



# Parliamo di chirurgia robotica: tutto bene con qualche ripensamento

***Prof. Bernardo Rocco***

Full Professor and Chief of the Department of Urology  
University of Modena and Reggio Emilia, Italy

# Bladder Cancer: what is stated



- Bca is the second most common genitourinary malignancy
  - 81,190 estimated new diagnoses for 2018 in the United States alone
  - Radical cystectomy (RC) with PLND: standard treatment for MI- and high risk NMI-BCa
  - However, RC is a complex procedure
  - RC population: older and more comorbid compared to other surgical patients
- ➔ RC carries a significant perioperative mortality and morbidity (up to 60%, EAU Guidelines)



VESCICA	
Incidenza	Nel 2019 sono attesi, complessivamente, 29.700 nuovi casi di tumore della vescica, 24.000 tra gli uomini e 5.700 tra le donne (12% e 3% di tutti i tumori incidenti, rispettivamente).
Mortalità	Nel 2016 sono stati 6.230 i decessi per tumore della vescica (4.883 uomini e 1.347 donne) in Italia.
Sopravvivenza a 5 anni	La sopravvivenza a 5 anni dei tumori della vescica in Italia è pari al 79%.
Sopravvivenza a 10 anni	La sopravvivenza a 10 anni dalla diagnosi è pari al 71%.
Fattori di rischio	Fumo di sigaretta ed esposizione occupazionale sono i più importanti. Al tabacco sono attribuiti i 2/3 del rischio complessivo nei maschi e 1/3 nelle femmine, alle esposizioni lavorative circa il 25% dei casi.

# Robotics: what is expected?



- To improve surgical outcomes, to decrease complication rate
  - To maintain (at least) oncological outcomes
- } Compared to ORC



# History of RARC

- First RARC publication: 2003 (Menon M, Hemal A, Tewari A, BJUI)
- IRCC (International Radical Cystectomy Consortium) database: 2010
- Pasadena Consensus to define the best practice: 2014
- First RCT comparing RARC and open: 2008
- Meta-analysis of RCTs in 2019: 4
- 10 years oncological analysis: delivered in 2019

## Opposite to robotic prostatectomy history ...



- No EBM evidences supporting robotics for Pca in 2019

Surgical treatment	
Inform patients that no surgical approach (open, laparoscopic- or robotic radical prostatectomy) has clearly shown superiority in terms of functional or oncological results.	Strong

BUT

RALP surpassed open in 2008-2009 and continued to increase thereafter

RALP is the first Robotic Procedure worldwide

# Bladder Cancer

Parliamo di chirurgia  
robotica: tutto bene con  
qualche ripensamento?



# Evidences for Robotic Cystectomy

[A systematic review and meta-analysis comparing the outcomes of open and robotic assisted radical cystectomy.](#)

Albisinni S, Veccia A, Aoun F, Diamand R, Esperto F, Porpiglia F, Roumeguère T, De Nunzio C. Minerva Urol Nefrol. 2019 Oct 10. doi: 10.23736/S0393-2249.19.03546-X. [Epub ahead of print]

PMID: 31619033

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[Robot-assisted Radical Cystectomy Versus Open Radical Cystectomy: A Meta-analysis of Oncologic, Perioperative, and Complication-related outcomes.](#)

Satkunasivam R, Tallman CT, Taylor JM, Miles BJ, Klaassen Z, Wallis CJD.

Eur Urol Oncol. 2019 Jul;2(4):443-447. doi: 10.1016/j.euo.2018.10.008. Epub 2018 Nov 16.

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[Robotic Assisted Radical Cystectomy vs Open Radical Cystectomy: Systematic Review and Meta-Analysis.](#)

Sathianathen NJ, Kalapara A, Frydenberg M, Lawrentschuk N, Weight CJ, Parekh D, Konety BR.

J Urol. 2019 Apr;201(4):715-720. doi: 10.1016/j.juro.2018.10.006.

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[Robotic versus open radical cystectomy for bladder cancer in adults.](#)

Rai BP, Bondad J, Vasdev N, Adshead J, Lane T, Ahmed K, Khan MS, Dasgupta P, Guru K, Chlosta PL, Aboumarzouk OM.

BJU Int. 2019 Jul 15. doi: 10.1111/bju.14870. [Epub ahead of print]

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[Robotic versus open radical cystectomy for bladder cancer in adults.](#)

Rai BP, Bondad J, Vasdev N, Adshead J, Lane T, Ahmed K, Khan MS, Dasgupta P, Guru K, Chlosta PL, Aboumarzouk OM.

Cochrane Database Syst Rev. 2019 Apr 24;4:CD011903. doi: 10.1002/14651858.CD011903.pub2.

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4 metanalysis of RCTs published in 2019

Cochrane, J Urol, Minerva Urologica, Eur Urol Oncolol, BJUI

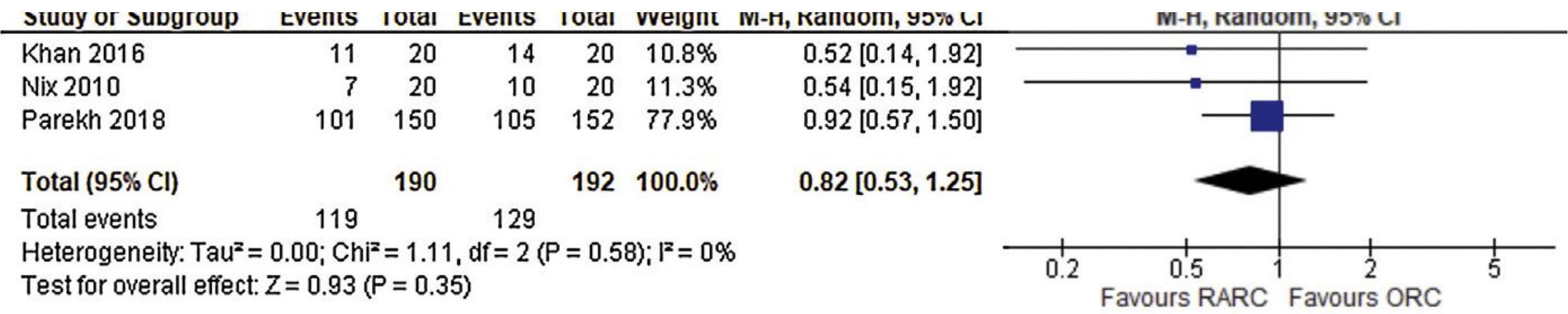
Focus on:

➔ Peri-op outcomes

➔ Complication rate

➔ Oncological outcomes

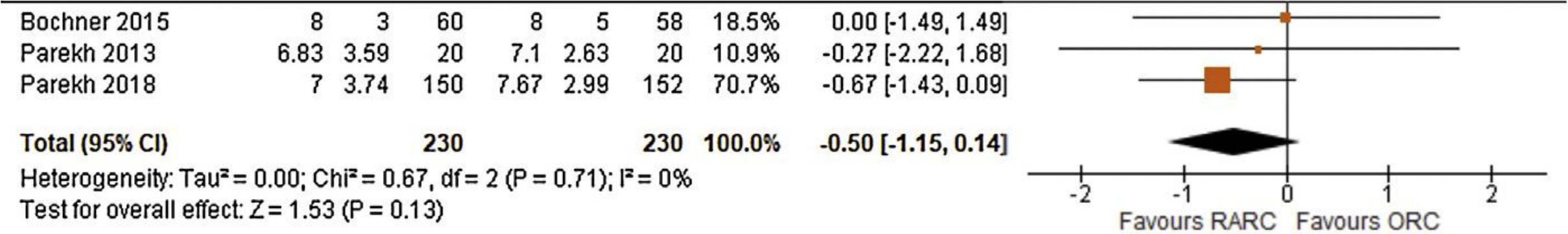
# Blood loss: in favor of RARC



difference -281 ml

Consistent results across all metanalaysis

# Operative Time: in favor of ORC



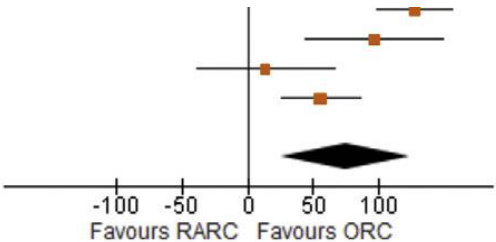
(D)

difference 75 min

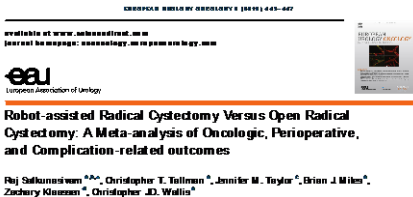
Consistent results across all metanalaysis

# LOS: substantially similar

Bochner 2015	456	82	60	329	77	58	27.6%	127.00 [98.31, 155.69]
Khan 2016	389	98	20	293	66	20	22.6%	96.00 [44.22, 147.78]
Parekh 2013	302	100.53	20	288.3	64.86	20	22.5%	13.70 [-38.73, 66.13]
Parekh 2018	419.6	139.98	150	364	126.49	152	27.3%	55.60 [25.50, 85.70]
Total (95% CI)			250			250	100.0%	75.00 [26.39, 123.61]
Heterogeneity: Tau <sup>2</sup> = 2018.03; Chi <sup>2</sup> = 19.16, df = 3 (P = 0.0003); I <sup>2</sup> = 84%								
Test for overall effect: Z = 3.02 (P = 0.002)								



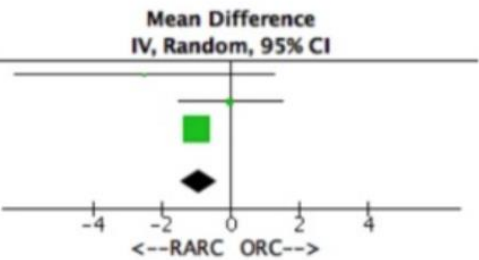
RARC provides -0,5 day  
non statistically significant



(C)

## Length of stay (days)

Study or Subgroup	RARC			ORC			Weight	Mean Difference IV, Random, 95% CI	Year
	Mean	SD	Total	Mean	SD	Total			
[22] Kain M et al	11.9	6.2	20	14.4	5.9	20	2.0%	-2.50 [-6.25, 1.25]	2015
[23] Bochner BH et al	8	3	60	8	5	58	11.6%	0.00 [-1.49, 1.49]	2018
[24] Parekh DJ et al	6	0.8	150	7	0.6	152	86.4%	-1.00 [-1.16, -0.84]	2018
<b>Total (95% CI)</b>			<b>230</b>			<b>230</b>	<b>100.0%</b>	<b>-0.92 [-1.46, -0.37]</b>	
Heterogeneity: $\tau^2 = 0.08$ ; $\chi^2 = 2.32$ , $df = 2$ ( $P = 0.31$ ); $I^2 = 14\%$									
Test for overall effect: $Z = 3.30$ ( $P = 0.0010$ )									



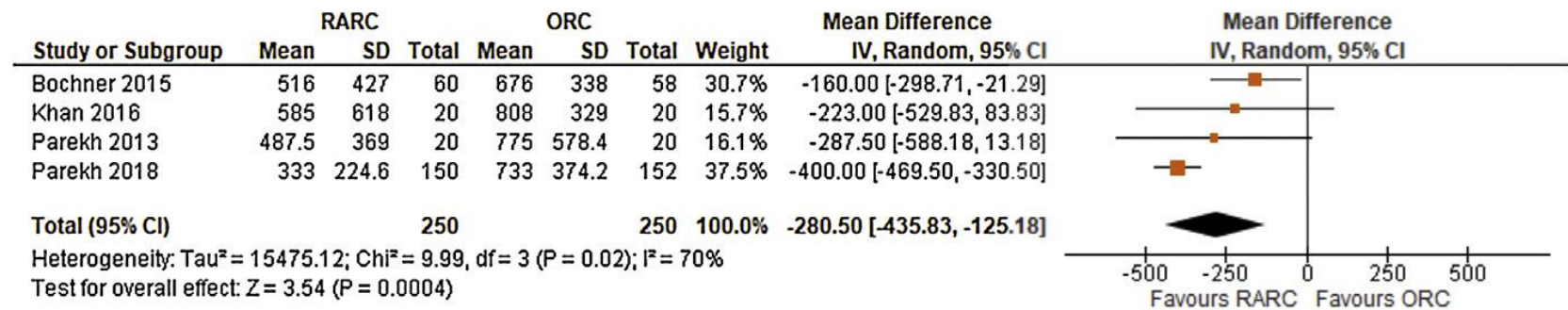
RARC provides -0,92 day  
(statistically significant)

