Considerations for radical cystectomy

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Conflicts of interest

Type of affiliation / financial interest	Name of commercial company
Receipt of grants/research supports	BMS, Photocure, Pacific Edge
Receipt of honoraria or consultation fees	Asieris Pharmaceuticals
Stock shareholder	Astrin Biosciences, Styx Biotechnologies, Geneverify
Other support (please specify):	

Patient selection

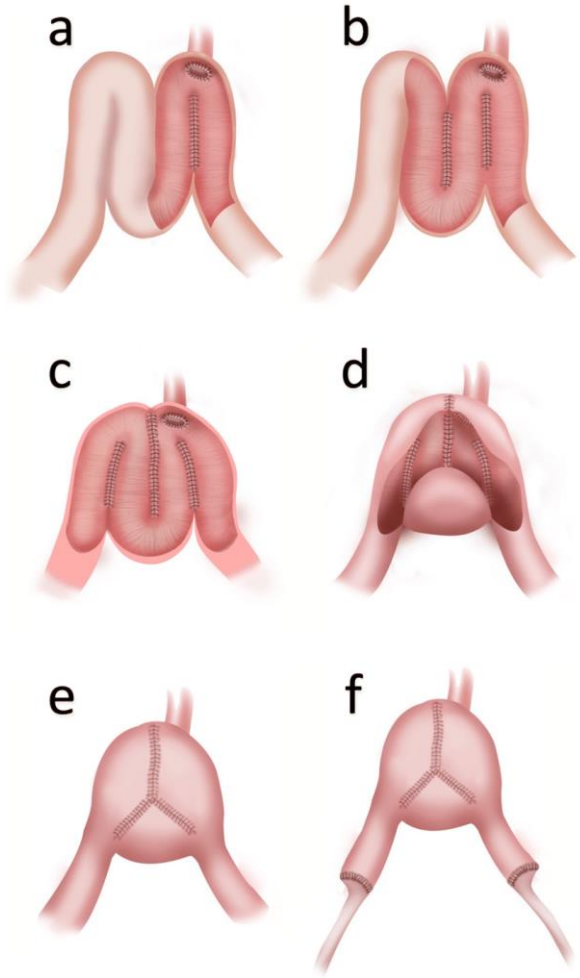
- Body habitus
- Comorbidity
- Willingness to catheterize
- Dexterity
- Social support
- Active stoma bag training

Selecting bowel segments

- Watershed areas
  - middle and right and left colic intersects
  - Sudecks junction of sigmoid and superior hemorrhoidal
  - Avoid distal ileum and terminal ileum in radiated patients
  - Ileum has higher likelihood of bowel obstruction vs colon (10% vs 4%)

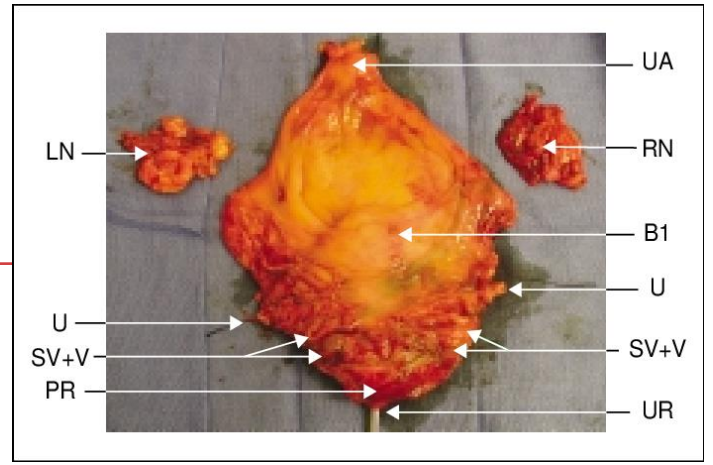
Continent diversion criteria

- Willing to accept need to cath
- Nightime incontinence
- Renal function adequate
  - Cr <2.0mg/dl
  - CrCl >40ml/min
  - *Urine pH <5.8 after NH4cl load*
  - *Urine osmolality >600 mOsm/kg after water deprivation*
  - *Minimal urine protein*



