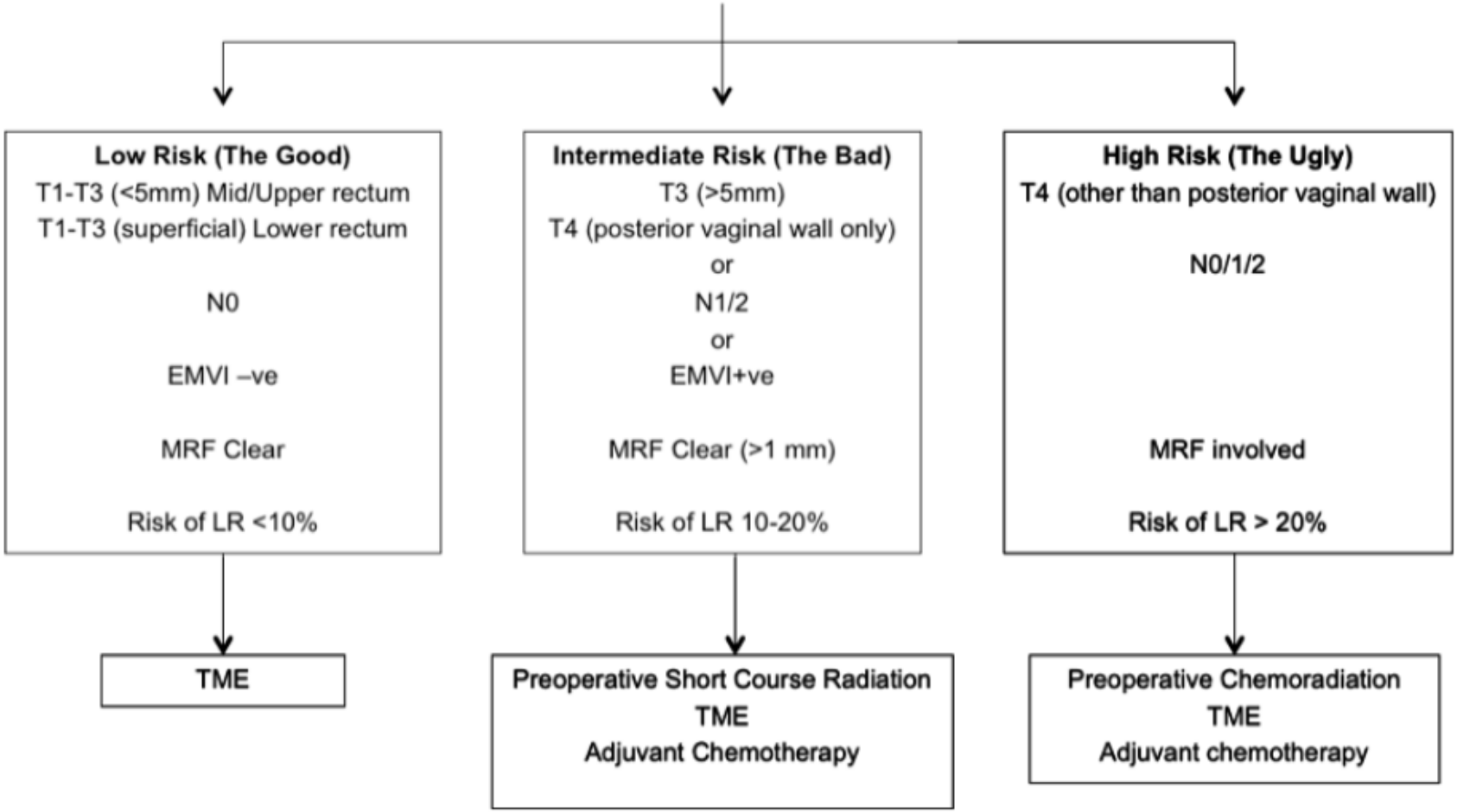


TME Specimen

Recurrence-Free Interval by Completeness of Mesorectal Excision

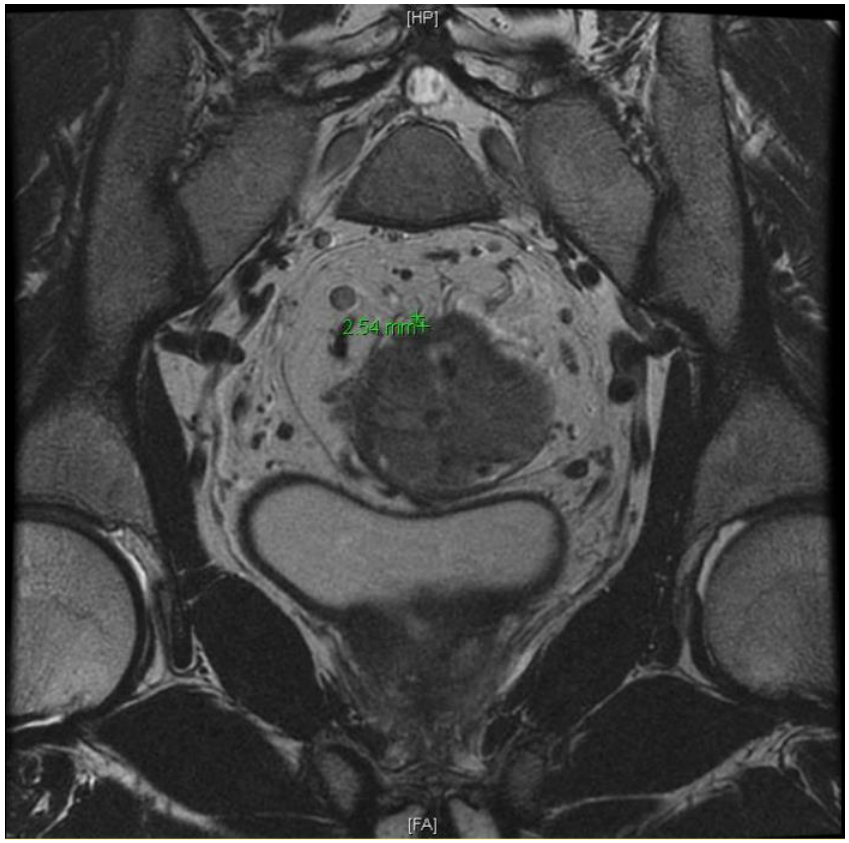


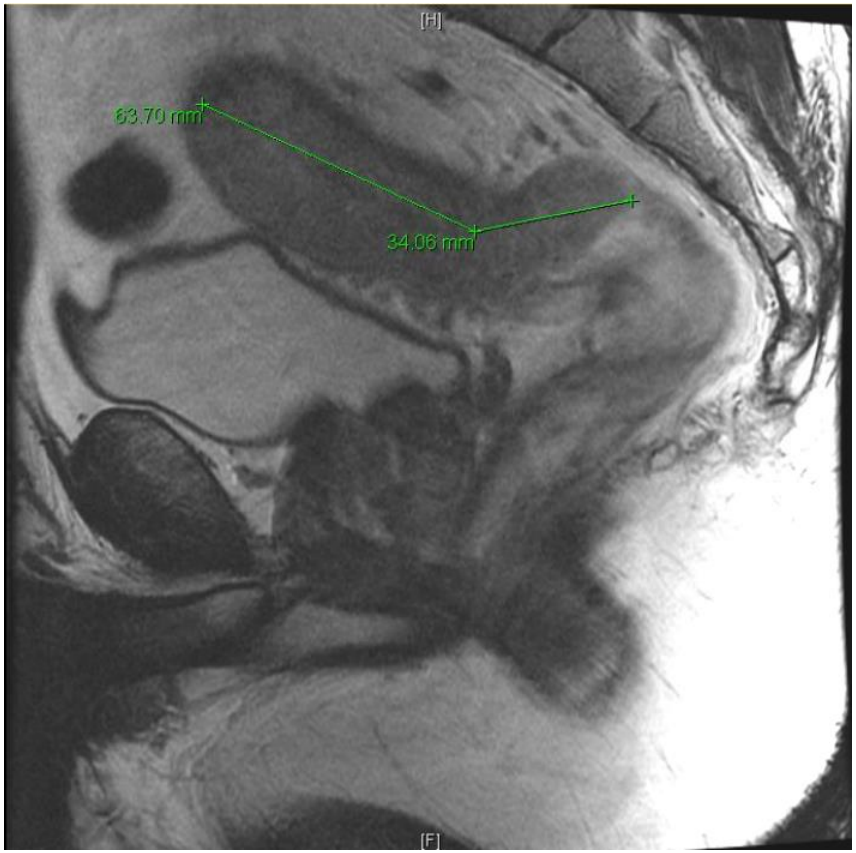
Risk Stratification
Rectal MRI



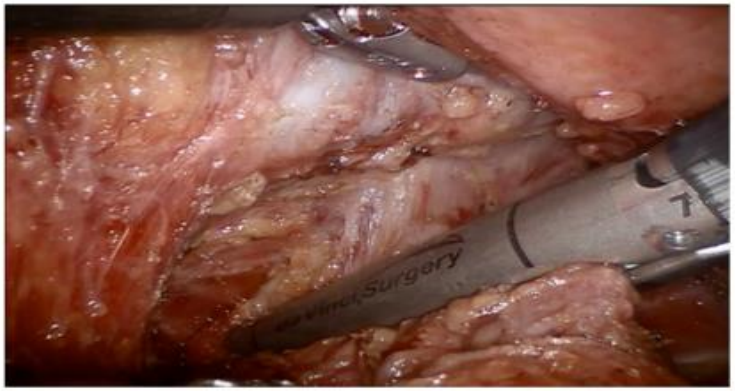
MRI helps selecting the best procedure for each patient