[A systematic review and meta-analysis comparing the outcomes of open and robotic assisted radical cystectomy.](#)  
Albisinni S, Vecchia A, Aoun F, Diamand R, Esperto F, Porpiglia F, Roumeguère T, De Nunzio C.  
Minerva Urol Nefrol. 2019 Oct 10. doi: 10.23736/S0393-2249.19.03546-X. [Epub ahead of print]  
PMID: 31619033  
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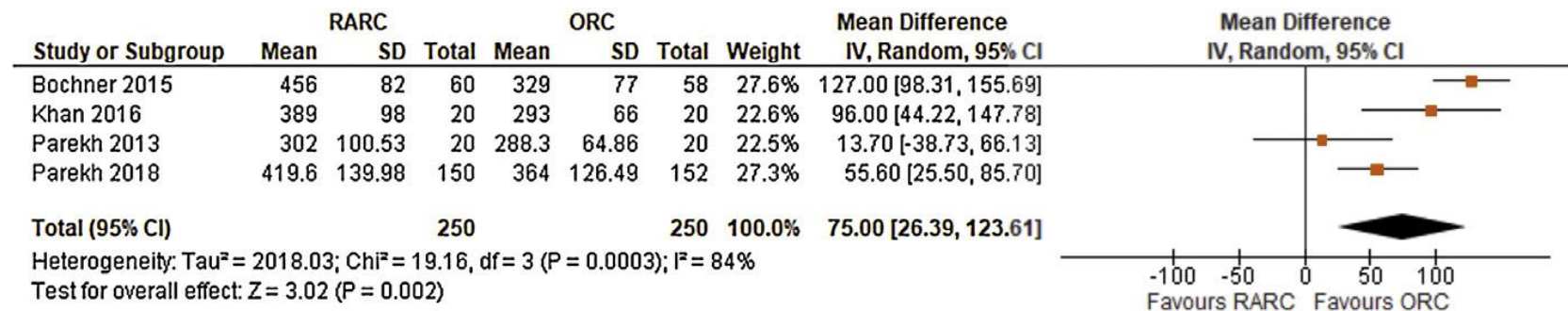
# Complication rate: similar

(A)



Overall

(B)



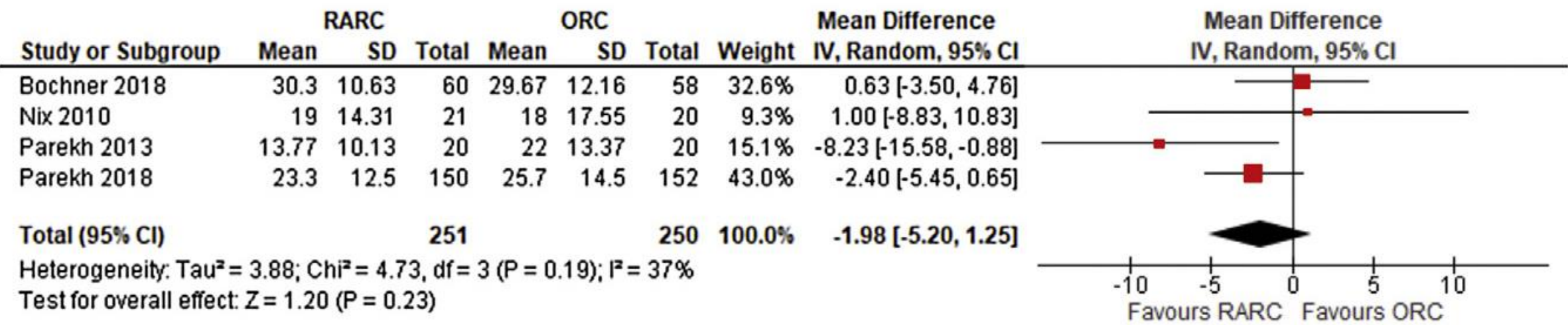
Clavien Dindo  $\geq 3$

Consistent results across all metanalaysis



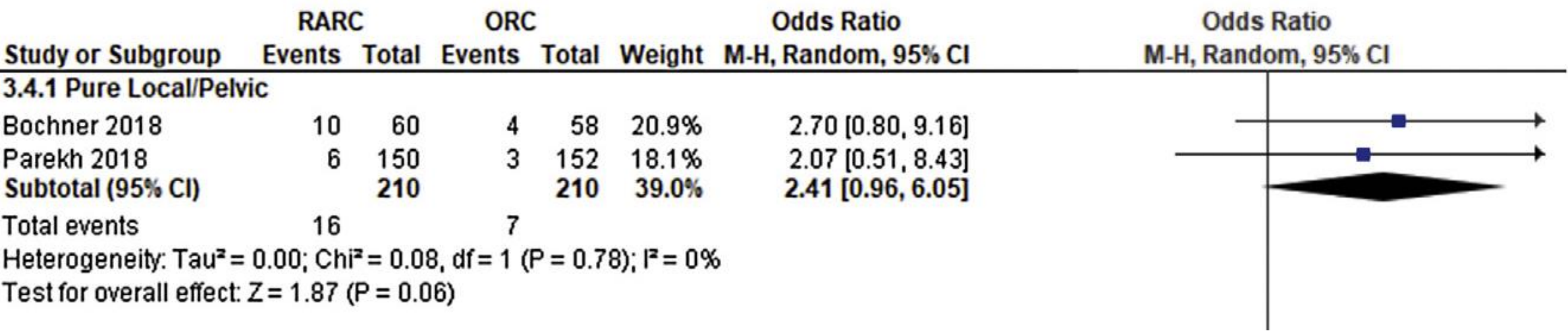
# Positive surgical margin rate: similar

(C)



Consistent results across all metanalaysis

# Nodal yield: similar



# Robotics: which are the evidences?

- Surgical outcomes
  - Blood loss ( $\downarrow$ )
  - OT ( $\uparrow$ )
  - LOS (=)
  - Complication rate (=)
  - PSM (=)



- Oncological outcomes



# Pattern of recurrences: monitored!



2015

## Recurrence Patterns After Open and Robot-assisted Radical Cystectomy for Bladder Cancer

Daniel P. Nguyen<sup>a,b,\*</sup>, Bashir Al Hussein Al Awamlh<sup>a</sup>, Xian Wu<sup>c</sup>, Padraic O'Malley<sup>a</sup>, Igor M. Inoyatov<sup>a</sup>, Abimbola Ayangbesan<sup>a</sup>, Bishoy M. Faltas<sup>d</sup>, Paul J. Christos<sup>c</sup>, and Douglas S. Scherr<sup>a</sup>

<sup>a</sup>Department of Urology, Weill Cornell Medical College-New York Presbyterian Hospital, New York, NY, USA <sup>b</sup>Department of Urology, Bern University Hospital, Bern, Switzerland <sup>c</sup>Department of Healthcare Policy and Research, Division of Biostatistics and Epidemiology, Weill Cornell Medical College, New York, NY, USA <sup>d</sup>Department of Medicine, Division of Hematology/Medical Oncology, Weill Cornell Medical College-New York Presbyterian Hospital, New York, NY, USA

**Table 2 – Distribution of locations among patients with recurrence and secondary urothelial carcinomas within 2 yr after open (ORC) and robot-assisted radical cystectomy (RARC)**

Variable	ORC	RARC
Any recurrence <sup>a</sup>	33/79 (42)	57/158 (36)
Local recurrence <sup>a</sup>	15/65 (23)	24/136 (18)
Cystectomy bed	11 (73)	14 (58)
PLND template	6 (40)	12 (50)
Distant recurrence <sup>a</sup>	26/73 (36)	43/147 (29)
Lung	9 (35)	14 (33)
Liver	9 (35)	10 (23)
Bone	12 (46)	16 (37)
Extrapelvic lymph node	4 (15)	10 (23)
Peritoneal carcinomatosis	2 (8)	9 (21)
Other (brain, adrenal)	3 (12)	0
Secondary urothelial carcinoma	0	4
Upper urinary tract	0	3 (75)
Urethra	0	1 (25)

Retrospective review of 383 consecutive pts who underwent ORC (120) or RARC (263) [2001-2014]

More extrapelvic lymph node location, more peritoneal carcinomatosis with RARC

# Pattern of recurrences: monitored!



2016

## Critical Analysis of Early Recurrence after Laparoscopic Radical Cystectomy in a Large Cohort by the ESUT

Simone Albisinni,\* Laurent Fossion, Marco Oderda, Omar M. Aboumarzouk, Fouad Aoun, Theodoros Tokas, Virginia Varca, Rafael Sanchez-Salas, Xavier Cathelineau, Piotr Chlost, Franco Gaboardi, Udo Nagele, Thierry Piechaud, Jens Rassweiler, Peter Rimington, Laurent Salomon and Roland van Velthoven

From the Department of Urology, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium (SA, FA, RvV), Department of Urology, Maxima Medisch Centrum, Eindhoven, The Netherlands (LF), Department of Urology, Clinique Saint Augustin, Bordeaux (MO, TP), Department of Urology, Institut Montsouris, Paris (RS-S, XC), and Department of Urology, CHU Henri Mondor, Creteil (LS), France, Department of Urology, Jagiellonian University, Krakow, Poland (OMA, PC), Department of Urology, Tirol Kliniken, Innsbruck, Austria (TT, UN), Department of Urology, San Raffaele – Turro Hospital, Vita Salute San Raffaele University, Milan, Italy (VV, FG), Department of Urology, SLK Kliniken, Heilbronn, Germany (JR) and Department of Urology, East Sussex Healthcare NHS Trust, Eastbourne, United Kingdom (PR)

- Analisi di 627 pazienti con patologia favorevole ( $\leq pT2$ )
- Follow up 46 mesi
- 8,7% progressione di malattia nei primi 24 mesi
- ➔ ➔ ➔ 5% Unusual pattern of recurrence