Timing of cystectomy

Authors Pub. Year Country	Mahmud [18] 2006 Canada	May [5] 2004 Germany	Sanchez–Ortiz* [6] 2003 USA	Chang [12] 2003 USA	Hara [14] 2002 Japan
pT stage	N/A	17% more pT4** $p = 0.009$	N/A	27% more pT3** $p = 0.01$	6% more pT3** 5% more pT4** NS
LNI	N/A	9% more N+** NS	4% more pN+** $p = 0.04$	17% more pN+**	10% more pN+** NS
pV+	N/A	9% more pV+** NS		N/A	27% more pV+** $p < 0.05$
NOC	N/A		36% more NOC** $p < 0.01$	N/A	
Diversion type[a]	N/A	20% more conduit** $p = 0.019$	N/A	N/A	53% more conduit** $p < 0.001$
Independent effects of delay a. 5-yr prog. free survival	N/A	HR = 1.62 (0.99–2.66) $p = 0.057$	N/A	N/A	NS[b]
b. 5-yr cancer sp. survival	N/A	N/A	HR = 1.93 (0.99–3.76) $p = 0.05$	N/A	NS[b]
c. 5-yr overall survival	HR = 1.2 (1–1.5) $p = 0.05$	N/A	N/A	N/A	NS[b]

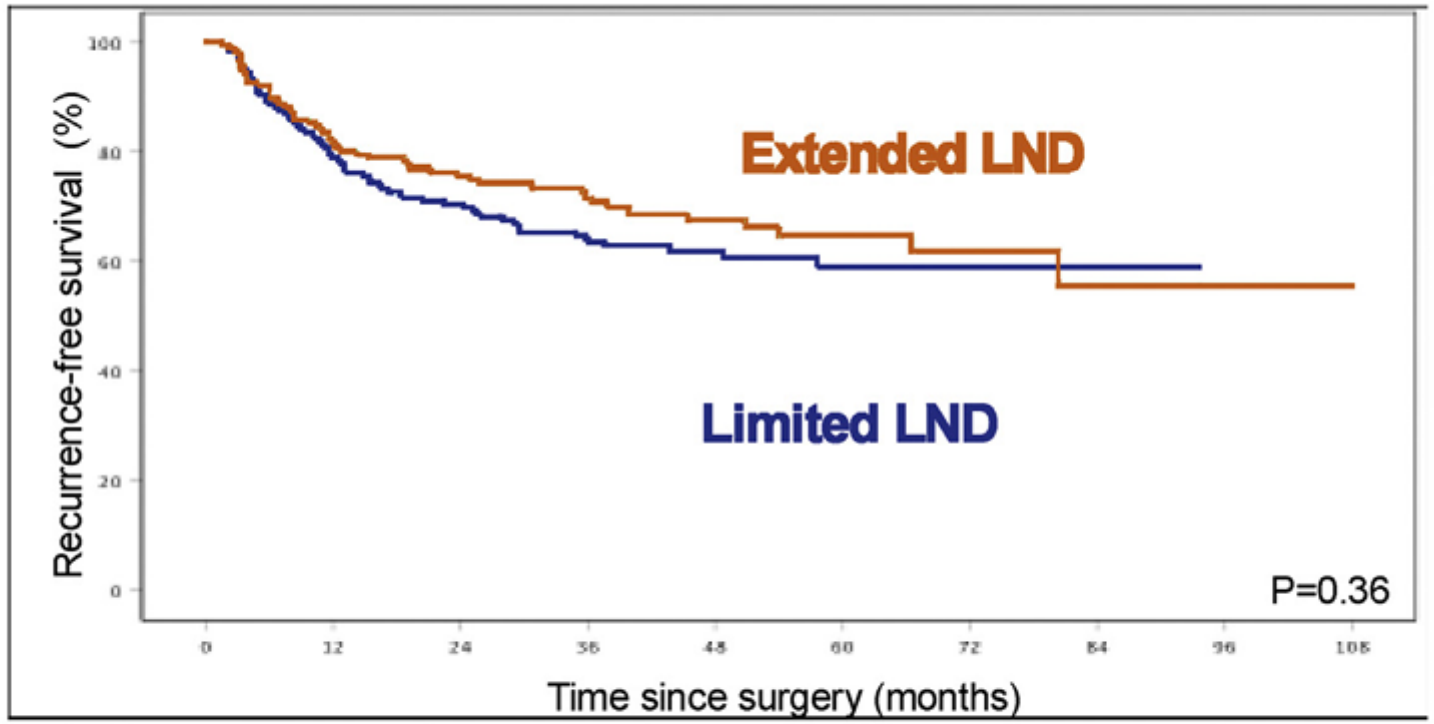


2 of 13 studies show delay affects survival
8 studies show higher path stage
3 studies show no correlation

Fahmy NM, et al. Eur Urol. 2006

Extended vs standard LND (LEA AUO AB/25-02)