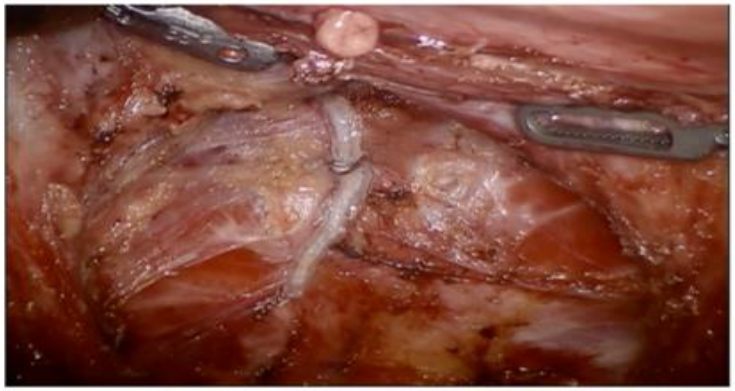
Mid rectal cancer

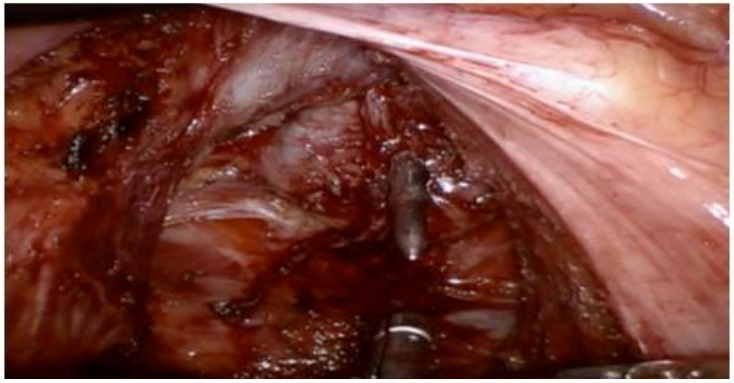




TME with double stapled anastomosis



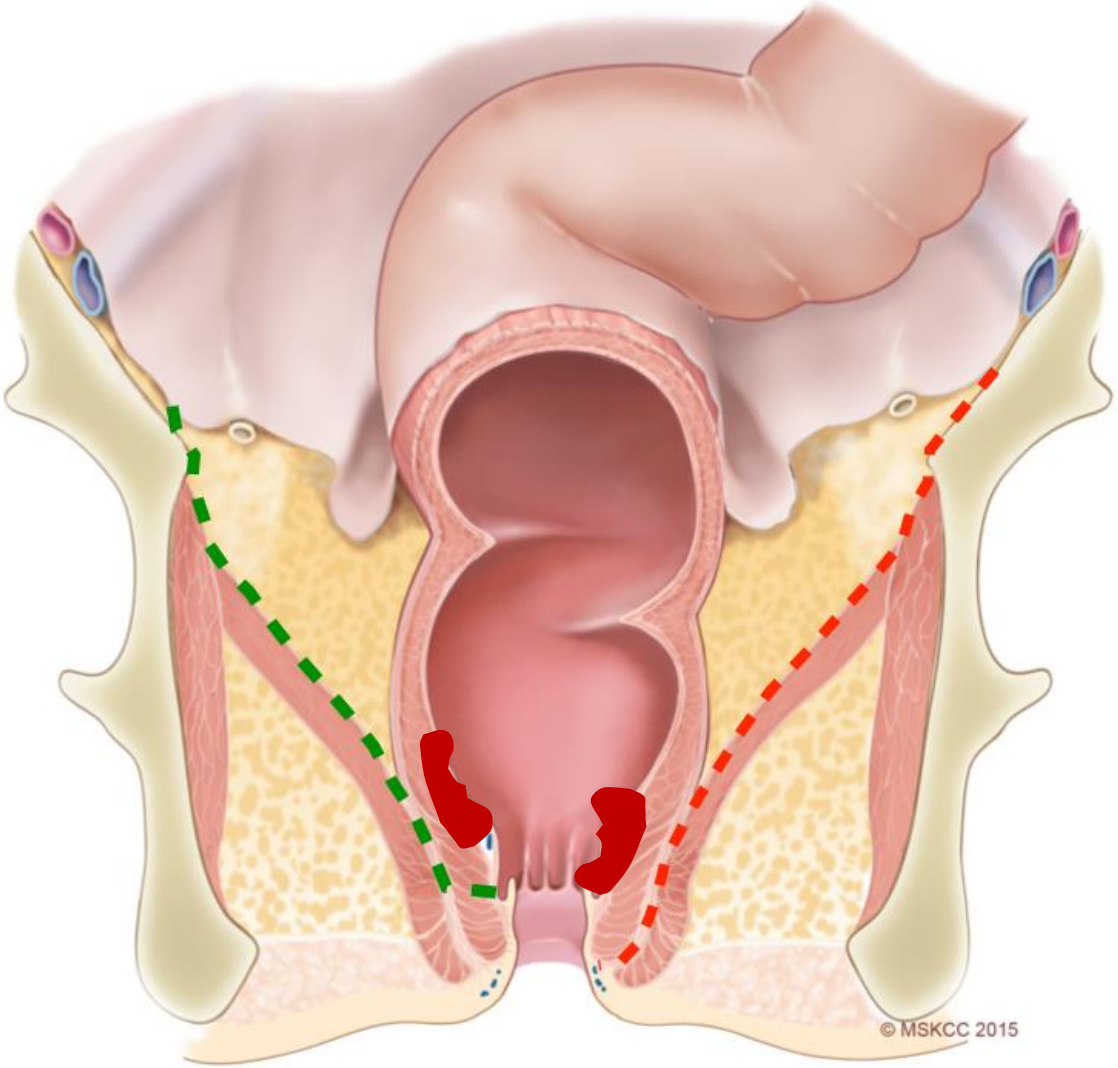




Functional outcomes after stapled LAR

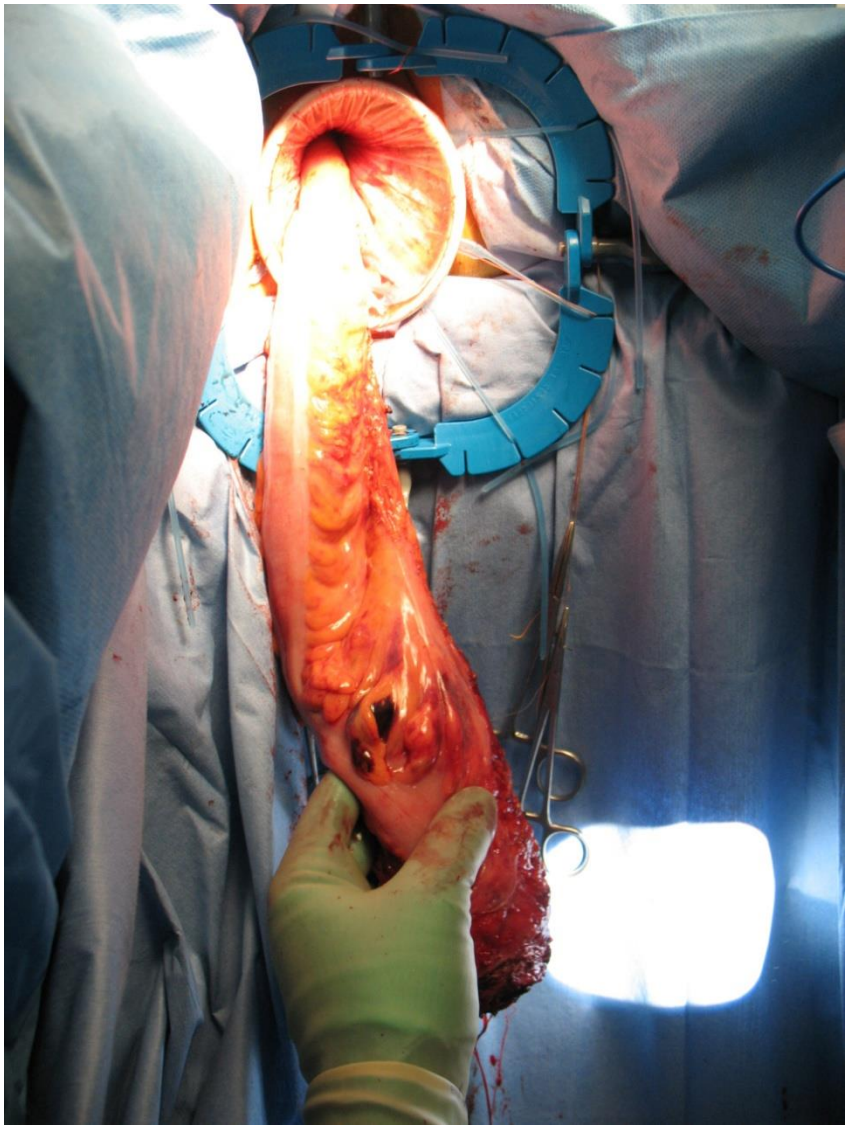
Urinary retention/incontinence		39%
Impairment of sexual function		
women	29%	
men	45%	
Bowel dysfunction (LAR syndrome)		38%

Ultralow (Intersphincteric) Anastomosis



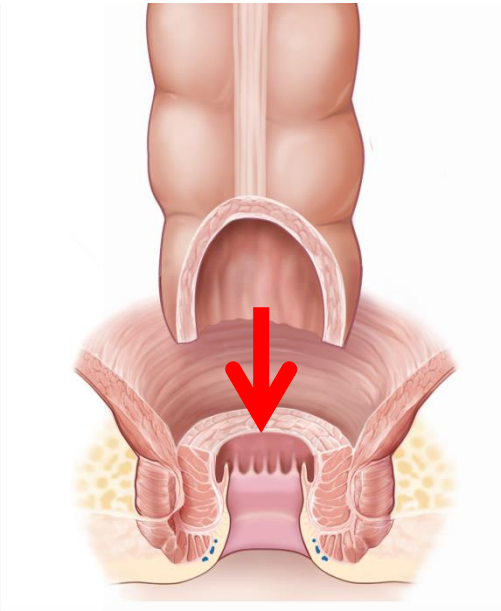
ring

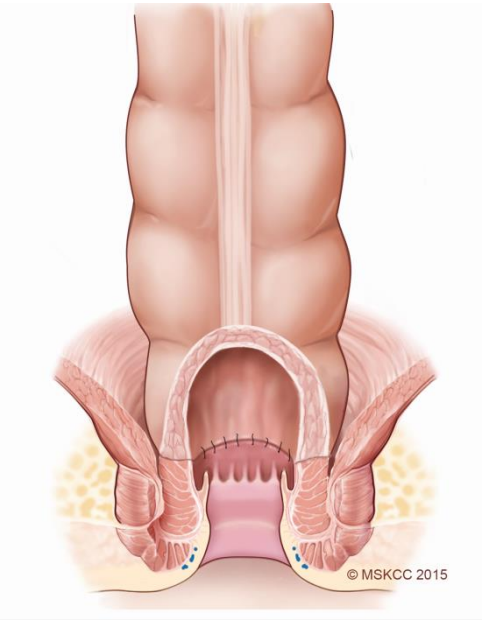
Transanal Extraction of Specimen

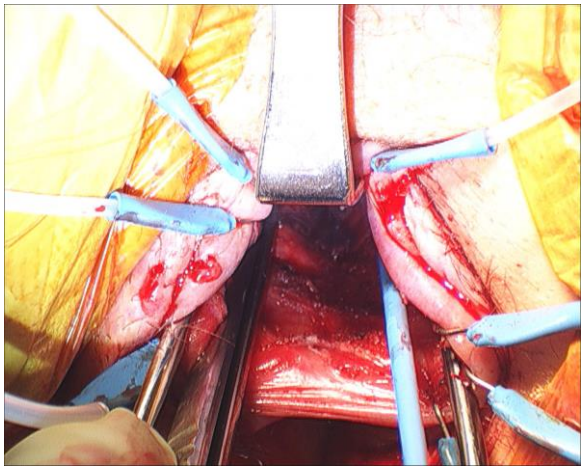


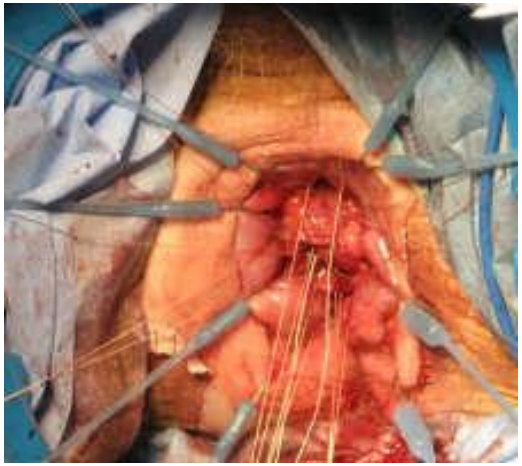
Memorial Sloan Kettering Cancer Center

Colo-anal Anastomosis









Distal Margin in Local Recurrence

627 patients, all stages rectal cancer treated with LAR at MSKCC

+ CRM	**1.4%**
Overall recurrence	
5 years	19%
10 years	25%
Pattern of Recurrence	
Distant	19%
Pelvic	5.4%
Mucosal	2.6%
Risk Factors for Local Recurrence	
Advanced stage	2- 5 X
Lymphovascular invasion	2 X
< 6 cm from anal verge	2 X
Distal resection margin < 8 mm	1 - 3 X