Center	Age	Sex	BMI	Smoker	Cis	LN	pT	Urinary Diversion	RFS	Recurrence localisation	N of Mets	Recurrence Treatment	Response	Mortality FU	Total FU
8	69	M	24.5	no	No	12	0	Ileal conduit	3	cerebral	1	Unknown	Partial	Dead, Non-cancer specific	18
8	42	F	17.2	no	No	17	2b	Ileal conduit	4	vulva; inguinal nodes; peritoneal carcinosis	Disseminated	Chemotherapy	None	Dead, Cancer Specific	6
9	59	F	19.7	no	Yes	1	a	Ileal conduit	5	pelvic mass	1	Palliative	Partial	Dead, Cancer Specific	13
2	68	M	19.0	yes	Yes	28	1	Ureterocutaneostomy	5	liver; retroperitoneal LN	Disseminated	Chemotherapy	None	Dead, Cancer Specific	6
1	56	F	24.0	yes	No	14	0	Orthotopic neobladder	6	bone; pelvic mass	Disseminated	Chemotherapy	None	Dead, Cancer Specific	12
1	78	F	20.6	yes	No	5	2b	Ileal conduit	6	bone (axial)	Disseminated	Palliative	None	Dead, Cancer Specific	6
5	75	M	27.1	Unknown	No	17	2a	Ileal conduit	6	Liver	Disseminated	Chemotherapy	None	Dead, Cancer Specific	9
10	73	M	25.6	Unknown	No	10	0	Ileal conduit	6	mediastinal and inguinal lymph nodes	5	Chemotherapy	Partial	Dead, Cancer Specific	29
5	68	M	25.4	no	Yes	8	2b	Orthotopic neobladder	7	Retroperitoneal lymph nodes	3	Chemotherapy	Partial	Dead, Cancer Specific	20
10	81	M	26.8	Unknown	No	1	0	Ileal conduit	8	pelvic mass	1	Chemotherapy	Partial	Alive	12
7	54	F	25.3	Unknown	No	9	2a	Ileal conduit	9	Bone, Liver	4	Unknown	Partial	Dead, Non-cancer specific	58
10	77	M	24.2	Unknown	No	12	2	Ileal conduit	10	lung	Disseminated	Chemotherapy	Partial	Alive	11
10	74	M	22.2	Unknown	No	14	1	Orthotopic neobladder	11	lung	5	Chemotherapy	Partial	Alive	33
3	59	M	20.0	Unknown	No	13	2a	Ileal conduit	12	cerebral	3	Unknown	None	Dead, Cancer Specific	18
5	75	M	22.7	Unknown	No	16	2b	Ileal conduit	12	Lung; liver; axillary nodes	Disseminated	Chemotherapy	None	Dead, Cancer Specific	20
7	78	M	24.5	Unknown	Yes	30	1	Ileal conduit	13	Bone	5	Unknown	Partial	Dead, Cancer Specific	61
5	66	M	23	Unknown	Yes	20	2b	Orthotopic neobladder	14	Liver; bone (axial); lungs	Disseminated	Chemo+radiotherapy	None	Dead, Cancer Specific	18
3	72	M	24.2	Unknown	No	3	1	Sigmoid neobladder	18	Retroperitoneal lymph nodes; liver	Disseminated	Unknown	Partial	Dead, Cancer Specific	36
3	75	M	28.7	Unknown	No	10	1	Ileal conduit	18	upper urinary tract	1	Unknown	None	Dead, Cancer Specific	24
3	70	M	27.4	Unknown	No	6	2b	Orthotopic neobladder	18	Pelvic mass	1	Unknown	Partial	Dead, Cancer Specific	36
4	74	M	29.1	yes	No	17	2b	Orthotopic neobladder	18	Lung; Liver	Disseminated	Chemotherapy	Partial	Alive	19
2	79	M	31.8	no	No	35	2a	Ileal conduit	19	lung; cerebral	3	Chemotherapy	None	Dead, Cancer Specific	22
2	79	M	21.3	no	No	0	2b	Ileal conduit	22	Inguinal lymph nodes; Corpora Cavemosa	5	surgery	Partial	Alive	30
1	58	M	21.8	yes	No	7	1	Orthotopic neobladder	24	bone (scapula); lung	3	Chemotherapy and surgery	Complete	Alive	60
1	68	M	24.4	no	No	14	2a	Ileal conduit	24	paraortic lymph node	1	chemotherapy and surgery	Complete	Alive	95
4	74	F	25.9	yes	No	21	2b	Orthotopic neobladder	24	pelvic mass	1	Chemotherapy	Partial	Alive	24
4	62	M	28.7	yes	No	21	2b	Orthotopic neobladder	24	Pelvic mass; Lung	4	Chemotherapy	Partial	Alive	24

Table 3.

# Pattern of recurrences: experts' reply



available at [www.sciencedirect.com](http://www.sciencedirect.com)  
journal homepage: [www.europeanurology.com](http://www.europeanurology.com)

**EAU**  
European Association of Urology

Platinum Priority – Brief Correspondence  
Editorial by Nieroshan Rajarubendra and Monish Aron on pp. 727–728 of this issue

**Early Recurrence Patterns Following Totally Intracorporeal Robot-assisted Radical Cystectomy: Results from the EAU Robotic Urology Section (ERUS) Scientific Working Group**

Justin W. Collins<sup>a</sup>, Abolfazl Hosseini<sup>a</sup>, Christofer Adding<sup>a</sup>, Tommy Nyberg<sup>b</sup>, Anthony Koupparis<sup>c</sup>, Edward Rowe<sup>c</sup>, Matthew Perry<sup>d</sup>, Rami Issa<sup>d</sup>, Martin C. Schumacher<sup>e</sup>, Carl Wijburg<sup>f</sup>, Abdullah E. Canda<sup>g</sup>, Melvin D. Balbay<sup>h</sup>, Karel Decaestecker<sup>i</sup>, Christian Schwentner<sup>j</sup>, Arnulf Stenzl<sup>j</sup>, Sebastian Edeling<sup>k</sup>, Saša Pokupić<sup>k</sup>, Fredrik D'Hondt<sup>l</sup>, Alexander Mottrie<sup>l</sup>, Peter N. Wiklund<sup>a,\*</sup>

<sup>a</sup>Karolinska University Hospital, Stockholm, Sweden; <sup>b</sup>Karolinska Institute, Stockholm, Sweden; <sup>c</sup>Bristol Urological Institution, Bristol, UK; <sup>d</sup>St. Georges Hospital London, London, UK; <sup>e</sup>Hirslanden Klinik, Aarau, Switzerland; <sup>f</sup>Carl Wijburg, Rijnsstate, Arnhem, The Netherlands; <sup>g</sup>Ankara Atatürk Hospital, Ankara, Turkey; <sup>h</sup>Memorial Sisi Hospital, Istanbul, Turkey; <sup>i</sup>Ghent University Hospital, Ghent, Belgium; <sup>j</sup>University of Tübingen, Tübingen, Germany; <sup>k</sup>Da Vinci Zentrum, Hanover, Germany; <sup>l</sup>O.L.V. Clinic, Aalst, Belgium

2017

Aim: to report early recurrence patterns among 717 RARC pts with intracorporeal urinary diversion at 9 institutions min follow-up of 12 mo

Conclusion: unusual recurrence patterns were not identified in this multi-institutional series and that recurrence patterns appear similar to those in open radical cystectomy series.

	Estimated recurrence rate (%)		
	3 mo	12 mo	24 mo
Any recurrence	4.1	19.8	25.4
Local recurrence	1.8	8.2	10.7
Cystectomy bed	0.7	2.8	3.4
Distal ureteric	0.1	0.3	0.5
Urethral	0.0	0.1	0.5
Pelvic lymph nodes	1.0	5.3	7.2
Distant recurrences	3.0	13.9	17.8
Lung	1.1	4.6	6.2
Liver	0.8	4.1	5.5
Bone	1.0	5.2	6.4
Brain	0.1	0.6	1.0
Adrenal	0.0	0.3	0.7
Bowel	0.0	0.3	0.3
Pancreas	0.0	0.1	0.1
Extrapelvic lymph nodes	1.4	4.9	6.6
Peritoneal carcinomatosis	0.3	0.7	0.7
Port site	0.0	0.3	0.3
Skin	0.0	0.1	0.1
Muscle	0.0	0.2	0.2
Secondary urothelial cancer			
Upper urinary tract	0.0	0.3	0.3
Multiple recurrences	2.0	8.0	11.0

# Need for evidences on oncological endpoints (recurrence free survival)

**2018**



2 RCTs planned to assess RFS/PFS as a primary endpoint → RAZOR + BOCHNER

RCT designed as «non-inferiority trials» → RAZOR



# Similar 2-yrs and 5-yrs recurrence free survival



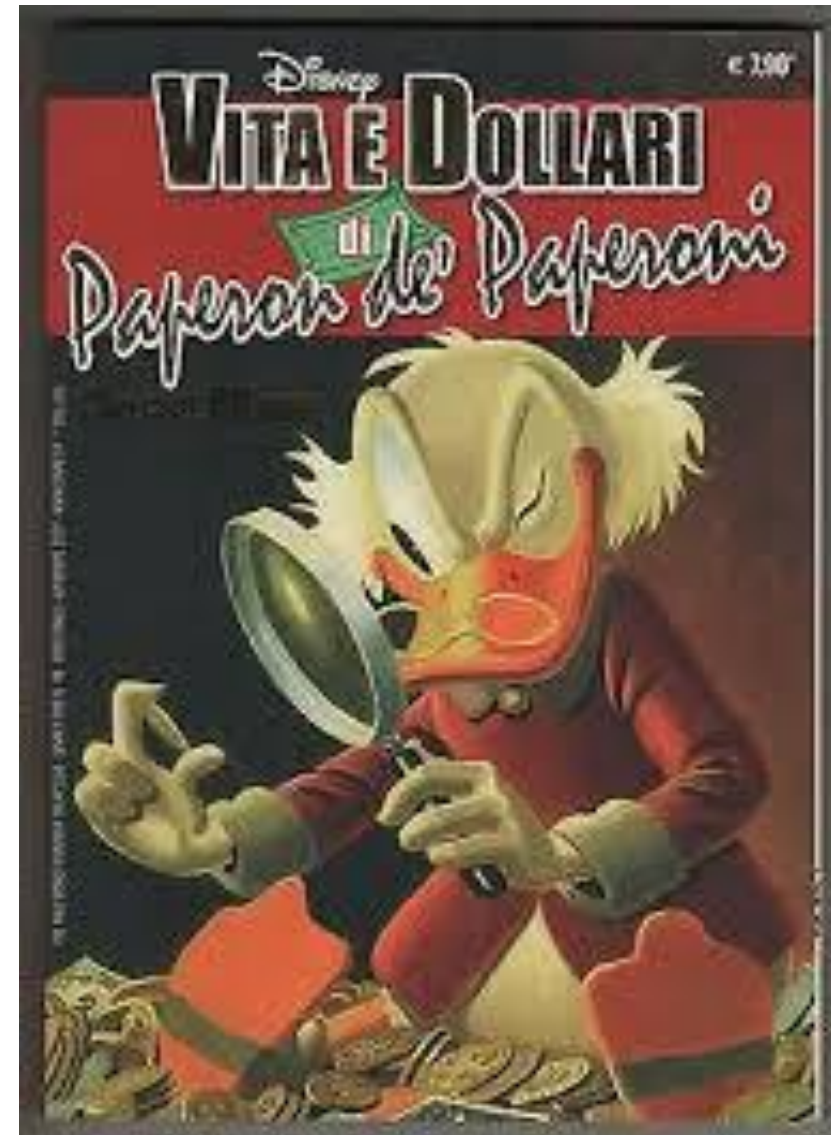
**BOCHNER 2018** (accrual 2010-2013, 60 vs 58 pts randomized to RARC or open):

- 5-yrs risk of recurrence 36% for RARC and 41% for ORC ( $p=0.4$ )
- CSS between RARC and ORC: similar ( $p = 0.4$ )

**RAZOR 2018** (accrual: 2011-2014, 176 vs 154 pts randomized to RARC or open)

- 2-year PFS was 72.3% in RARC and 71.6% in open → non-inferiority of robotic cystectomy

Are there questions still open?



# 1) Is long term oncological safety reproducible?

## **Ten-Year Oncologic Outcomes Following Robot-Assisted Radical Cystectomy: Results from the International Robotic Cystectomy Consortium**



Ahmed A. Hussein,\* Ahmed S. Elsayed,\* Naif A. Aldhaam, Zhe Jing, Jennifer Osei, Jihad Kaouk, Juan Palou Redorta, Mani Menon, James Peabody, Prokar Dasgupta, Mohammed Shamim Khan, Alexandre Mottrie, Michael Stöckle, Ashok Hemal, Lee Richstone, Abolfazl Hosseini, Peter Wiklund, Francis Schanne, Eric Kim, Koon Ho Rha and Khurshid A. Guru†

High volume surgeons, high volume institutions

43% pT3 or greater and positive soft tissue surgical margin in 7% !!!

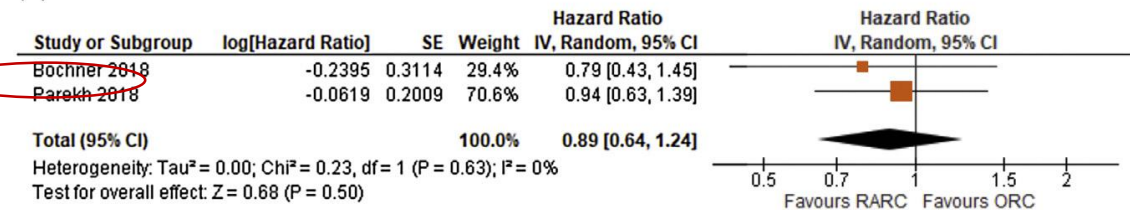
## 2) Are doubt of unusual pattern of recurrence completely ruled out?