A Recurrence-free survival



Number at risk										
Extended LND	198	127	108	81	53	34	14	8	1	1
Limited LND	203	127	101	79	54	35	20	6	0	0

RCT results:

- Expected RFS difference: 15%
- Difference seen: 5.45%
- No difference in CSS or OS
- No difference in complications
- All endpoints favored extended LND

Gschwend J et al. Eur Urol. 2018

Reported complication rates

Author	Years	N	Complication %
Knapp	2002-2008	268	57%
Lee	1993-2003	262	Men – 33% Women – 43%
Chang	1995-2000	304	Minor 4.9% Major 30.9%
Figueroa	1971-1996	1166	<70 years – 25% ≥70 years – 32%
Konety	1998-2002	6577	28%

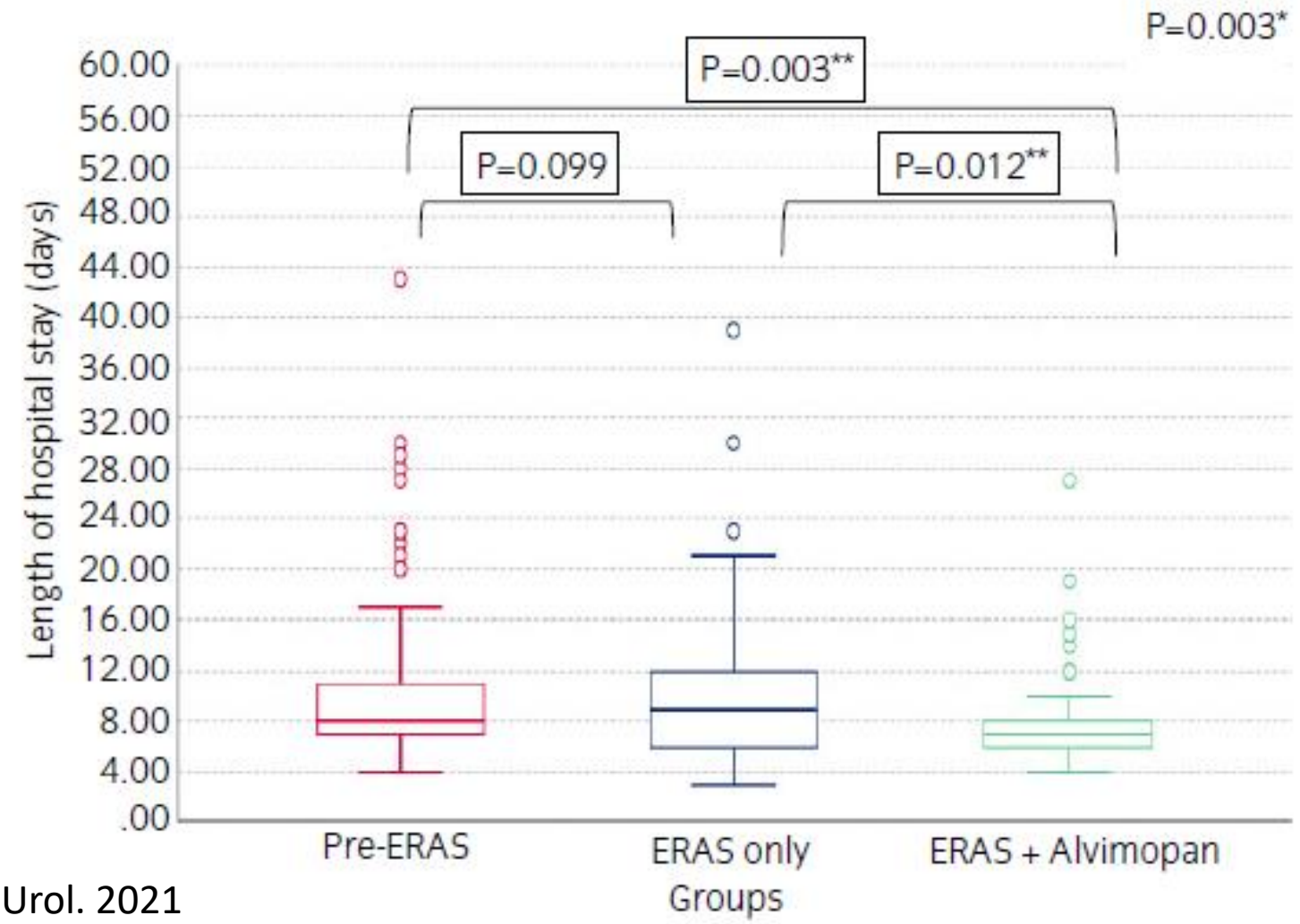
Benefit of using ERAS

Table 2. *Postoperative assessment of complications*

	% ERAS	% CR	p Value
Hydronephrosis	10	13	0.622
Urinary tract infection	40	38	0.852
Antibiotics for urinary tract infection	35	33	0.825
Cardiovascular complications	8	13	0.436
DVT	0	8	0.027
Lung emboli	2	8	0.127
Wound healing disorders	15	38	0.006
Paralytic ileus	15	28	0.093
Fever	26	54	0.004