Intersphincteric Resection Morbidity/Mortality

%	Leak	Stricture	Fistula	Pelvis Sepsis	Wound Comp	Bleeding	Bowell Obstruction	Mortality
Braun 1992	10	3	0	0	8	0	3	3
Bannon 1995	0.9	0.9	0.9	0.9	1.8	0.9	0.9	1
Kohler 2000	49	10	19	0	3	6	10	0
Kim 2001	6.2	6.2	4.2	NR	NR	NR	8.3	NR
Luna-Perez 2003	9.4	6.2	6.25	9.3	6.25	NR	6.25	NR
Rullier 2005	11	0	2	3	0	7	0	0
Saito 2006	10.1	0	1.3	4.4	0	1.3	0	0.4
Krand 2009	4	2	0	2	9	0	2	0
Weiser 2009	5	16	5	7	0	7	0	0
Yamada 2009	4.7	8.4	0	0	3.7	0	8.4	0
Lim 2011	1.8	6.3	0.9	2.7	NR	NR	1.8	0
Benis 2012	7	NR	NR	NR	NR	1.6	2.6	0.4
Konanz 2013	NR	NR	NR	NR	NR	NR	15	NR
Akagi 2013	8.4	4.8	1.2	1.2	NR	NR	2.4	0

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Akagi 2013	8.4	4.8	1.2	1.2	NR	NR	2.4	0

Overall Morbidity 7.5%-38%

Intersphincteric Resection Functional Outcomes

%	n	ARM	Tool	Bowel Mov/24hs	Perfect Continence	Flatus Incont.	Soiling	Urgency
Braun 1992	63	No	Mayo	2.2	75	23	15	22
Kohler 2000	31	Yes	Gen. Questionnaire	3.3	30	11	63	NR
Kim 2001	48	No	Kirwan	4.4	NR	NR	NR	NR
Tiret 2003	25	No	NR	2.5	50	23	27	19
Schissel 2005	121	Yes	Williams & Johnson Class.	2.2	86.3	NR	13.7	NR
Saito 2006	228	No	CCII	NR	32.7	29.1	29.1	NR
Chamlou 2007	90	No	CCII	2.3	41	25	59	19
Yamada 2009	107	No	CCII	3.7	42.3	NR	27.9	NR
Han 2009	40	No	Kirwan	2.7	43	29	29	31
Krand 2009	47	No	Kirwan	2.3	80	9	11	2
Kuo 2011	22	No	CCII	4.7	NR	NR	NR	19
Akagi 2012	83	Yes	CCII/Kirwan	5.1	NR	16	22	33
Koyama 2014	37	No	CCII	3.7	NR	NR	NR	22-57

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Saito 2006	228	No	CCII	2.2-5.1	32.7	9-29%	29.1	2-57%
Chamlou 2007	90	No	CCII	2.3	30-80%	25	11-59%	19
Yamada 2009	107	No	CCII	3.7	42.3	NR	27.9	NR
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Intersphincteric Resection Oncologic Results

%	n	Median FU	LR	5Y DFS	5Y OS
Braun 1992	63	80	11	62	NR
Marks 1993	52	50	14	85	NR
Bannon 1995	109	40	11	87	NR
Mohiuddin 1998	48	48	15	82	NR
Kohler 2000	31	82	10	79	NR
Kim 2001	48	26	4.1	NR	NR
Nakagoe 2004	184	47.4	9.5	NR	73.6
Rullier 2005	92	40	2	81	70
Schiessel 2005	121	94	5.3	88	NR
Saito 2006	228	41	3.6	92	83
Akasu 2008	120	42	6.7	91	77
Krand 2009	47	68	2	85	82
Weiser 2009	44	47	0	93	86
Yamada 2009	107	41	2.5	92	87
Han 2010	310	84	11.6	66	NR
Lim 2011	111	29.4	5.4	NR	NR
Kuo 2011	162	5.5	7.7	83	76
Reshef 2011	986	60	3	71	69
Akagi 2012	83	60	11.3	74	87
Koyama 2014	77	76.5	6	NR	76.4

Intersphincteric Resection Oncologic Results

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Braun 1992	63	80	11	62	NR
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Saito 2006	228	41	2-15%	62-93%	69-87%
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Reshef 2011	986	60	3	71	69
Akagi 2012	83	60	11.3	74	87
Koyama 2014	77	76.5	6	NR	76.4

Intersphincteric Resection
Quality of Life

	n	Tool	Control Group	Results
Renner 1999	65	Specific questionnaire	Anterior Resection	Worse results ISR
Bretagnol 2004	40	SF36/FIQL	Conventional Coloanal anastomosis	-No diff. SF36 -ISR worse Embarrassment scores in FIQL
Barisic 2011	45	EORTC QLQ C30 FIQL	Partial vs total ISR	-No diff. EORTC -FIQL worse results with more IAE resection
Konanz 2013	25	EORTC C30-CR38	AR-APR	Overall similar QOL ISR more gastrointestinal symptoms

Intersphincteric Resection
Quality of Life

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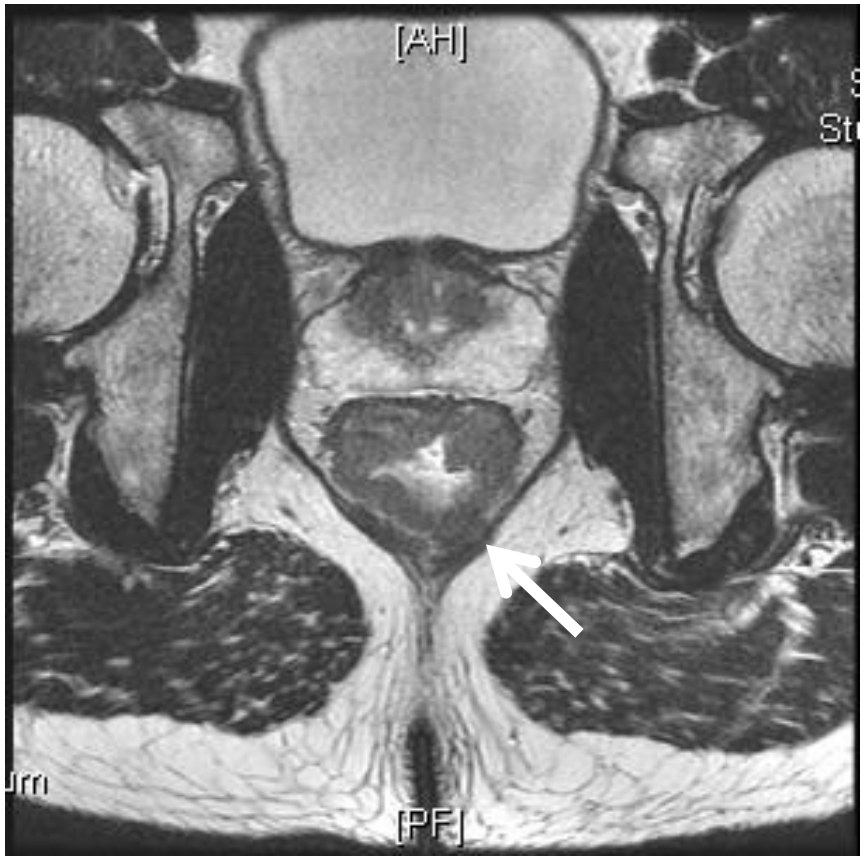
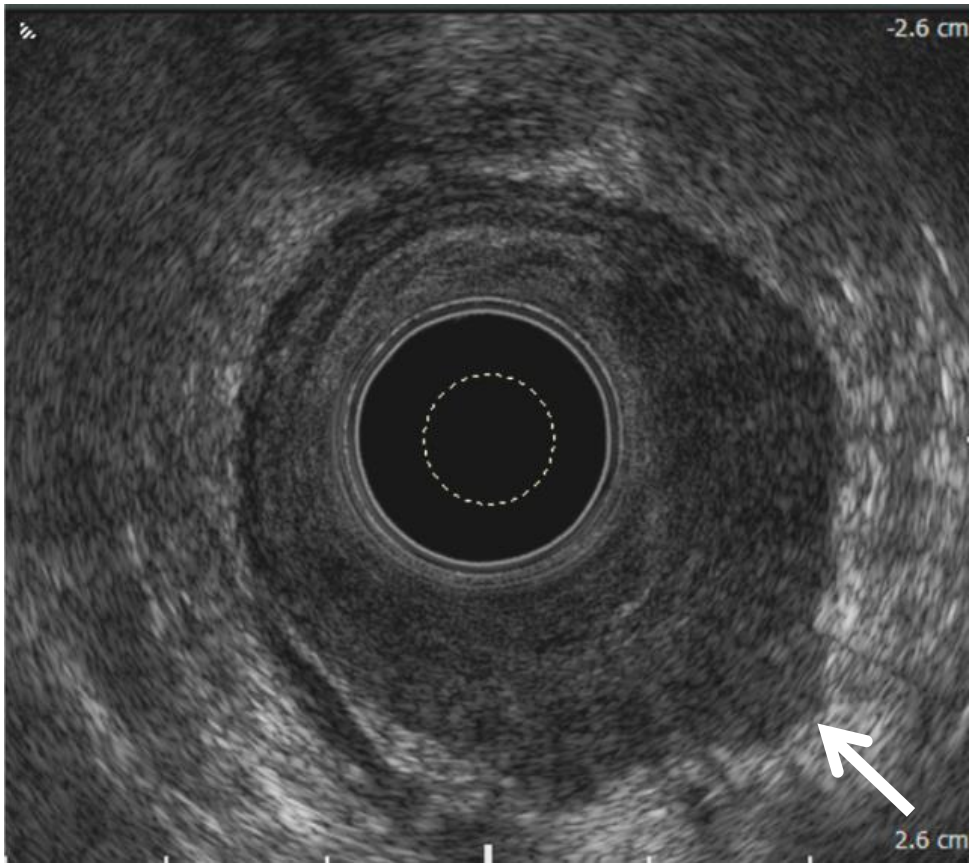
		C30 FIQL	ISR	-FIQL worse results with more IAE resection
Konanz 2013	25	EORTC C30-CR38	AR-APR	Overall similar QOL ISR more gastrointestinal symptoms