Metanalysis Eur Urol Oncol 2019:

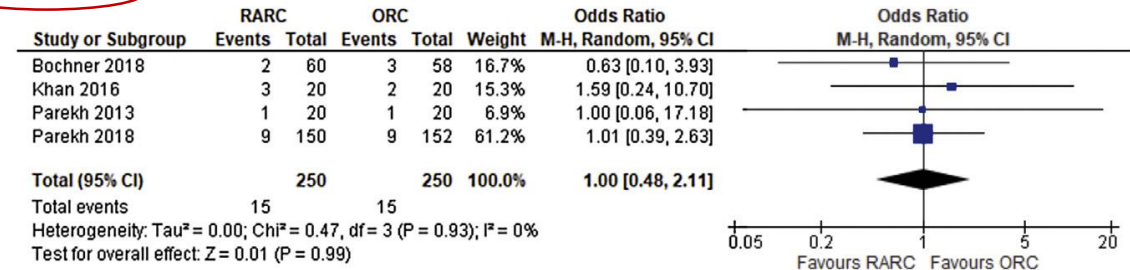
significantly different patterns of recurrence between RARC and ORC ( $p = 0.04$ )



(A)



(B)



BOCHNER 2018

More local/abdominal sites for RARC ( $p=0,035$ )

More distant metastatic site in ORC ( $p<0.05$ )

# Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer

Pedro T. Ramirez, M.D., Michael Frumovitz, M.D., Rene Pareja, M.D., Aldo Lopez, M.D., Marcelo Vieira, M.D., Reitan Ribeiro, M.D., Alessandro Buda, M.D., Xiaojian Yan, M.D., Yao Shuzhong, M.D., Naven Chetty, M.D., David Isla, M.D., Mariano Tamura, M.D., [et al.](#)

**CONCLUSIONS** In this trial, minimally invasive radical hysterectomy was associated with lower rates of disease-free survival and overall survival than open abdominal radical hysterectomy among women with early-stage cervical cancer. (Funded by the University of Texas M.D. Anderson Cancer Center and Medtronic; LACC ClinicalTrials.gov number, [NCT00614211](#).)

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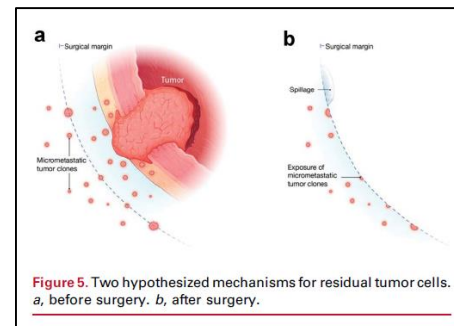
### 3) Biology of local recurrence still under investigation

#### Accurate Quantification of Residual Cancer Cells in Pelvic Washing Reveals Association with Cancer Recurrence Following Robot-Assisted Radical Cystectomy



2019

Lei Wei,\* Ahmed A. Hussein,\* Yingyu Ma,\* Gissou Azabdaftari, Youssef Ahmed, Lai Ping Wong, Qiang Hu, Wei Luo, Victoria N. Cranwell, Brittany L. Bunch, Justen D. Kozlowski, Prashant K. Singh, Sean T. Glenn, Gary Smith, Candace S. Johnson, Song Liu and Khurshid A. Guru†



Conclusions: Residual cancer cells detected in approx half of the pelvic washing after (but not before) RARC

..... Which is the source of residual cancer cells?

Synchronous or preexisting metastases, or iatrogenic dissemination? .....

Reply:

Is local, abdominal, port site metastasis more likely associated with tumor aggressiveness and biology (pT,pN)?

Jancke, Wiklund, Eur Urol 2018

## 4) Could the type of urinary diversion (extra vs intra) impact on benefits?



- RCTs are based on extracorporeal reconstruction urinary diversion
- Robotic Experts suggest that this may limit the advantage of a minimally invasive approach on peri-op outcomes (ileus, mobilization, LOS ...)

➔ NO answers yet, but an ongoing RCT

**Open access****Protocol**

**BMJ Open** Robot-assisted radical cystectomy with intracorporeal urinary diversion versus open radical cystectomy (iROC): protocol for a randomised controlled trial with internal feasibility study

James W F Catto,<sup>1,2</sup> Prmit Khetrpal,<sup>2</sup> Gareth Ambler,<sup>3</sup> Rachael Sarpong,<sup>4</sup> Muhammad Shamim Khan,<sup>5</sup> Melanie Tan,<sup>4</sup> Andrew Feber,<sup>2</sup> Simon Dixon,<sup>6</sup> Louise Goodwin,<sup>1</sup> Norman R Williams,<sup>4</sup> John McGrath,<sup>7</sup> Edward Rowe,<sup>8</sup> Anthony Koupparis,<sup>8</sup> Chris Brew-Graves,<sup>4</sup> John D Kelly<sup>2</sup>



# COSTS

**Table 5** Operating costs

Author	Urinary diversion	Operating cost (ORC) (%)	Operating cost (RARC) (%)	ORC mean operating time (min)	RARC mean operating time (min)
Bansal [13]	Ileal conduit, Orthotopic neobladder	<u>\$6464 (47.8%)</u>	<u>\$10,140 (63.1%)</u>	192 <sup>a</sup>	265 <sup>a</sup>
Bochner [23]	Ileal conduit, Orthotopic neobladder	included in total cost		330 <sup>b</sup>	464 <sup>b</sup>
Martin [21]	Ileal conduit	N.A. (for institutional reason)		320 <sup>a</sup>	280 <sup>a</sup>
Lee [22] <sup>c</sup>	Ileal conduit, Orthotopic neobladder, Continent cutaneous	\$10,384 (40.7–50.1%)	\$14,556 (64.1–70.5%)	420 <sup>d</sup>	444
Smith [11]	N.A.	\$9304 (57.3%)	\$9527 (65.3%)	228 <sup>e</sup>	246 <sup>e</sup>



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Bladder Cancer

## Defining a “High Volume” Radical Cystectomy Hospital: Where Do We Draw the Line?

*Sohrab Arora<sup>a,b,\*</sup>, Jacob Keeley<sup>a,b</sup>, Amit Patel<sup>a</sup>, Sriram V. Eleswarapu<sup>c</sup>, Chandler Bronkema<sup>d</sup>, Shaheen Alanee<sup>a</sup>, Mani Menon<sup>a</sup>*

<sup>a</sup>Department of Urology, Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA; <sup>b</sup>Center for Outcomes Research, Analytics and Evaluation, Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA; <sup>c</sup>Department of Urology, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, USA; <sup>d</sup>Wayne State University School of Medicine, Detroit, MI, USA

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**Results and limitations:** The inpatient complication rate was 4769/6790 (70.2%), of which 1572/6790 (23.2%) were major complications. Restricted cubic spline analysis revealed a significant inverse nonlinear association between hospital volume and complications. The odds of complications decreased with increasing volume, with a plateau at 50–55 cases/yr for any complications ( $p = 0.024$ ) and 45–50 cases/yr for major complications ( $p = 0.007$ ).

# EAU GUIDELINES

Summary of evidence	LE
Robot-assisted radical cystectomy (RARC) has longer operative time (1-1.5 hours) and major costs, but shorter length of hospital stay (1-1.5 days) and less blood loss compared to open radical cystectomy (ORC).	1
Robot-assisted radical cystectomy series suffer from a significant stage selection bias as compared to ORC.	1
Grade 3, 90-day complication rate is lower with RARC.	2
Most endpoints, if reported, including intermediate-term oncological endpoint and quality of life, are not different between RARC and ORC.	2
Surgeons experience and institutional volume are considered the key factor for outcome of both RARC and ORC, not the technique.	2
Recommendations on how to define challenging patients and an experienced RARC surgeon are still under discussion.	3
The use of neobladder after RARC still seems under-utilised, and functional results of intracorporeally constructed neobladders should be studied.	4

Recommendations	Strength rating
Inform the patient of the advantages and disadvantages of open radical cystectomy (ORC) and robot-assisted radical cystectomy (RARC) to allow selection of the proper procedure.	Strong
Select experienced centres, not specific techniques, both for RARC and ORC.	Strong

# Conclusions

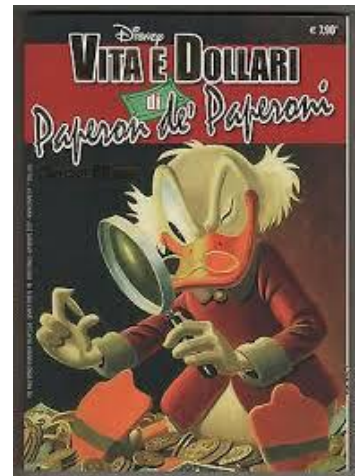
## CURRENT EVIDENCES FROM RCTs

- Complication rate: similar
- Oncological outcomes: «non inferior»

## QUESTIONS STILL OPEN

- 1) Is long term oncological safety reproducible?
- 2) Are doubt of unusual pattern of recurrence completely ruled out?
- 3) Biology of recurrence still under investigation
- 4) Could the type of urinary diversion (extra vs intra) impact on benefits?
- 5) ORC and in case, RARC and should be performed only in high volume centers

**Last open question is ... are RARC costs justified?**



**RICERCA CLINICA E PATIENT ENGAGEMENT:  
DALLA TEORIA ALLA PRATICA IN URO-ONCOLOGIA**

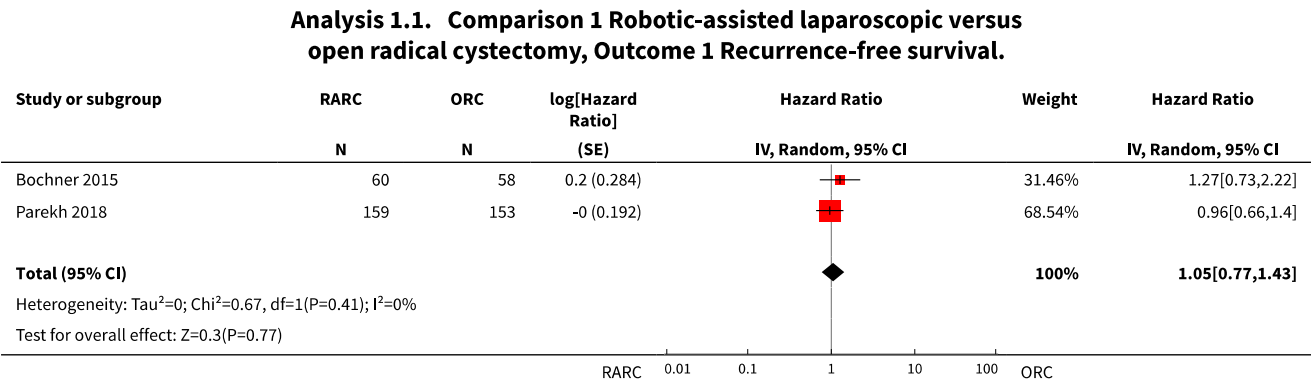
**Milano 30 Novembre 2019**

Palazzo Pirelli, via Fabio Filzi n.22, Milano



@bernardorocco73

# Recurrence free survival: meta-analysis

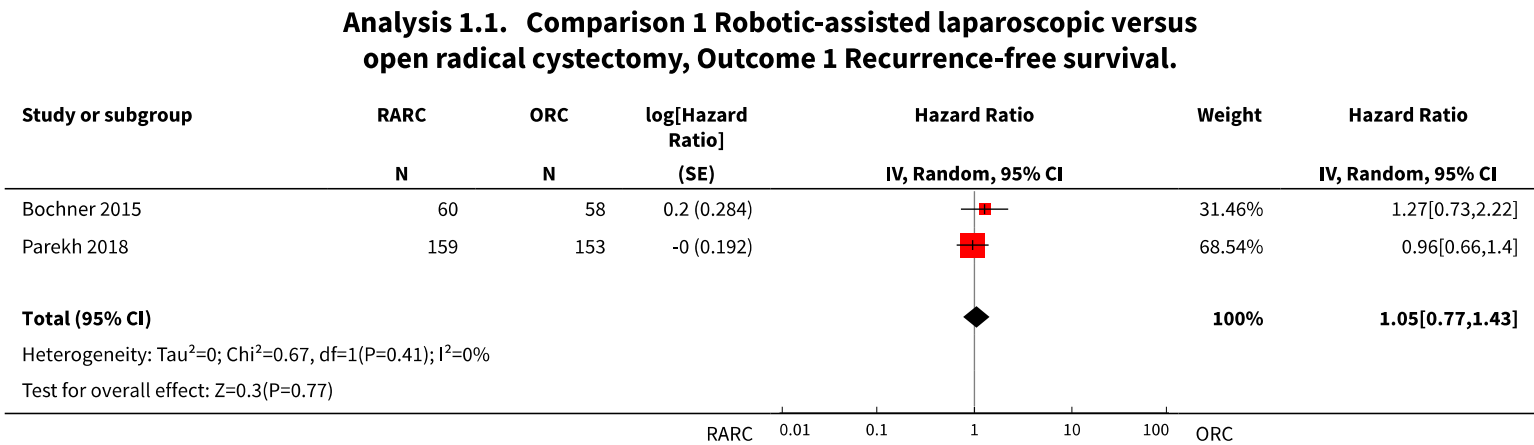




# Recurrence free survival: evidences

RCTs planned to assess RFS/PFS as a primary endpoint → RAZOR + Bochner, 2018  
RCT designed as «non-inferiority trials» → RAZOR

RAZOR: 2-year progression-free survival was 72.3% (95% CI 64.3 to 78.8) in the robotic cystectomy group and 71.6% (95% CI 63.6 to 78.2) in the open cystectomy group (difference 0.7%, 95% CI -9.6% to 10.9%;  $p_{\text{non-inferiority}}=0.001$ ), indicating non-inferiority of robotic cystectomy.