- ERAS:
  No bowel prep
- High calorie drinks day before
- Clears till 2h pre-op
- NO NGT
- Early ambulation
- Early feeding
- Alvimoplan
- Early drain removal
- Restrict intraop fluids

The alvimoplan difference



Hanna P et al. Int. J Urol. 2021

Effects of Immunonutrition for Cystectomy on Immune Response and Infection Rates: A Pilot Randomized Controlled Clinical Trial

Jill M. Hamilton-Reeves[a,b,], Misty D. Bechtel[a], Lauren K. Hand[a], Amy Schleper[a], Thomas M. Yankee[c], Prabhakar Chalise[d], Eugene K. Lee[b], Moben Mirza[b], Hadley Wyre[b], Joshua Griffin[b], Jeffrey M. Holzbeierlein[b]*

European Association of Urology

- MDSCs significantly lower in SIM group than oral supplement group at POD 2
- 33% decrease postop complications and 39% decrease infections during late-phase recovery

Table 1 – Postoperative complications of men after bladder cancer surgery[1]

	Specialized immunonutrition, *n* = 14 men	Oral nutrition supplement, *n* = 15 men	Differences between groups, % (95% CI)
Complications, *n* (%)			
30 d	10 (71)	11 (73)	−2 (−36 to 33)
90 d*	2 (14)	7 (47)	−33 (−70 to −5.7)
High-grade complications, *n* (%)			
30 d	2 (14)	2 (13)	1 (−25 to 27)
90 d	0 (0)	2 (13)	−13 (−37 to 11)
Antibiotic use, *n* (%)[2]			
30 d	5 (36)	9 (60)	−24 (−66 to 18)
90 d**	2 (14)	8 (53)	−39 (−77 to −0.94)
Intra-abdominal infection, *n* (%)			
30 d	1 (7)	4 (27)	−20 (−53 to 14)
90 d	0 (0)	1 (7)	−7 (−26 to 13)
Ileus >5 d, *n* (%)	4 (27)	2 (13)	14 (−21 to 51)
Length of stay	6.3 (3.1)	6.1 (1.9)	0.2 (−1.79 to 2.23)
SIRS, *n* (%)[3]	1 (7)	2 (13)	−6 (−34 to 22)
Readmission, *n* (%)			
Yes	4 (29)	6 (40)	−11 (−53 to 30)
No	10 (71)	9 (60)	11 (−29 to 53)
Clavien-Dindo grade 30 d, *n* (%)[4]			
Grade 0	0 (0)	0 (0)	
Grade 1	2 (14)	1 (7)	7 (−22 to 37)
Grade 2	8 (57)	8 (53)	4 (−36 to 44)
Grade 3a	0 (0)	1 (7)	−7 (−26 to 13)
Grade 3b	0 (0)	1 (7)	−7 (−26 to 13)
Grade 4–5	0 (0)	0 (0)	
Clavien-Dindo grade 90 d, *n* (%)			
Grade 0	0 (0)	0 (0)	
Grade 1	0 (0)	0 (0)	
Grade 2	2 (14)	5 (33)	−19 (−56 to 18)
Grade 3a	0 (0)	2 (13)	−13 (−37 to 11)
Grade 3b	0 (0)	0 (0)	
Grade 4–5	0 (0)	0 (0)	

CI = confidence interval; SIRS = systemic inflammatory response syndrome.

[1] Recruitment and follow-up occurred from September 2013 to April 2015. Clinical outcomes data abstracted at 30 and 90 d were analyzed from all participants who signed the informed consent and who received any allocated supplements. Rates were compared using a chi-square test using intention to treat for categorical variables. A $p < 0.05$ was considered statistically significant.

[2] Infectious complications were defined by the need for intervention or prescription of nonprophylactic antibiotics. All patients followed the same antibiotic protocol according to the standard pathways of the University of Kansas Medical Center. All patients receive 24 h of Mefoxin followed by 1 mo of Macrodantin 100 mg every day.