Worse QoL compared to stapled LAR
Related to amount of IAE resected

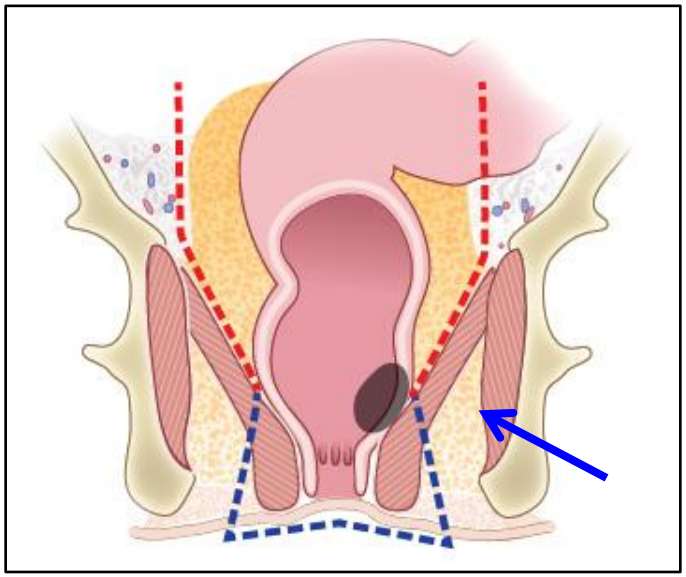
Levator Ani Involvement



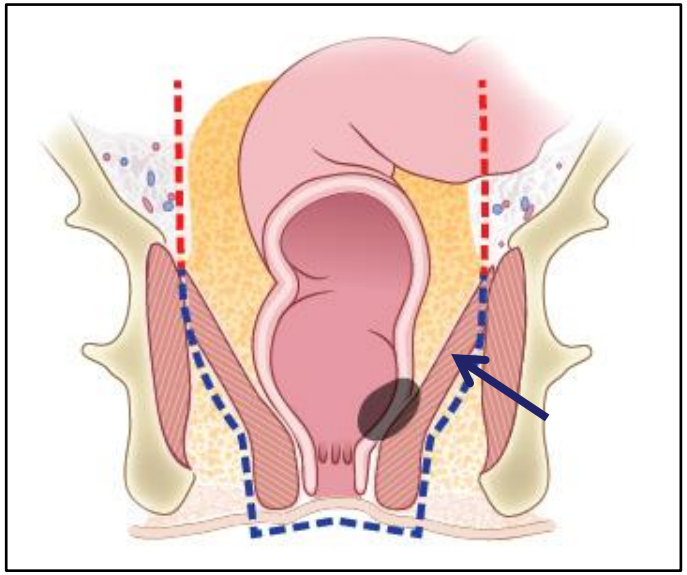


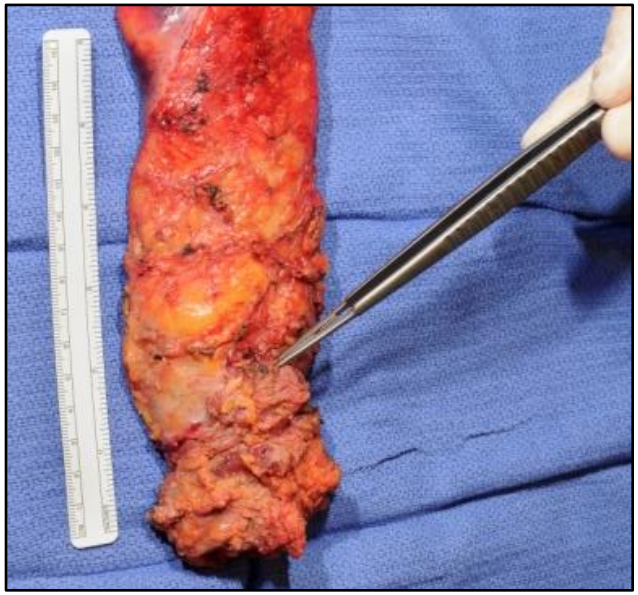
APE in distal rectal cancer

Standard

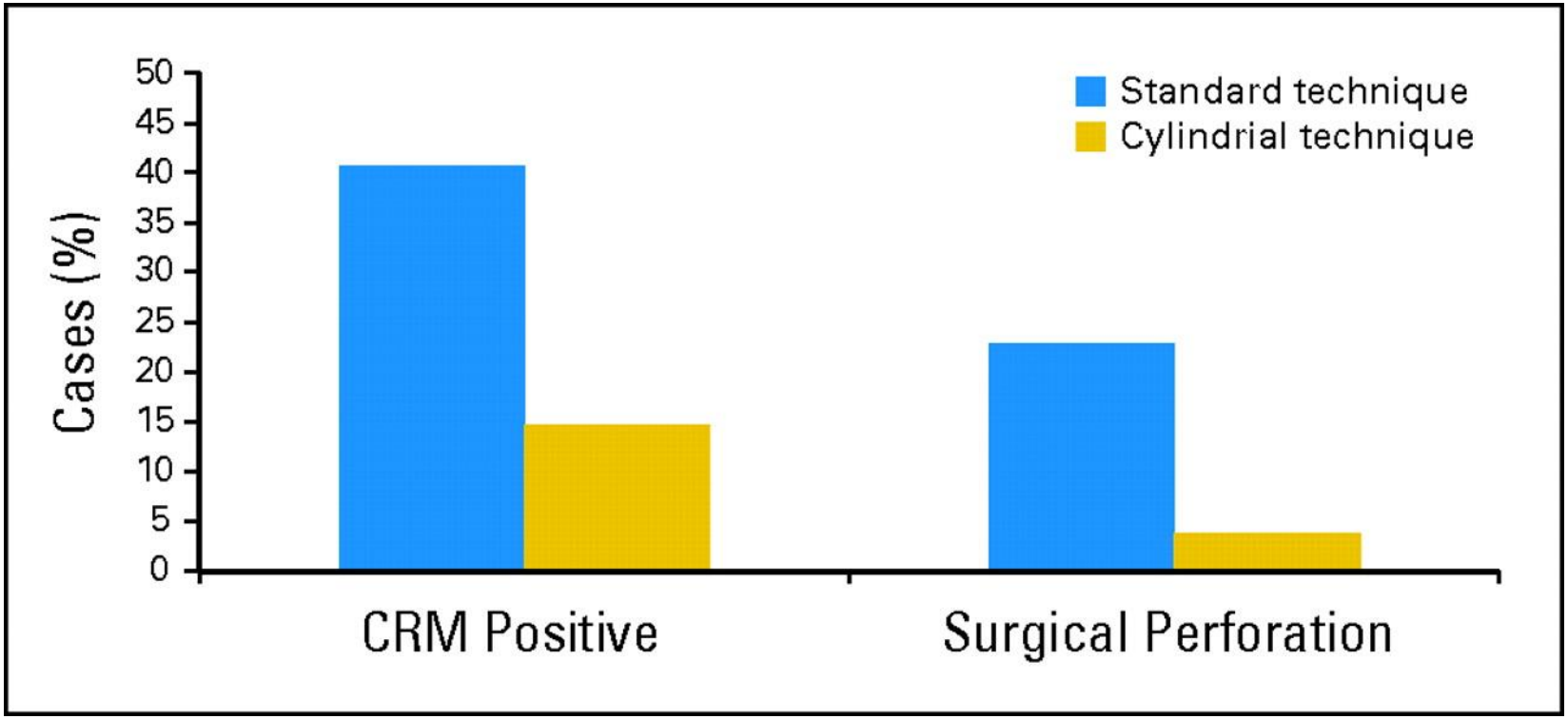


Extralevator



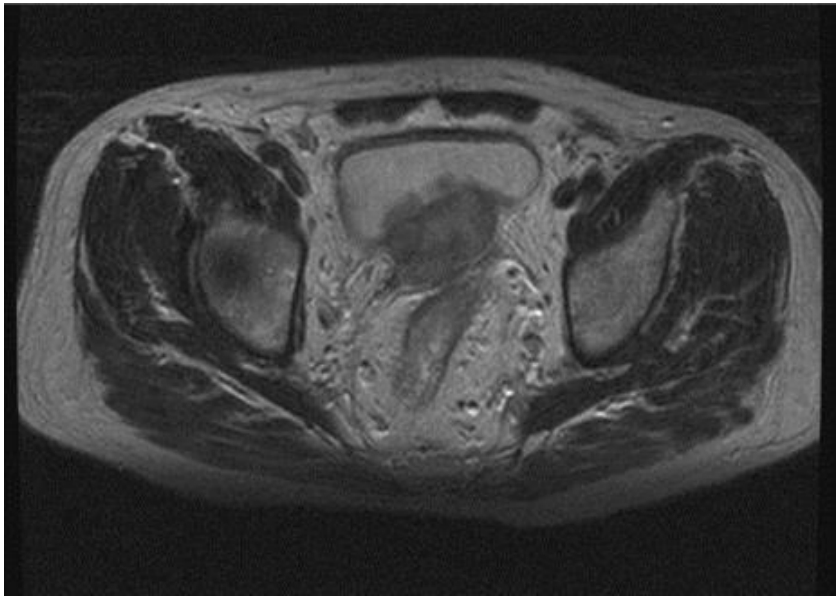


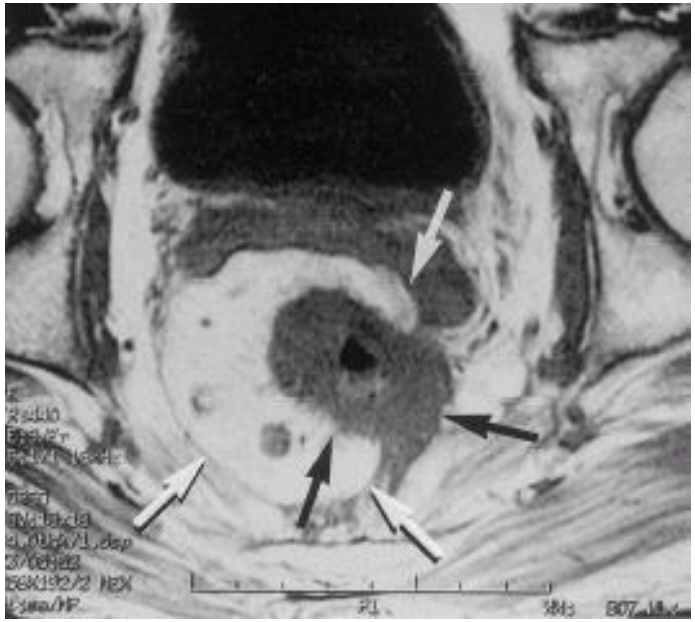
CRM Positivity and Surgical Perforation Rates According to the APE Method



Nicholas P. West et al. JCO 2008;26:3517-3522

Tumors requiring extended resections





Minimally Invasive Surgery for Rectal Cancer

RCT comparing open with laparosocpic surgery for colon cancer

Open/Laparoscopic	COST	COLOR	CLASICC	Leung	ALCCAS
Patients	863	1248	794 (413 colon)	403	594
Operative Time (min)	95/150 p<0.001	115/145 p<0.001	135/185	189/144 p<0.001	107/158 p=<0.001
Blood Loss	NR	175/100 p<0.001	NR	238/169 p=0.06	100/100 p=0.17
Length of Incision (cm)	18/6 p<0.001	NR	22.8/7	NR	20.6/8 p<0.001
Conversion %	21%	17%	25%	23%	14%
LN removed (mean/median)	12/12 (median)	10/10 (median)	13.5/12 (mean)	12./11 (mean)	13/13 (mean)
Overall Morbidity (%)	20/21 p=0.64	20/21 p=0.88	26/26 p=n/s	22/19 p=n/s	45/38 p=0.062
Length of Stay (days)	6/5 p<0.001	9.3/8.2 p<0.001	10/8	8.7/8.2 p<0.001	10.6/9.5 p0.068
5Y -DFS	68/69 p=0.94	68/66 p=0.7	64/58 p=0.399	78/75 p=0.45	71/73 p=0.7
5Y-OS	75/76 p=0.93	74/74 p=0.45	63/56 p=0.253	8076 p=0.61	76/77 p=0.64