2 yrs PFS  
2 yrs PFS

**Oncological Risk : need for strong evidences**



High volume centers

Extracorporeal diversion

Chemotherapy use left to clinical discretion





**Cochrane**  
**Library**

Cochrane Database of Systematic Reviews

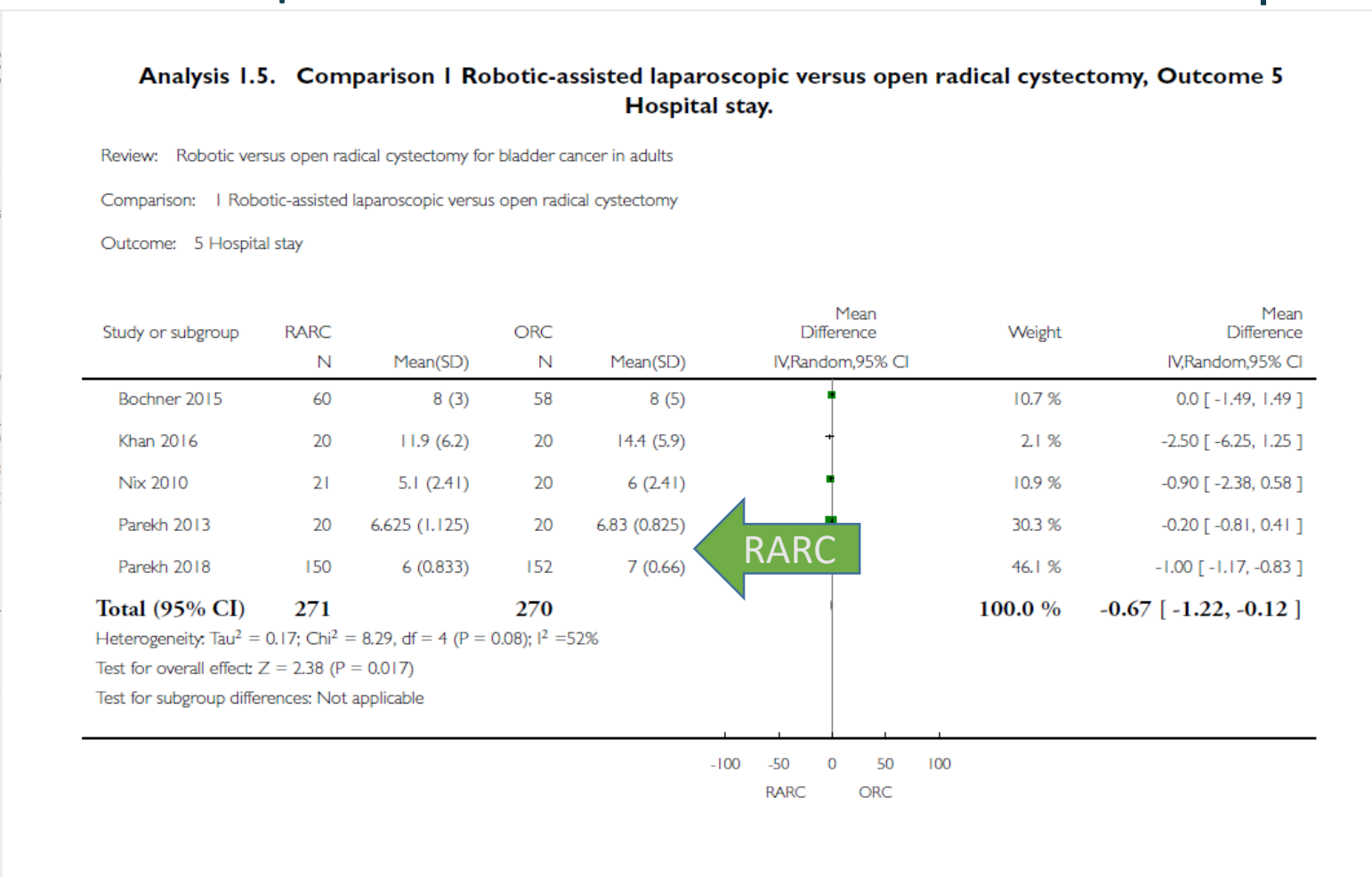
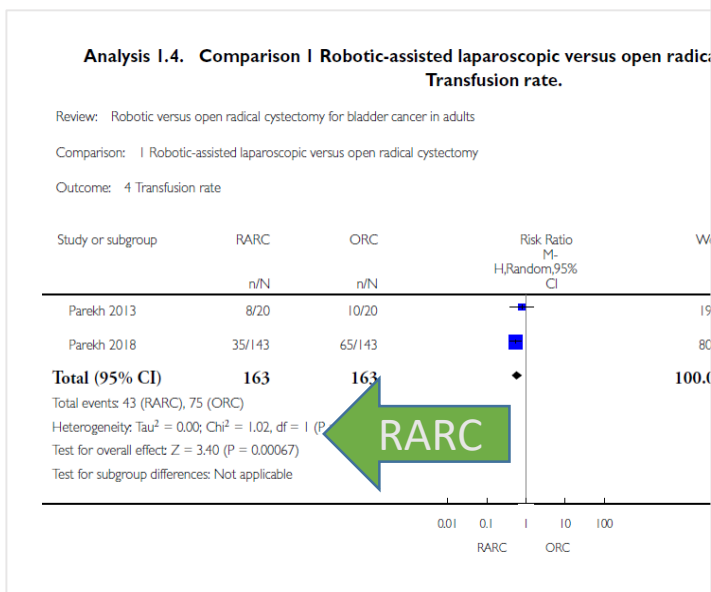
## **Robotic versus open radical cystectomy for bladder cancer in adults (Review)**

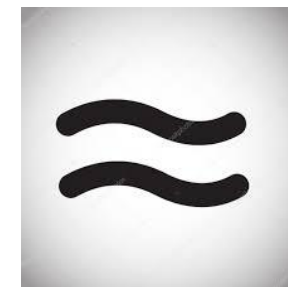
Rai BP, Bondad J, Vasdev N, Adshead J, Lane T, Ahmed K, Khan MS, Dasgupta P, Guru K, Chlosta PL, Aboumarzouk OM

Review of 5 RCT comprising a total of 541 participants (ORC: 270; RARC 271)

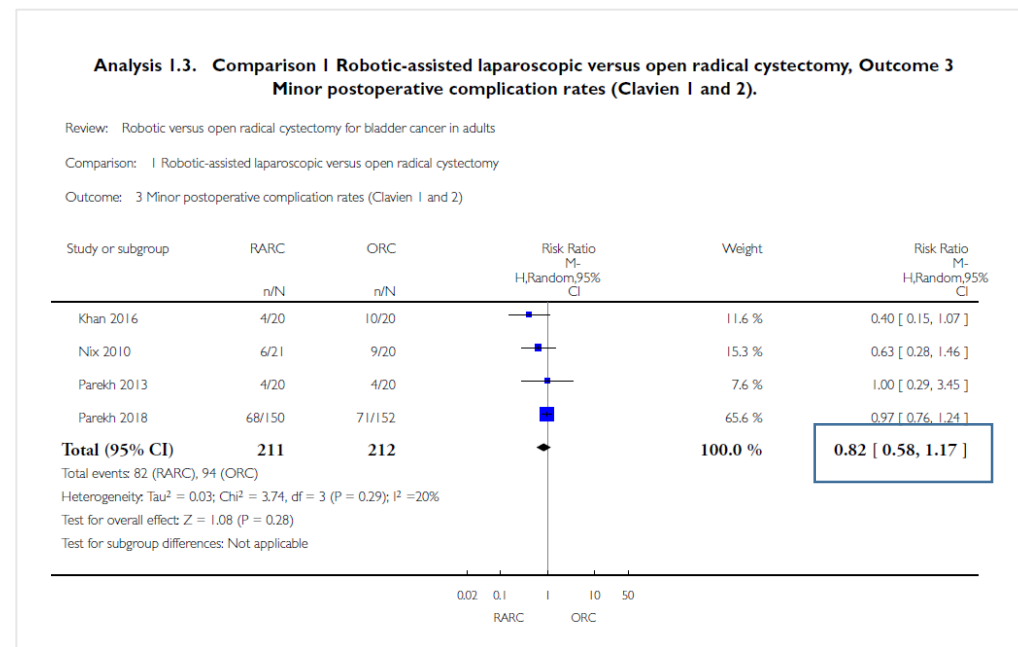
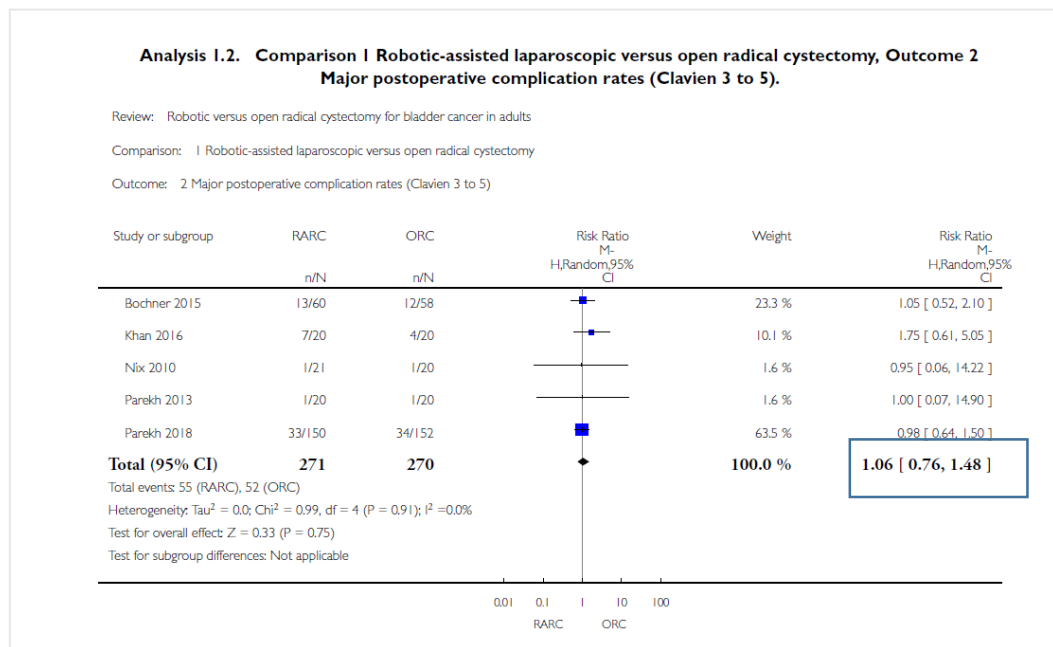


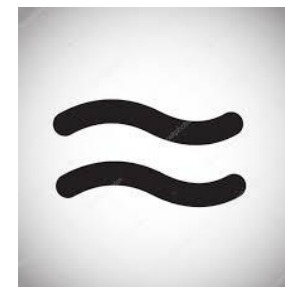
- Transfusion rate: RARC better than open → 193 fewer transfusions/1000 pts
- Hospital Stay: RARC better