COST Study
Short-term Results

		Laparoscopy	
	Open	Convert.	No Convert.
Intravenous narcotics (days)	4.0	4.4	2.8
Oral analgesics (days)	2.2	2.3	1.7
Length of stay (days)	6.4	7.4	5.1

Weeks et al, JAMA 2002

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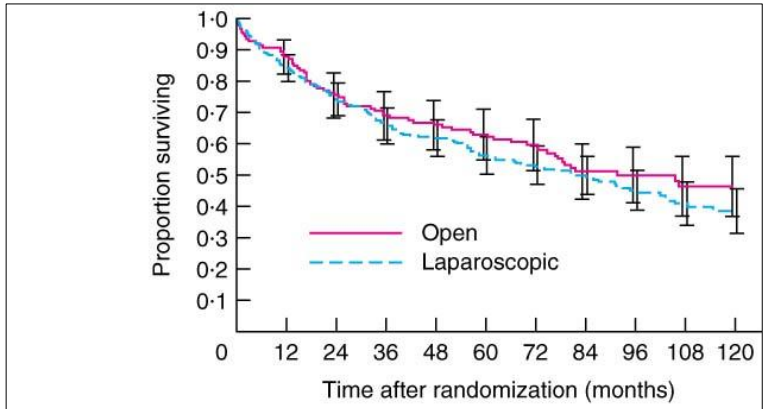
RCT Comparing Open and Laparoscopic TME

Open/Lap	CLASICC	COLOR II	COREAN	ALaCaRT	Z6051
Patients	381[1] [2]	1103[2]	340	475	486
Participating Institutions	27 centers, UK	30 centers, 8 countries	3 centers, South Korea	24 centers, Australia New Zealand	35 centers USA Canada
Tumor stage	All	T1-3 (>2mm MRF)	cT3N0-2	All (exclude T4)	Stage II – III (exclude T4)
Operative Time (min)	135/180[3]	188/240 p<0.001	197/224.9 p=0.001	190/210 P=0.007	220/266 p<0.001
Conversion Rate (%)	34	17	1	9	11
Complete TME (%)	67/79	92/88 p=0.250	88/92 P=0.55	92/87 P=0.06	87/81 P=0.41*
CRM +ve	14/16 p=0.8	10/10 P=0.850	4/3 p=0.770	3/7 p=0.06	8/12 p=0.11
Complications	13/14	37/40 p=0.42	23.5/21.1 p=0.603	No dif.	58/57 p=0.93
LOS	13/10	9/8 p=0.036	9/8 p=0.056	8/8 p=0.21	7/7 p=0.1

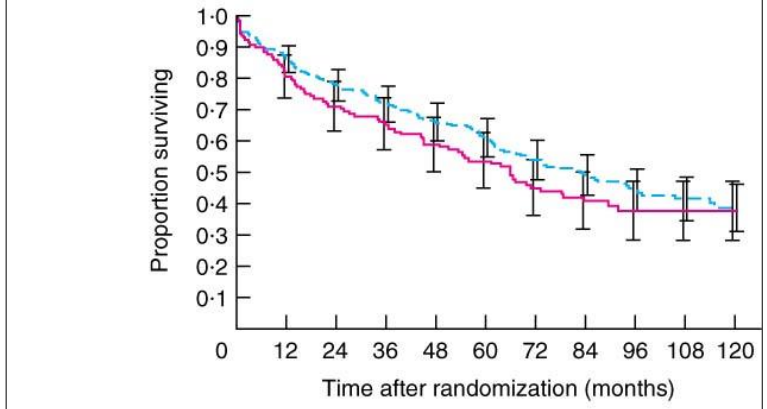
Long-term follow-up of the CLASICC trial of open *versus* laparoscopically assisted resection in colorectal cancer



No. at risk

Open	140	122	105	95	87	83	67	50	40	23	14
Laparoscopic	273	228	201	176	160	143	123	99	59	40	21

a Colonic cancer



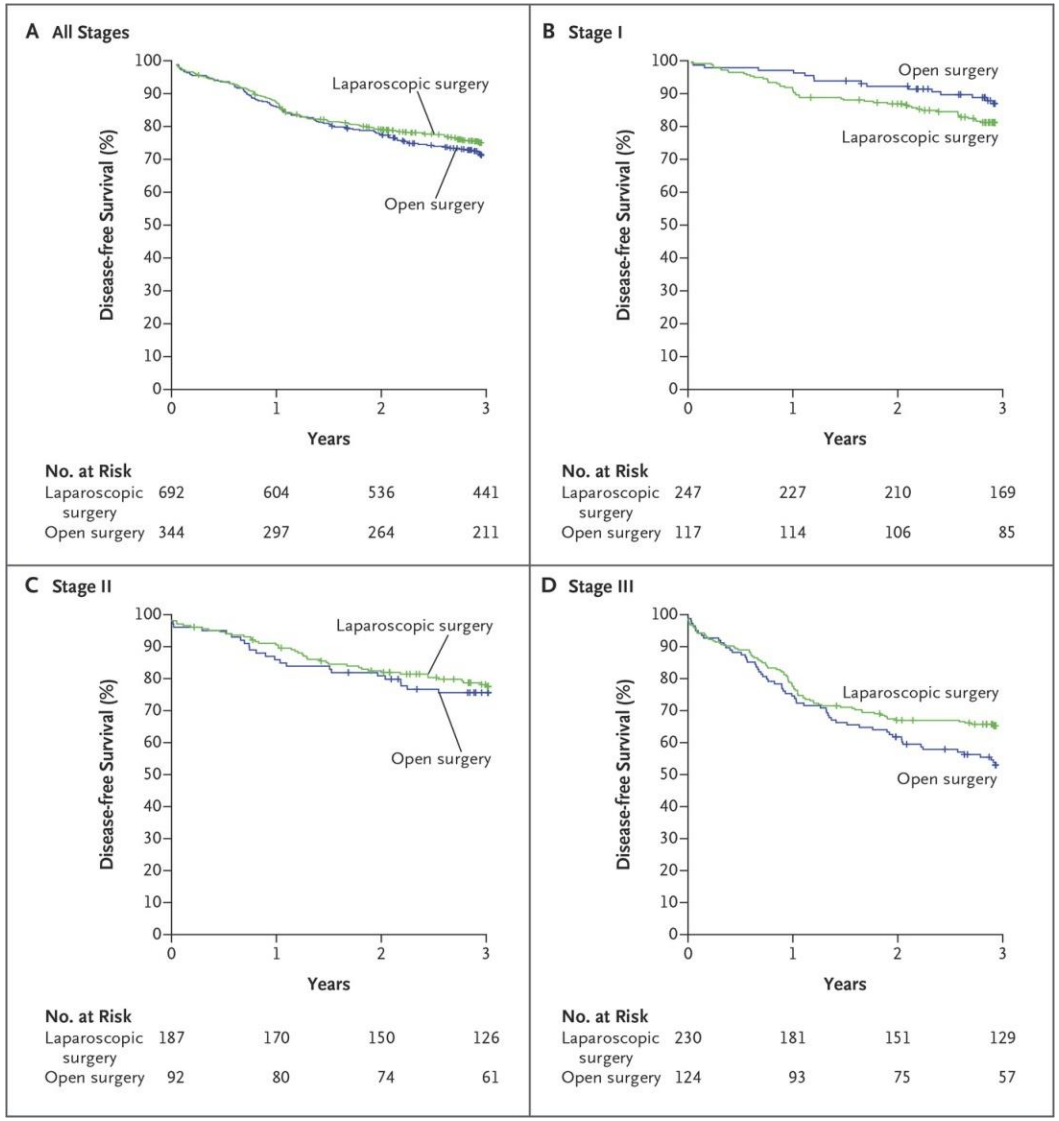
No. at risk

Open	128	103	89	81	70	60	47	37	21	15	7
Laparoscopic	253	217	195	180	161	142	109	94	94	38	20

b Rectal cancer

Green et al. Br. J Surg 2013, 100:75-82

Results of the COLOR II Trial Comparing Open and Laparoscopic TME for Rectal Cancer Disease-free Survival According to Disease Stage

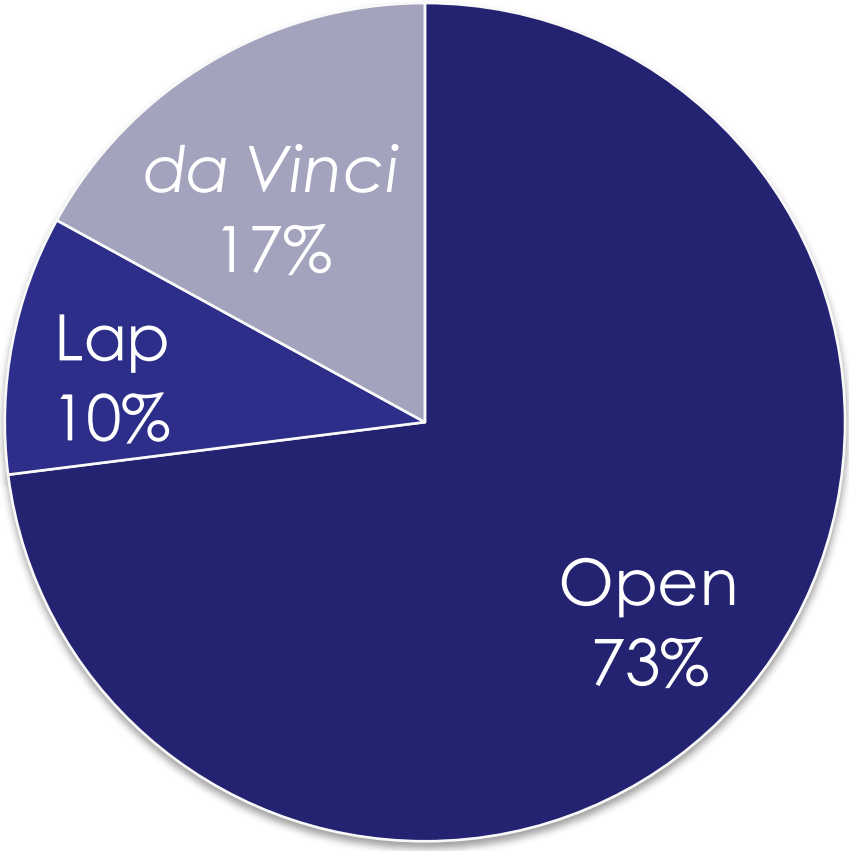


Bonjer HJ et al. N Engl J Med 2015;372:1324-1332.

Summary of laparoscopy in rectal cancer

- Similar length of stay
- Mixed results about completeness of TME
- Equivalent survival ?