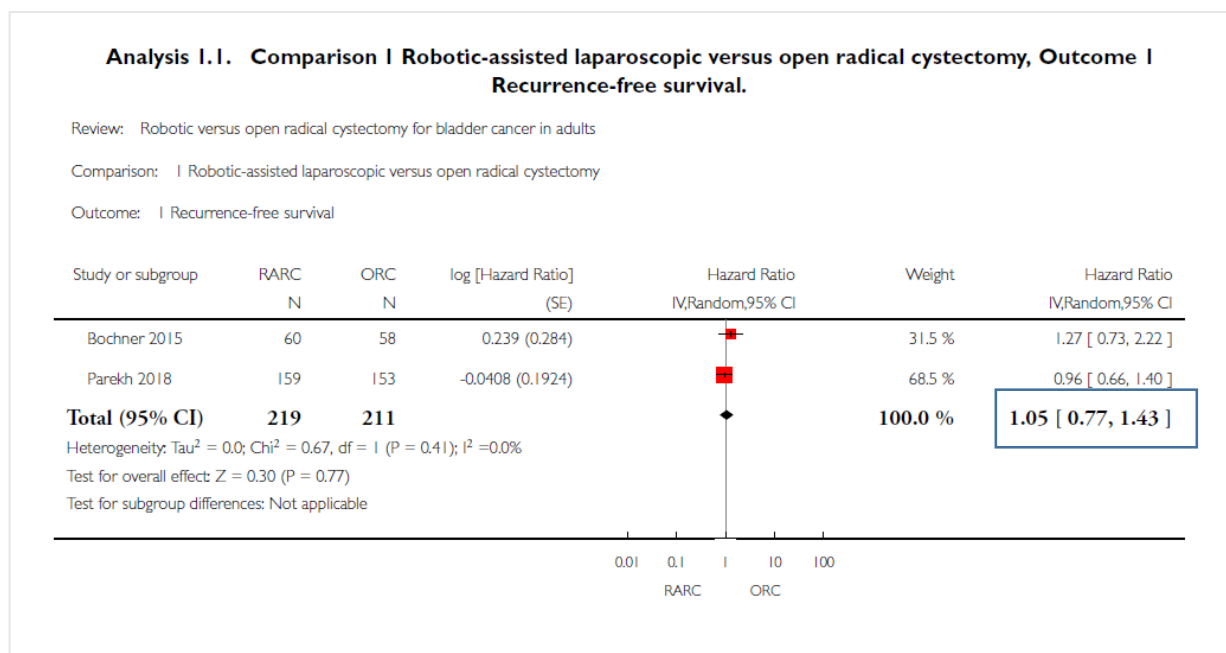


- Major complications (Clavien 3-5): RARC and open are similar
- Minor complications: RARC and open are similar





- Positive margin rates: RARC and open have similar positive margin rates

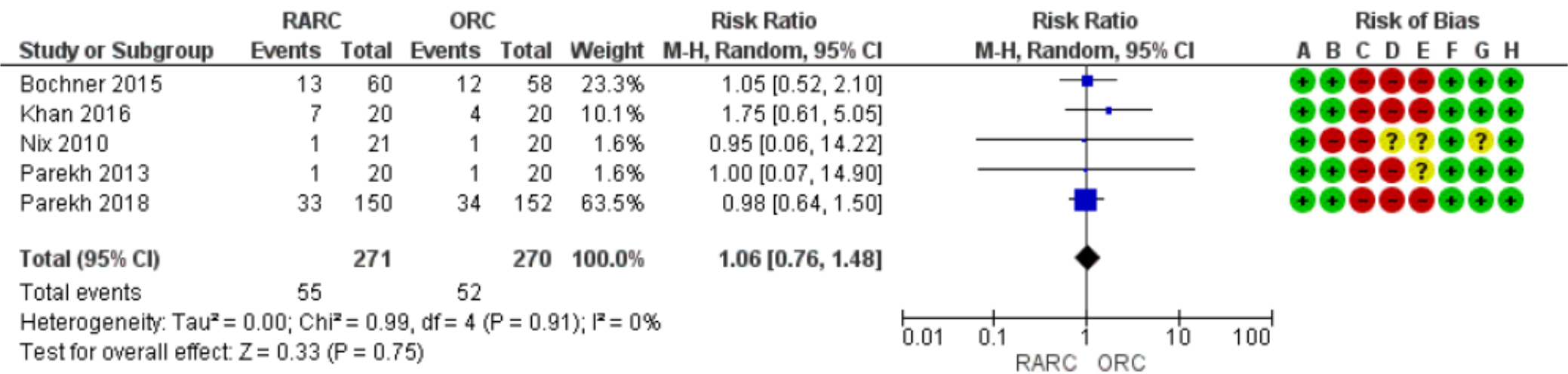


# Peri-operative

- f

Outcomes	No. of participants (studies) Follow-up	Certainty of the evidence (GRADE)
Time to recurrence (here: recurrence rate at 5 years) <sup>1</sup> assessed with clinical examination and imaging	277 (2 RCTs)	⊕⊕⊕⊕ LOW <sup>a,b</sup>
Major postoperative complications assessed with Clavien-Dindo system (rated grade 3 to 5)	541 (5 RCTs)	⊕⊕⊕⊕ LOW <sup>b,c</sup>
Minor postoperative complications assessed with Clavien-Dindo system (rated grade 1 or 2)	423 (4 RCTs)	⊕⊕⊕⊕ VERY LOW <sup>c,d</sup>
Positive margins assessed through pathological evaluation of cystectomy specimen	541 (5 RCTs)	⊕⊕⊕⊕ LOW <sup>b,c</sup>
Hospital stay assessed in days	541 (5 RCTs)	⊕⊕⊕⊕ LOW <sup>b,c</sup>

**Figure 4. Forest plot of comparison: 1 Primary outcome, outcome: 1.1 Major postoperative complication rates (Clavien 3 to 5).**



RARC may result in similar rates of major complications as ORC (risk ratio (RR) 1.06, 95% CI 0.76 to 1.48); 5 trials; low-certainty evidence

We downgraded the certainty of evidence for study limitations and imprecision

# Evidences for Robotic Cystectomy

- Nell'ultimo anno fiorire di metaanalisi su RCT
- J Urol
- Cochrane + BJUI
- Minerva



# Who is performing RARC? Insights into LC

- PASADENA definition:  $> 30$  RARC
- Razor definition:  $> 10$  RARC

# Case Presentation (1)

F.M. 59 yo male

- Married, current job as a Lawyer, IIEF 24
- Absence of concomitant cardiovascular and metabolic disease
- No medications
- Absence of previous abdominal surgery
- BMI 24

# History of RARC: milestones

- First RARC publication: 2003 (Menon M, Hemal A, Tewari A, BJUI)
- IRCC (International Radical Cystectomy Consortium) database: 2010
- Pasadena Consensus, 2014: to define the best practice
- First RCT comparing RARC and open:
- First meta-analysis:
- Long term oncological outcomes: 2019
- Cost-effectiveness analysis: yet undefined

# Case Presentation (1)

F.M. 59 yo male

## UROLOGICAL HISTORY

### **October 2017:**

- He reported a 3 months history of disuria and frequency, treated with solifenacin without benefit, and one episode of terminal hematuria
- USS: right bladder echogenic intravesical mass
- Urine cytology: atypia on 3/3 samples
- PSA 1,46 ng/ml ; Creatinine 0,9 (GFR 80 ml/min)
- Clinical examination: no abdominal masses, DRE: soft, mildly enlarged prostate

### **November 2017:** CYSTOSCOPY & TURBT : pT2G3 + CIS

- Bladder: 3 cm exophytic mass of bladder dome + multiple reddish areas
- Pathology: Urothelial cell carcinoma T2G3

Multiple biopsies: multifocal CIS (cold cup prostatic urethral biopsy: positive)

## Clinical Case - staging

# Case Presentation (1)

**Chest Xray:** normal

**Abdominal CT scan:**

normal upper urinary tract, no lymphadenopathies, no visible residual mass in the bladder



# Case Presentation (1)

Patient refuses neoadjuvant chemotherapy

Highly motivated for neobladder reconstruction

(may refuse surgery if an attempt to perform an internal continent diversion is not considered)

Extremely keen to maintain erectile function

(baseline IIEF = 24)

No preference for surgical technique (open or robotic)

Setting: Academic Center equipped with DaVinci Xi

## Case Presentation (1)

Which approach?  
Open or Robotic?



# What really happened in this case...

## Case Presentation (1)

Patient underwent robotic LND + radical cystectomy

Frozen section of:

- 1) Terminal ureters: no tumour
- 2) wedge of membranous urethra  
+ prostatic apex: no tumour

Extracorporeal neobladder (Y shaped) + ureteral-neobladder anastomosis on lateral wall of each chimney (no antireflux)

# Case Presentation (1)

- Post-operative course: uneventful
- Pathological report: pT2a, R0, N0
- At 2-years follow up, absence of local relapse or distant metastasis
- Continence: no pad requirement during day (ICIQ questionnaire : 4)
- IIEF: 18, use of oral PDE5-I



Different clinical case ...

Twins could be actually disparate?



## Case Presentation (2)

- Male, 74 years old patient
  - Diabetes mellitus
  - Previous hernioplasty
  - Relapsing episodes of hematuria (HB: 9.8)
  - Dysuria
- 
- Ultrasound: 50 mm mass in the left bladder aspect, mild homolateral hydronephrosis

## Case Presentation (2)

TURB-T: High-grade urothelial carcinoma, pT2,.lymphovascular invasion

Contrast CT: grade I left hydronephrosis, slightly enlarged left pelvic nodes (max size: 13 mm)

Charlson Comorbidity index: 6

Which approach?  
Open or Robotic?

## Case Presentation (2)

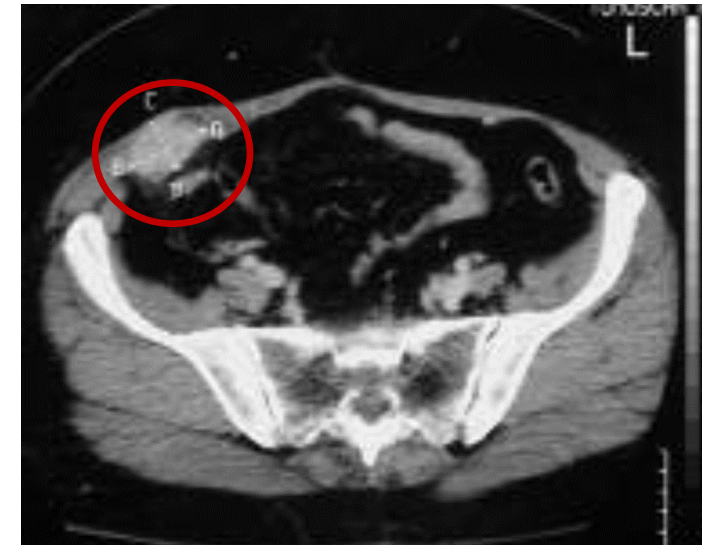
➔ The patient underwent RARC (April 2015) with an ileal conduit

Pathological report: urothelial carcinoma of the bladder, high grade, lymphovascular invasion, pT3a, negative surgical margins, pN1



## Case Presentation (2)

- October 2016
- Follow up: 4 cm nodule on the right abdominal wall (CT)
- Surgical removal: metastatic site of urothelial carcinoma





# Open and Robotics ... Which differences?



## 1) TECHNIQUE AND OUTCOMES

- If you perform it robotically, which urinary diversion: extra- or intra-corporeal ?
- Has robotic advantages to restore erectile function by a nerve sparing approach?
- Is robotic a guarantee of better post-op outcomes (blood loss, complication rate, LOS)?  
Or could ERAS protocol be the major drivers of a faster post-op course?

## 2) ONCOLOGICAL OUTCOMES

- Could the approach (open or robotic) impact on major oncological endpoints?

# Open and Robotics ... Which differences?



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## 2) ONCOLOGICAL OUTCOMES

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## Extra- or intra-corporeal diversion?

### Randomized Clinical Trial of Intra-corporeal vs Extra-corporeal Urinary Diversion after Robot Assisted Radical Cystectomy (RECEIVE trial)

- Primary endpoint: to determine whether RARC followed by ICD provides **superior** postoperative outcomes compared to ECD, resulting in a 20% reduction of 90-day postoperative complications.
- Secondary endpoints: perioperative outcomes, functional recovery, morbidity, mortality.