Approach to rectal resection, USA 2014



Why is laparoscopic TME not widely adopted ?

- Rectal cancer surgery is challenging, particularly in obese patients, with narrow pelvis and distal tumors

- Laparoscopy is technically challenging
  - Long instruments – magnify involuntary motion
  - Rigid and non reticulating - reduce dexterity
  - Limited control: Surgeon handles two instruments at a time
  - Poor ergonomics
  - Two dimensional visualization

- Require expert help
  - Camera position
  - Traction and triangulation

- Rectal cancer surgery performed by low volume surgeons at low volume centers

MIS alternatives to laparoscopic TME

- Robotic TME
- Transanal TME (TaTME)

Potential Benefits of the Robotic Platform

- 3D view of the field
- Articulating instruments
- Motion scaling
- Enhanced precision
- Suppression of hand tremor
- More surgeon control
- Improved ergonomics
- Facilitates teaching

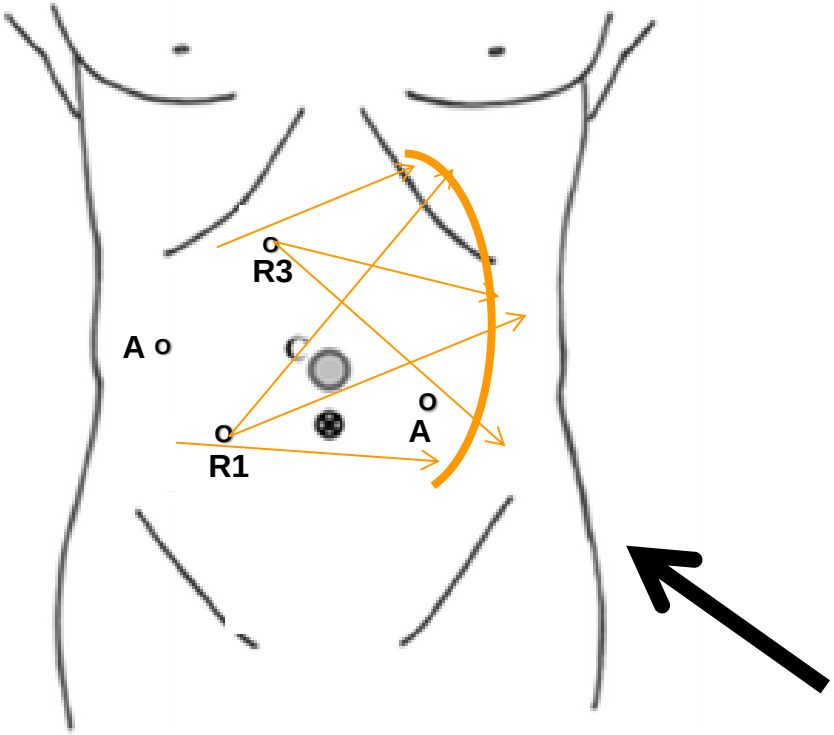
Potential Drawbacks of the Robotic Platform

- Docking and undocking time
- Lack of tactile sensation
- Need for expert field assistance
- Costs
  - Capital
  - Disposables
  - Maintenance

Robotic technology and technique have evolved

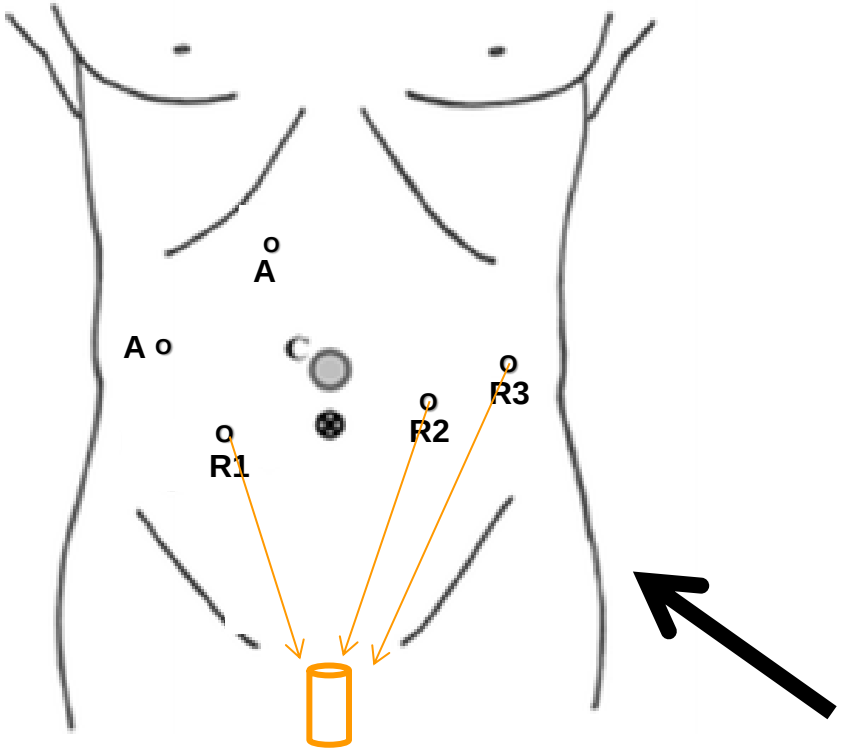
Colon Mobilization

- Left side down
- Minimal Trendelenburg



Mesorectal dissection

- No lateral tilt
- Steep Trendelenburg

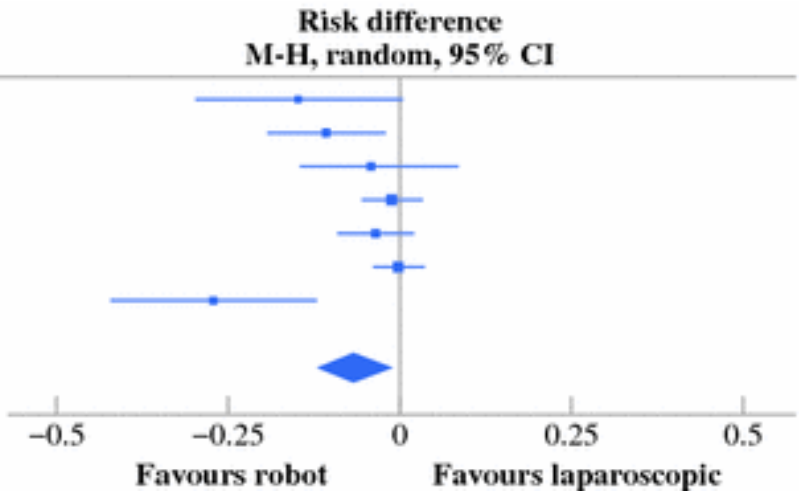


Robotic vs. Laparoscopic TME – Conversion Rates

Study or subgroup	Robot Events	Robot Total	Laparoscopic Events	Laparoscopic Total	Weight	Risk difference M-H random, 95% CI
Baek	3	41	9	41	8.9%	−0.15 [−0.30, 0.00]
Balk	0	56	6	57	14.5%	−0.11 [−0.19, −0.02]
Bianchi	0	25	1	25	12.6%	−0.04 [−0.14, 0.06]
Kim NK	2	100	3	100	18.6%	−0.01 [−0.05, 0.03]
Kwak	0	59	2	59	17.4%	−0.03 [−0.09, 0.02]
Park	0	41	0	82	19.1%	0.00 [−0.04, 0.04]
Patriti	0	29	10	37	8.9%	−0.27 [−0.42, −0.12]
Total (95% CI)		**351**		**401**	**100%**	**−0.07 [−0.12, −0.01]**
Total events	**5**		**31**			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 30.07$, df = 6 ($P < 0.0001$); $I^2 = 80\%$

Test for overall effect: Z = 2.16 (P = 0.03)



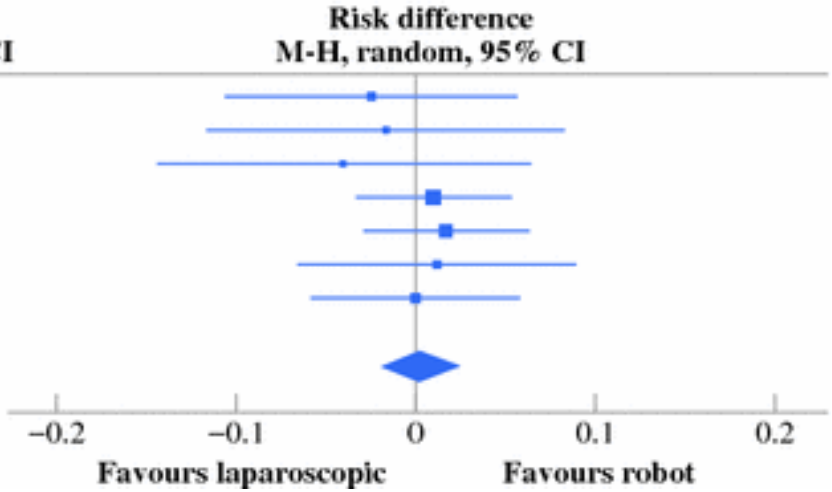
Memon S et al. Ann Surg Oncol. 2012 Jul;19(7):2095-101

Robotic vs. Laparoscopic TME – CMR status

Study or subgroup	Robot Events	Robot Total	Laparoscopic Events	Laparoscopic Total	Weight	Risk difference M-H random, 95% CI
Baek	1	41	2	41	8.4%	−0.02 [−0.11, 0.06]
Balk	4	56	5	57	5.5%	−0.02 [−0.12, 0.08]
Bianchi	0	25	1	25	5.1%	−0.04 [−0.14, 0.06]
Kim NK	3	100	2	100	29.4%	−0.01 [−0.03, 0.05]
Kwak	1	59	0	59	26.3%	−0.02 [−0.03, 0.06]
Park	2	41	3	82	9.2%	0.01 [−0.07, 0.09]
Patriti	0	29	0	37	16.1%	−0.00 [−0.06, 0.06]
Total (95% CI)		**351**		**401**	**100%**	**0.00 [−0.02, 0.03]**
Total events	**11**		**13**			