# Intracorporeal vs Extracorporeal Urinary Diversion After Robot Assisted Radical Cystectomy

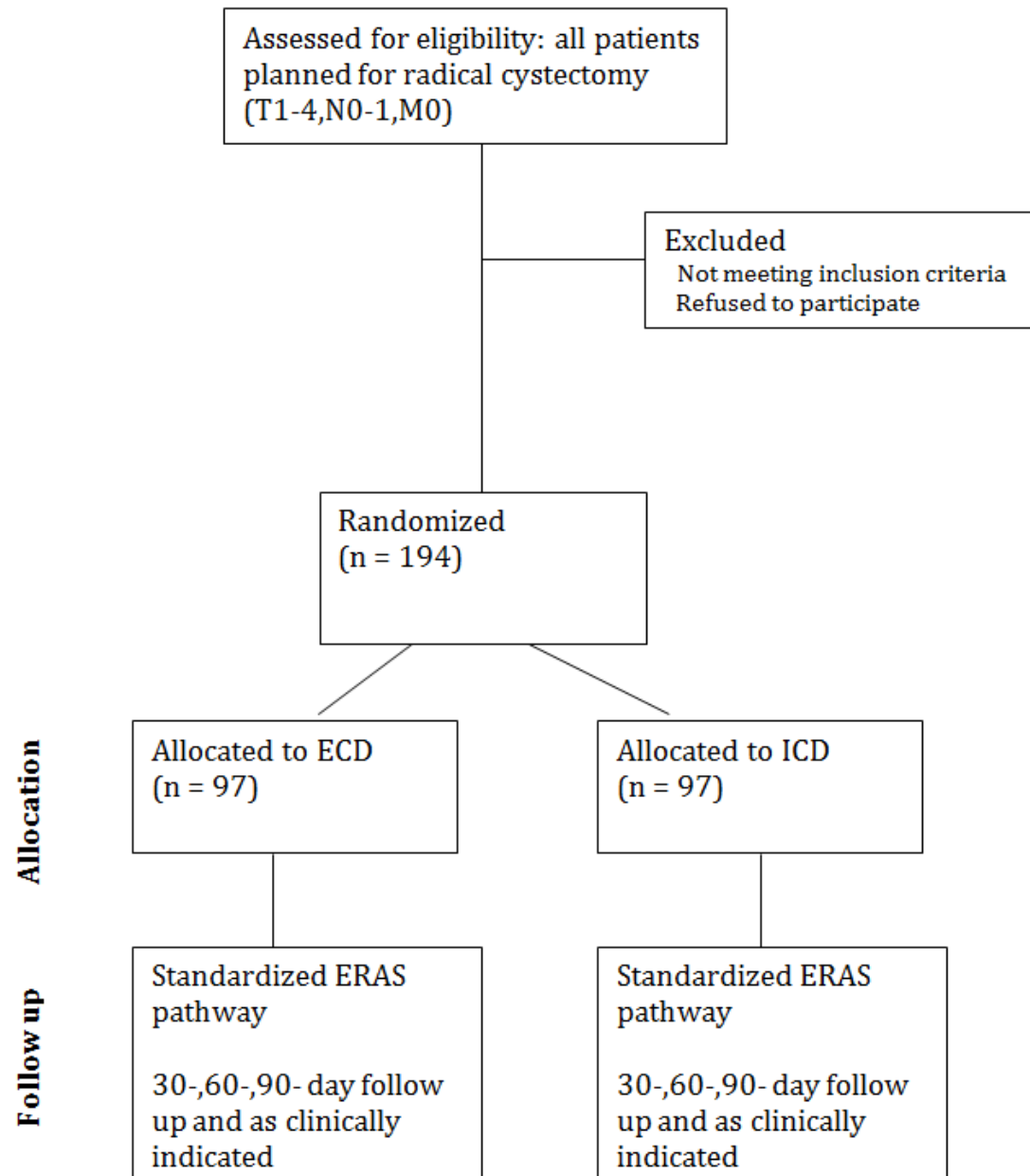
ClinicalTrials.gov Identifier: NCT03469362

Recruitment Status ⓘ : Recruiting

First Posted ⓘ : March 19, 2018

Last Update Posted ⓘ : January 18, 2019

See [Contacts and Locations](#)



## Extra- or intra-corporeal diversion?

### Intracorporeal UD: a step forward for RARC?

## Declining Use of Orthotopic Reconstruction Worldwide—What Went Wrong?

**Richard E. Hautmann**

*From the Department of Urology, University of Ulm, Ulm (Germany)*

- **The rate of continent urine diversion is declining in recent years:**
  - **USA:** from 6.9% 2010 to 4.7 in 2013 (*Kosinsky 2017*)
  - **Germany:** from 36.7% in 2006 to 29.7% in 2013 (*Goreben 2017*)
- **Reason?**
  - **Low surgical volume (as a result of dissemination of the procedure)?**
  - **Imperfect continence?**

**IUD with RARC:**

**-any implication in this trend?**

**-Any hint that it will reverse this trend?**

## Extra- or intra-corporeal diversion?

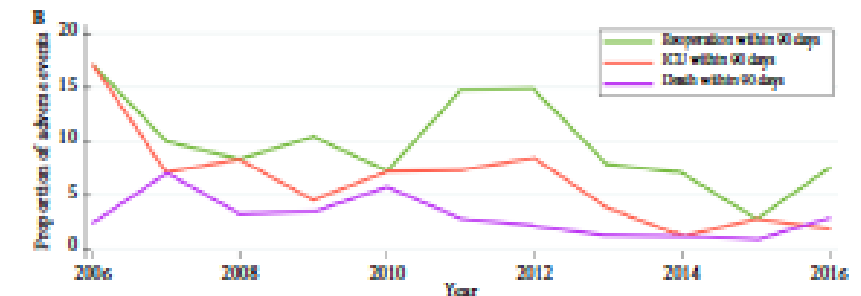
### No evidence that intracorporeal UD has improved cystectomy outcomes

- **The (positive) facts:**

- Since 2013 all RC were RARC and **the majority had IUD**
- Neobladder were twice more likely with RARC than ORC
- RARC patients less fit for surgery (> ASA III)
- 90d mortality, ICU admission and reinterventions were significantly lower in RARC

- **The problem:**

- reduction of risk with RARC lost after propensity score matching
- Improvements in patients care (ERAS...) to be accounted for



### Evolution of cystectomy care over an 11-year period in a high-volume tertiary referral centre

Aldo Brassetti\*, Axel Möller\*, Oscar Laurin\*, Jonas Höijer†, Christofer Adding\*, Ayako Miyakawa\*, Abolfazl Hosseini\* and Peter Wiklund\*

# Open and Robotics ... Which differences?



## 1) TECHNIQUE AND OUTCOMES

- If you perform it robotically, which urinary diversion: extra- or intra-corporeal ?
- **Has robotics advantages to restore erectile function by a nerve sparing approach?**
- Is robotic a guarantee of better post-op outcomes (blood loss, complication rate, LOS)?  
Or could ERAS protocol be the major drivers of a faster post-op course?

## 2) ONCOLOGICAL OUTCOMES

- Could the approach (open or robotic) impact on major oncological endpoints?



# Would you do a nerve sparing robotic cystectomy?

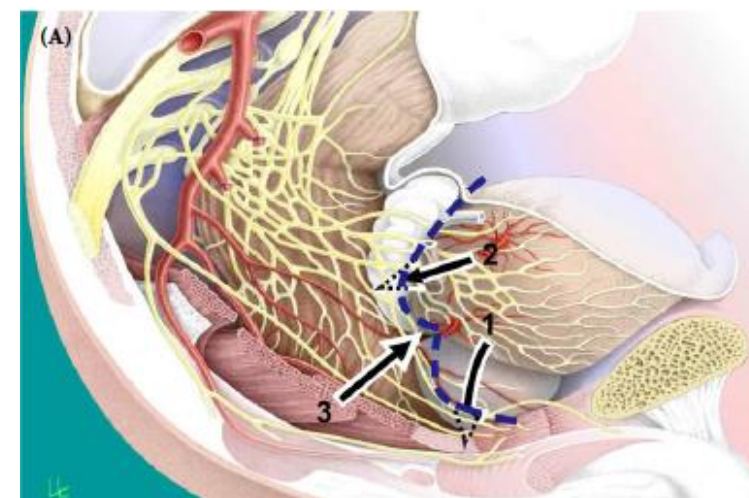
Prof. Gontero

## “Nerve sparing”: what do we mean?

Technical variants for sparing sexual function

- 1.- Prostate sparing
- 2.- Prostate capsule sparing
- 3.- Seminal sparing
- 4.- Nerve sparing (only)

## Nerve sparing “only” technique (male)



## NERVE SPARING CYSTECTOMY: FOR WHOM?

### Patient selection:

- Patients willing to preserve sexual function
- Preoperative sexual function
- Organ confined disease
- Absence of any type of tumour at the prostate, prostatic urethra, bladder neck (for prostate-seminal sparing techniques)

*Hernandez V et al, Urol Oncol 2017*

**Do not offer sexual preserving cystectomy as a standard therapy for MIBC**

NERVE SPARING CYSTECTOMY: efficacy and safety (SR)

Oncological safety:

- No evidence that oncological results are compromised
- No evidence of unusual metastases

Functional results (nerve sparing only):

- Postoperative potency better with NS compared to controls (20-90% vs 0-4%)

Study ID	Postoperative sexual function assessment				Sexual outcomes-potency			
	Time frame (mo)	Questionnaire	Self-impression	n evaluated (intervention vs. control)	Intervention	Control	P	Treatment ED
<i>Nerve sparing</i> Vilaseca et al. [20]	NR	Yes, EHS	No	30 (9–21)	77.8%	4.5%	<0.001	100% intervention, 23.0% control (PDE-5)
El-Bahnasawy et al. [21]/Hekal et al. [22]	12	Yes, IIEF-5	No	21	78.8%	0%	<0.05	21.0% PDE-5
Kessler et al. [7]	3–24	Yes, NR	Yes	331 (256–75)	77.0%	–	<0.001	8.0% PDE-5, 16.0% PG
Jacobs et al. [23] (NS group)	12	Yes, BCI	Yes	20	45.0%	–	–	–
Colombo et al. [24] (NS group)	24	Yes, IIEF-5	Yes	35	28.6%	–	–	–

## Nerve sparing cystectomy: ANY IMPACT ON CONTINENCE?

- 180 cons patients who survived > 10 y
  - NNS 13%
  - Unilateral NS 56%
  - Bilateral NS 31%
- Most baseline characteristics did not differ between groups
- Degrees of nerve sparing progressively affected both daytime and night-time continence

Variable	Univariate		Multivariable	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.03 (1.00–1.06)	0.048	1.03 (1.003–1.061)	0.03
Female	1.15 (0.47–2.83)	0.8	1.28 (0.50–3.23)	0.6
Body mass index	1.04 (0.99–1.10)	0.2	1.05 (0.99–1.11)	0.1
Charlson-Age Comorbidity Index ≥2	1.11 (0.73–1.70)	0.6	0.98 (0.64–1.51)	>0.9
Pathological stage				
≤T1	Reference	–	Reference	–
T2	0.92 (0.59–1.43)	0.7	0.93 (0.60–1.46)	0.8
T3a	0.91 (0.51–1.60)	0.7	1.07 (0.59–1.92)	0.8
NS status				
No NS	Reference	–	Reference	–
Any NS	2.08 (0.91–4.76)	0.05	2.51 (1.08–5.85)	0.03
Unilateral NS	1.84 (0.79–4.28)	0.15	2.25 (0.96–5.31)	0.06
Bilateral NS	2.63 (1.10–6.25)	0.03	3.49 (1.40–8.68)	0.007

# Open and Robotics ... Which differences?



## 1) TECHNIQUE AND OUTCOMES

- If you perform it robotically, which urinary diversion: extra- or intra-corporeal ?
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**Or could ERAS protocol be the major drivers of a faster post-op course?**

## 2) ONCOLOGICAL OUTCOMES

- Could the approach (open or robotic) impact on major oncological endpoints?

The degree of certainty for better perioperative outcomes of RARC remains low

Outcomes	No. of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with open radical cystectomy	Risk difference with robotic-assisted laparoscopic cystectomy
Major postoperative complications assessed with Clavien-Dindo system (rated grade 3 to 5)	541 (5 RCTs)	⊕⊕○○ LOW <sup>b,c</sup>	RR 1.06 (0.76 to 1.48)	Study population 185 per 1000	11 more per 1000 (44 fewer to 89 more)
Minor postoperative complications assessed with Clavien-Dindo system (rated grade 1 or 2)	423 (4 RCTs)	⊕○○○ VERY LOW <sup>c,d</sup>	RR 0.82 (0.58 to 1.17)	Study population 443 per 1000	80 fewer per 1000 (186 fewer to 75 more)
Transfusion rate assessed with transfused units of packed red blood cells	326 (2 RCTs)	⊕⊕⊕○ MODERATE <sup>c</sup>	RR 0.58 (0.43 to 0.80)	Study population 460 per 1000	193 fewer per 1000 (262 fewer to 92 fewer)
Hospital stay assessed in days	541 (5 RCTs)	⊕⊕○○ LOW <sup>b,c</sup>	-	Mean hospital stay ranged from 5.1 to 11.9 days	MD 0.67 days lower (1.22 lower to 0.12 lower)

# Mid-term follow up of surgery: similar

[Comparing Open Radical Cystectomy and Robot-assisted Laparoscopic Radical Cystectomy: A Randomized Clinical Trial.](#)

**Bochner** BH, Dalbagni G, Sjoberg DD, Silberstein J, Keren Paz GE, Donat SM, Coleman JA, Mathew S, Vickers A, Schnorr GC, Feuerstein MA, Rapkin B, Parra RO, Herr HW, Laudone VP.

**Eur Urol.** 2015 Jun;67(6):1042-1050. doi: 10.1016/j.eururo.2014.11.043. Epub 2014 Dec 8.

PMID: 25496767 **Free PMC Article**

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- 90-days complication rate
- 3- and 6-mo QOL outcomes

# Open and Robotics ... Which differences?



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- If you perform it robotically, which urinary diversion: extra- or intra-corporeal ?
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## 2) ONCOLOGICAL OUTCOMES

- **Could the approach (open or robotic) impact on major oncological endpoints?**



# Major oncological endpoints: equal

- Meta-analysis of RCT (Jul 2019)
- Robotic = open → surgical margin rate, nodal yield, RFS, PFS

*Eur Urol Oncol*. 2019 Jul;2(4):443-447. doi: 10.1016/j.euo.2018.10.008. Epub 2018 Nov 16.

## **Robot-assisted Radical Cystectomy Versus Open Radical Cystectomy: A Meta-analysis of Oncologic, Perioperative, and Complication-related outcomes.**

Satkunasivam R<sup>1</sup>, Tallman CT<sup>2</sup>, Taylor JM<sup>3</sup>, Miles BJ<sup>2</sup>, Klaassen Z<sup>4</sup>, Wallis CJD<sup>5</sup>.

### **Author information**

- <sup>1</sup> Department of Urology, Houston Methodist Hospital, Houston, TX, USA; Center for Outcomes Research, Houston Methodist Hospital, Houston, TX, USA. Electronic address: raj.satkunasivam@gmail.com.
- <sup>2</sup> Department of Urology, Houston Methodist Hospital, Houston, TX, USA.
- <sup>3</sup> Department of Urology, Baylor College of Medicine and Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX, USA.
- <sup>4</sup> Division of Urology, Medical College of Georgia-Augusta University, Augusta, GA, USA.
- <sup>5</sup> Division of Urology, Department of Surgery, University of Toronto, Toronto, Canada.

### **Abstract**

Robot-assisted radical cystectomy (RARC) is increasingly being used to treat muscle-invasive bladder cancer in an attempt to improve functional outcomes and complication rates over open radical cystectomy (ORC). We performed a meta-analysis of randomized controlled trials (RCTs) to compare patient outcomes between RARC and ORC. The primary outcome measure was a composite of recurrence-free survival (RFS) or progression-free survival (PFS). As a secondary measure, we examined other surrogate oncologic endpoints, perioperative outcomes, and complications. We found no difference between RARC and ORC with respect to RFS/PFS (hazard ratio 0.89, 95% confidence interval 0.64-1.24), surgical margin rates, or lymph node dissection yield. Analysis of patterns of recurrence for (pelvic) versus distant/abdominal sites indicated a significant difference between RARC and ORC ( $p=0.04$ ). This analysis represents a combination of post hoc analyses using RCT data and inconsistent between-study definitions of recurrence sites, and must be interpreted with caution. Lastly, RARC was associated with an advantage in estimated blood loss, but a longer operative time, with no difference in hospital length of stay or complication rates. These data support the oncologic safety of RARC; however, further research is required to assess potential differences in recurrence patterns. **PATIENT SUMMARY:** We synthesized data from recent randomized controlled trials to examine differences in cancer control between minimally invasive, robot-assisted radical cystectomy and traditional, open radical cystectomy. Our study shows that cancer control outcomes are comparable between robotic and open techniques, supporting the safety of minimally invasive surgery. Blood loss was lower in robotic surgery, but the robotic procedure was longer and did not have lower complications rates after surgery.

# Major oncological endpoints: equal

## • 3-years updates from the RAZOR trial (RCT on 302 pts)

- PFS at 36 months was 68.4% in the robotic and 65.4% in the open groups ( $p=0.600$ ).
- OS at 36 months was 73.9% in the robotic and 68.5% (95% CI 59.8-75.7%) in the open group ( $p=0.334$ ).
- There was no significant difference in the cumulative incidence rates of recurrence ( $p=0.802$ ).

### Author's Accepted Manuscript

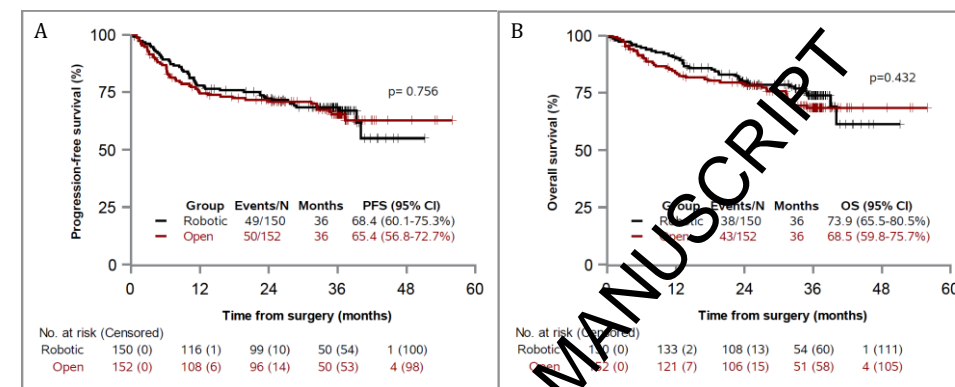
Predictors of recurrence, progression-free and overall survival following open versus robotic radical cystectomy: Analysis from the RAZOR trial with a 3-year follow-up

Venkatramani V, Reis IM, Castle EP, Gonzalgo ML, Woods ME, Svatek RS, Weizer AZ, Konety BR, Tollefson M, Krupski TL, Smith ND, Shabsigh A, Barocas DA, Quek ML, Dash A, Kibel AS, Pruthi RS, Montgomery JS, Weight CJ, Sharp DS, Chang SS, Cookson MS, Gupta GN, Gorbos A, Uchio EM, Skinner E, Soodana-Prakash N, Becerra MF, Swain S, Kendrick K, Smith JA Jr, Thompson IM, Parekh DJ

DOI: [10.1097/JU.0000000000000565](https://doi.org/10.1097/JU.0000000000000565)

Reference: JU-19-1272

Figure 1. Progression-free survival (A) and overall survival (B) by surgical groups.

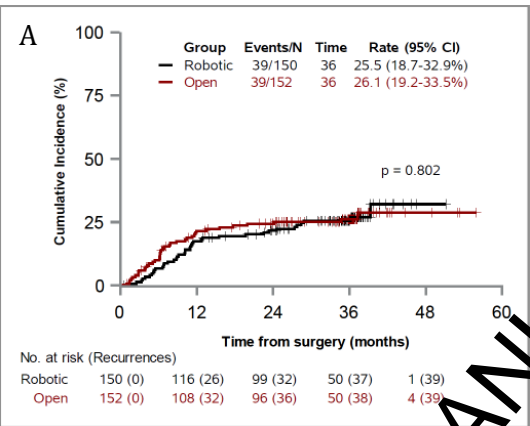


† Tick marker for censored observations.

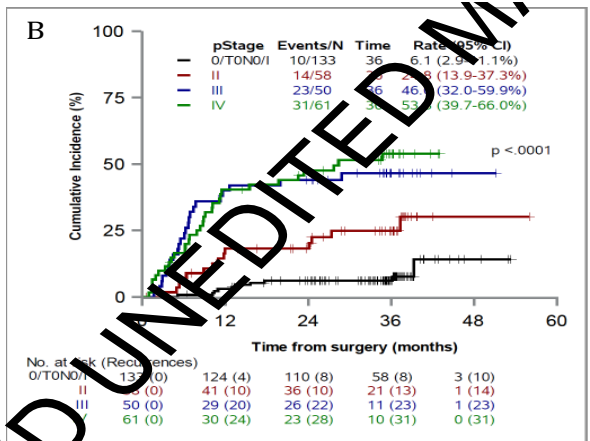
*Atypical site of recurrences: no difference from the RAZOR updates (sept 2019)*

Factors affecting overall recurrences:

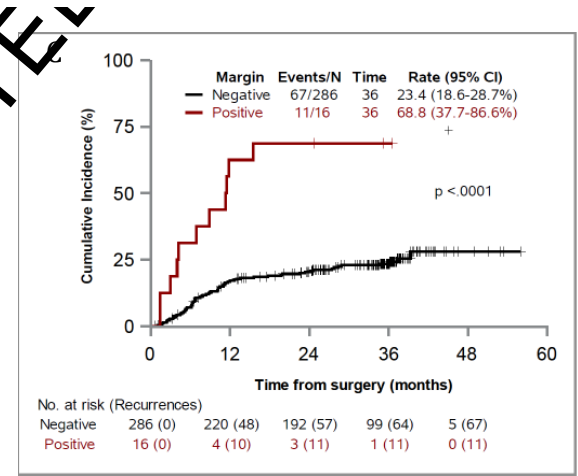
- Surgical approach: no impact (p=0.802)



Pathological stage (p<0.0001)



Positive surgical margins (P<0.0001)



† Tick marker for censored observations.

## .... unusual recurrence sites for RARC

Single center, single surgeon, retrospective

N= 120 ORC, 263 RARC

More LA disease in ORC (20% T4 in ORC vs 11% RARC)

*Median f.u. 30 m*

No difference in local recurrences **but distinct pattern of distant recurrence:**

- *Extrapelvic node locations (4/26 ORC vs 10/43 RARC)*

- *Peritoneal carcinomatosis (2/26 (8%) ORC vs 9/43 (21%) RARC)*

(No port site recurrence)

## Same concern from RCT

Memoria RCT study, oncological outcomes (2ry end point)

N= 60 RARC and 58 ORP

*Median f.u.: 4.9 y*

**Combining pelvic + abdominal recurrences = significantly higher in RARC:**

- *Pelvic recurrences (14 RARC vs 5 ORC)*
- *Abdominal wall rec (5 RARC vs 2 ORC)*
- *Bowel rec (5 RARC vs 0 ORC)*

(No difference in peritoneal carcinomatosis)

## The alert for unusual local recurrence with RARC warrants further investigations

*“It is concerning that we observed a potentially clinically meaningful increased risk of local recurrence with RARC [RR 2.08, CI 0.96-4.50]”*

*The Authors of the systematic review of 5 RCT: Sathianathan NJ et al, J Urol 2019*

### **Equivalence of RARC rec. rate should be interpreted cautiously:**

- The follow up does not usually go beyond 2-3 y (except the Memorial study)
- RARC series are likely to be selected (low rate of T3-T4 disease), thus preventing a fair comparison with RC series
- Large case series on RARC are biased and RCTs have low sample size
- Notably, the recent RCT comparing open vs MIT hysterectomy for early cervical cancer had 300 pt per arm & 4.6 y follow up...

*Ramirez PT, NEJM 2018*