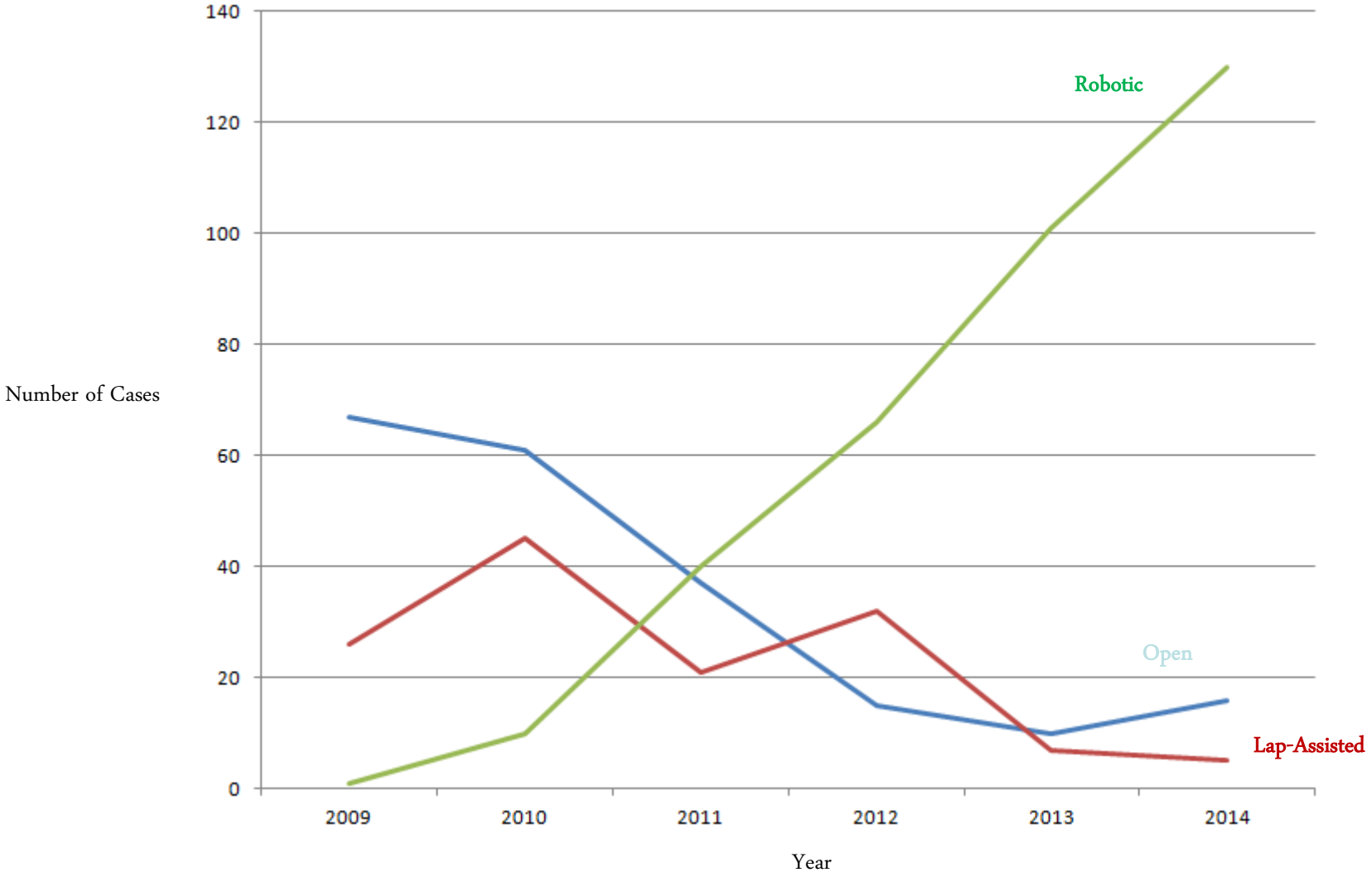
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 8$; df = 6 (P = 0.93); $I^2 = 0\%$

Test for overall effect: Z = 0.30 (P = 0.77)



Memon S et al. Ann Surg Oncol. 2012 Jul;19(7):2095-101

Robotics in Rectal Cancer at MSK



Robotic LAR vs. Lap-Assist. vs. Open Demographics

	Open = 155	Lap-Assist = 107	Robotic = 371	*p*
Age (SD)	58.3 (13.4)	54.6 (13.0)	53.3 (12.8)	0.0006
Gender				0.49
Male	59%	52%	55%	
Female	41%	48%	45%	
BMI	28.4 (6.6)	28.1 (6.9)	27.2 (5.5)	0.35
ASA				0.57
1	3 (2%)	2 (2%)	3 (1%)	
2	57 (37%)	49 (46%)	150 (40%)	
3	93 (60%)	54 (50%)	215 (58%)	
4	2 (1%)	2 (2%)	3 (1%)	
Dist. Anal Verge (cm)	8.5 (3.4)	8.3 (3.6)	9.0 (3.4)	0.11
Chemoradiation	63%	63%	55%	0.11
Induction Chemo	17%	21%	45%	<.0001
Prev. Abd. Surgery	30%	24%	26%	0.45
Associated Procedure	26%	18%	20%	0.21

Robotic LAR vs. Lap-Assist vs. Open Surgical outcomes

	Open (155)	Lap-Assist (107)	Robotic (371)	*p*
Positive CRM (%)	5.2%	2.8%	3.2%	0.49
Mean Distal Margin (mm)	25.6	23.0	29.1	0.02
Lymph nodes (median)	16	17	18	<0.0001
EBL ml	310	215	118	<0.0001
Op Time min (SD)	235 (89.2)	290 (87.6)	317 (102.8)	<0.0001

Robotic LAR vs. Lap-Assist. vs. Open
Short-term clinical outcmes

Complications	Open (155)	Lap-Assist (107)	Robotic (371)	*p*
Any Complication	48%	41%	32%	0.0011
Grade III or higher	14%	10%	8%	0.141
Any SSI	24%	17%	7%	<0.0001
Superficial SSI	12.9%	12.14%	2.2%	<0.0001
Organ space SSI Abscess/Leak	13.6%	5.6%	7.8%	0.047
Readmission 90 days	17%	8%	13%	0.1416
Length of stay (days) median	7	6	5	<0.001
Hospital costs	**$10,800**	**$11700**	**$14250**	<0.0001

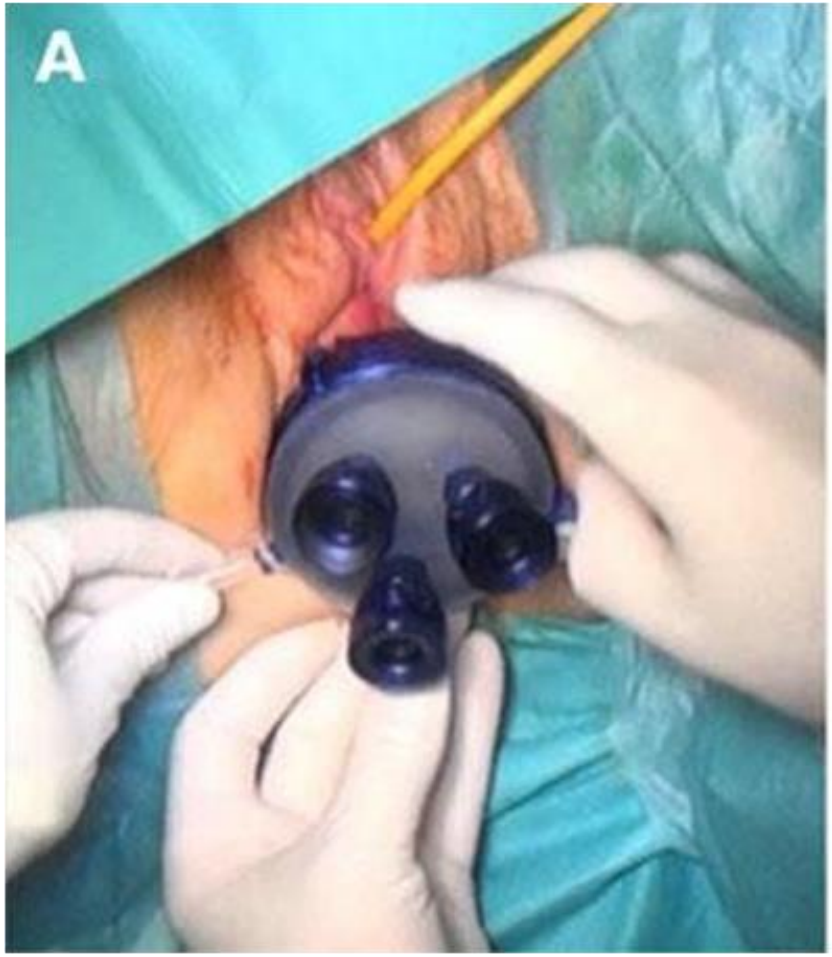
Multivariable Analysis (Mixed Effect Model)

Any Complication	OR	p
Year	0.805	<.0001
Ileostomy	1.503	0.0152
SSI		
Robot	0.576	0.0012
Year	0.831	0.0035
LOS		**p**
Robot	-1.4	0.0003
Age	0.03	0.0016
Any Complication	2.4	<.0001
COST		
Laparoscopic	884	0.0431
Robot	2653	<.0001
Any Complication	2237	<.0001

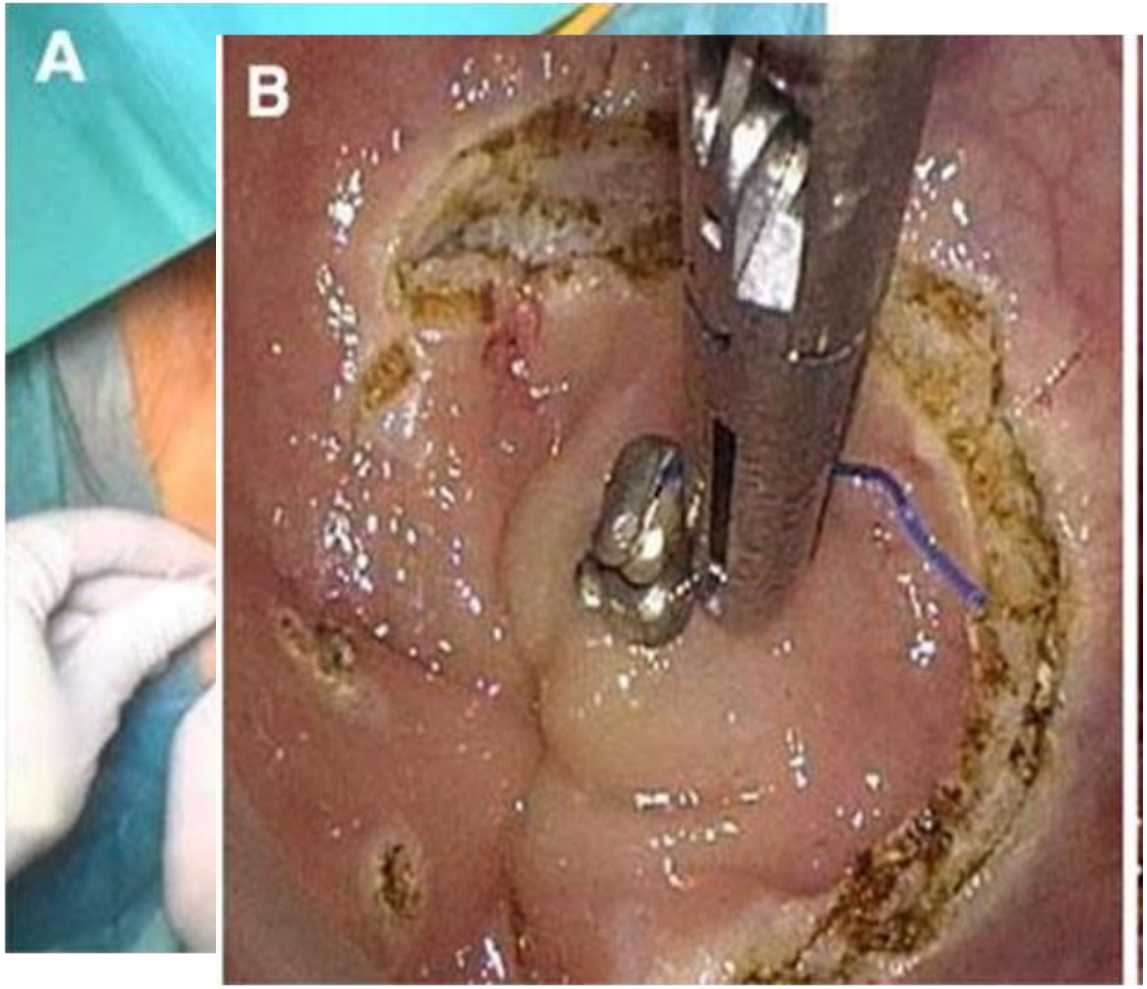
Robotic vs. Open APE

	Open (75)	Robotic (77)	*p*
CRM +ve (< 1mm)	9 (12%)	6 (8%)	0.27
Lymph nodes examined, median (IQR)	15 (12-19)	16 (12.5-21)	0.26
Any Complication	48 (64%)	41 (53%)	0.15
Mean number of complications per patient	2.03	1.47	0.01
Grade III or higher	8 (11%)	7 (9%)	0.74
SSI	26 (35%)	19 (25%)	0.18
Perineal Wound Complications	22 (42%)	16 (30%)	0.17
LOS	8 (7-10)	5 (5-7)	<0.001
90-Day Readmission	22 (29)	14 (18)	0.11

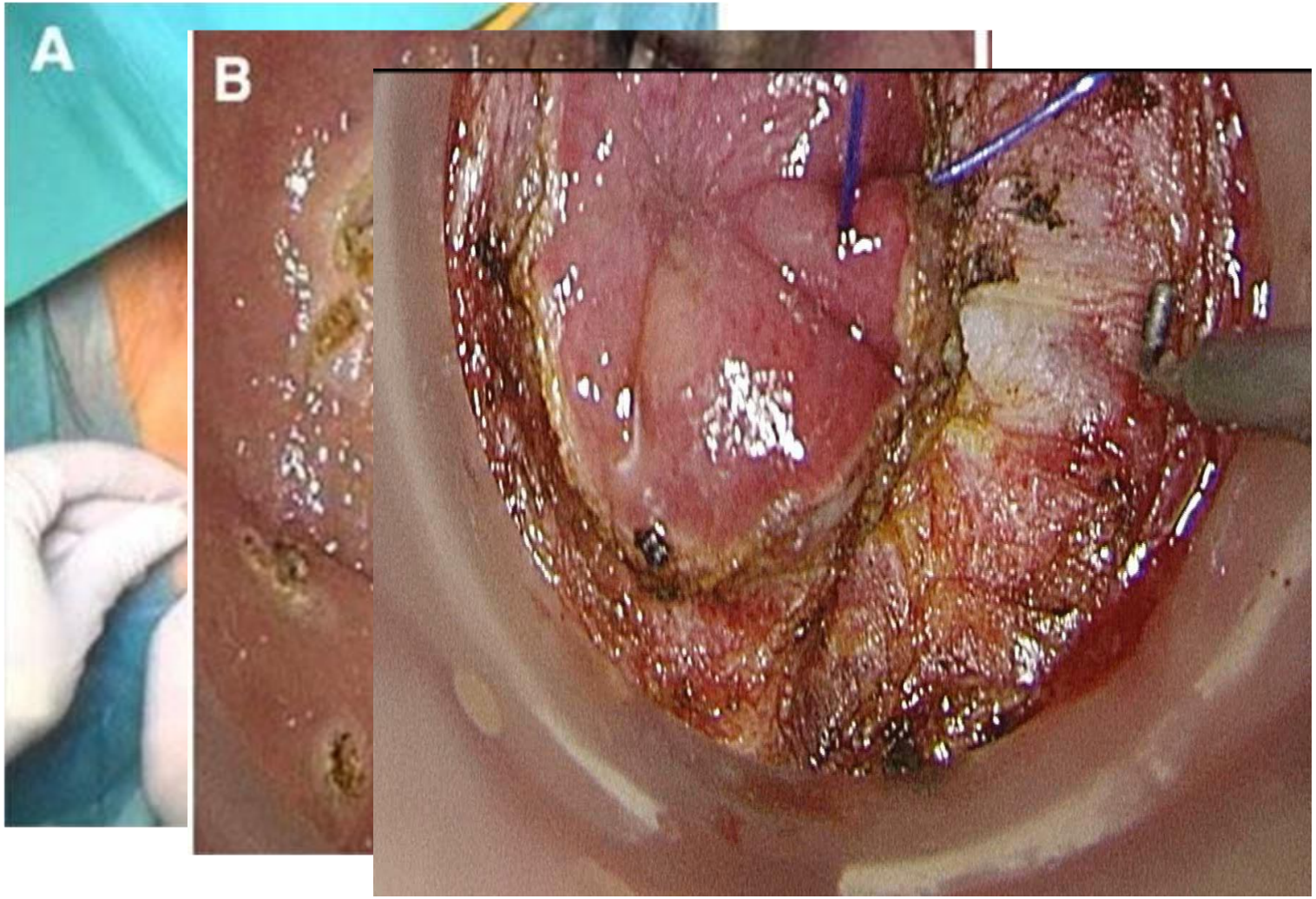
Transanal TME (TaTME)



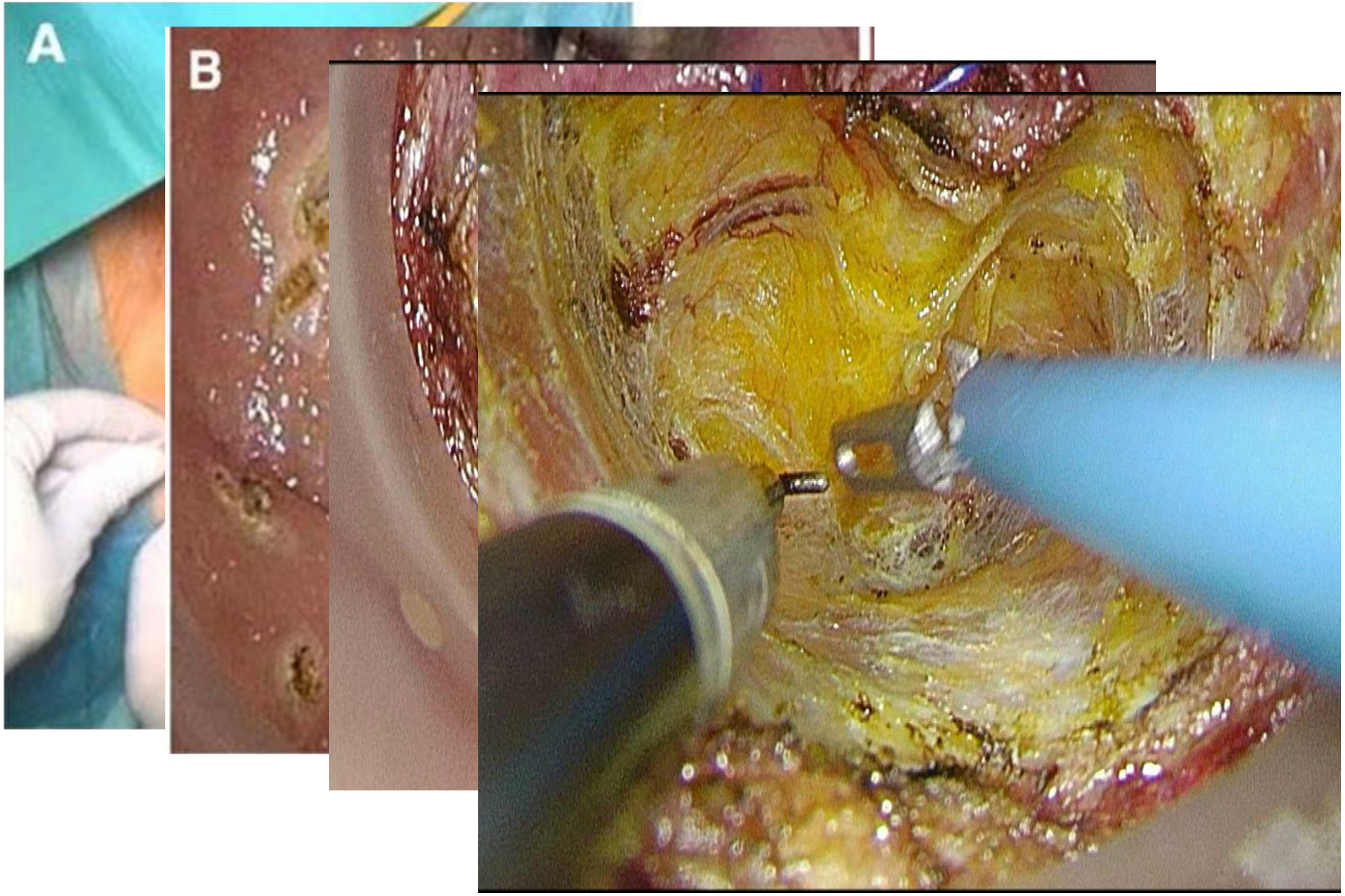
Transanal TME (TaTME)



Transanal TME (TaTME)



Transanal TME (TaTME)



Why TaTME?

- Difficult exposure and dissection in distal tumors
  - Obese, male, narrow pelvis
- Surgical clearance in anteriorly located tumors
- Difficulty transecting the distal rectum to perform a safe stapled anastomosis
- Avoid conversion rates

Systematic Review of TaTME series

Patients	**510**
Age	23-87
BMI	26 (21.7 to 31.8)
Peoperative radiation	78%
Median distance from anal verge (cm)	4 to 9.7
Intraoperative Complications	9% (27/282)
Postoperative Complications	33.5% (126/376)
Positive CRM	5%
Coloanal/Stapled Anastomosis	2/1
Average anastomotic Leak	6%
Length of stay (days)	4.3 to 16.6

Simillis et al, Colorcetal Disease 2016, 18(1): 19-36

TaTME

- Does not eliminate the need for a laparocospic abdominal time to control vessels, take-down splenic flexure, and mobilize the colon
- Two sets of equipment
    - Abdominal (Laparoscopic)/Rectal (TAMIS)
- Requires opening the rectum in patients who would be candidates for a double stapling anastomosis
    - Bacterial contamination
    - Tumor cell spillage

TaTME

- Tendency to perform colo-anal anastomosis in patients who don’t need it – worse outcomes
- Interesphincteric plane easily found at the upper anal canal; mesorectal fascia difficult to identify in the midrectum
- Need to identify neurovascular bundle and pelvic plexus first at the point where they are at maximal risk of injury
- Laparoscopic transanal dissection is difficult – all the problems of laparoscopy magnified by the restricted port and instruments placement

TaTME

- Not needed for most rectal cancer, specially when robotic technology and expertise is available
- A useful tool in selected patients, when distal dissection is difficult (combined with laparoscopic, robotic, and even open abdominal approach)

Summary

- Selection of patients for sphincter-preserving surgery facilitated by MRI imaging
- Minimally invasive TME for rectal cancer is feasible, but technically challenging
- The robotic platforms facilitates minimally invasive TME for rectal cancer, but is expensive
- The TaTME is a useful tool to have in the surgical armamentarium; may facilitate TME in some cases when the robotic equipment is not available

Thank You