[3] SIRS, based on temperature (<36 °C or >38 °C), heart rate (>90 beats/min), respirations (>20 breaths/min or $Paco_2$ <4.3 kPa), white blood cell count (<4000 cells/mm^3 or >12 000 cells/mm^3 or >10% bands present).

[4] Clavien-Dindo classification of surgical complications; a higher grade indicates a greater severity of complication.

* $p = 0.060$.

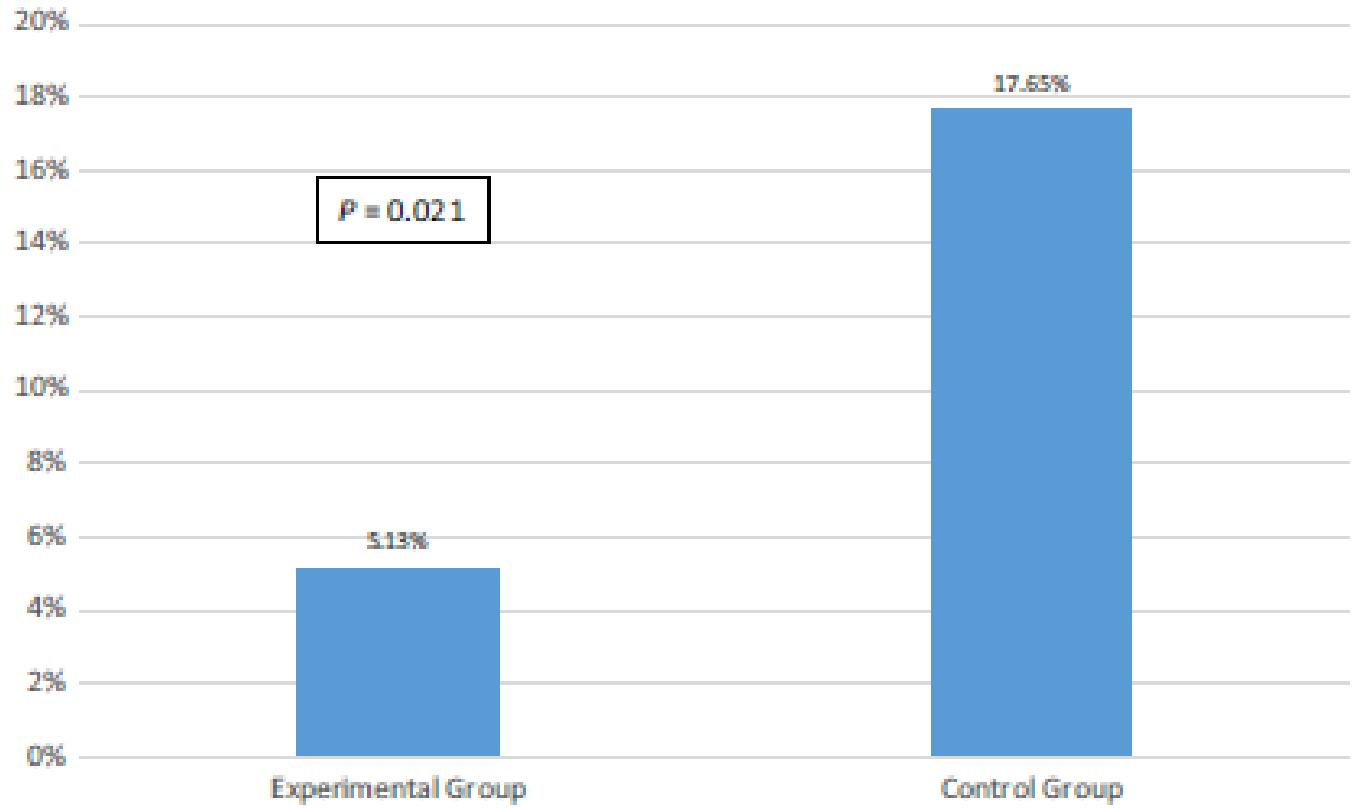
** $p = 0.027$.

Benefits of Immunonutrition

Postop Outcome	Overall Incidence (%)	No. Pts	Incidence in Pts Who Received Pre-INS vs Control	p Value
All complications (Clavien-Dindo I—V)	70.1	143	63.5% vs 77%	0.046
High-grade (Clavien-Dindo III—V) complication	22.2	45	22.1% vs 22%	1
Readmission within 30 days	34.3	70	39.8% vs 36%	0.66
Ileus requiring NGT decompression	28.9	59	23.3% vs 35%	0.09
Received TPN	25.5	52	17.3% vs 35.6%	0.015
Postop infection	34.8	71	25% vs 45%	0.003

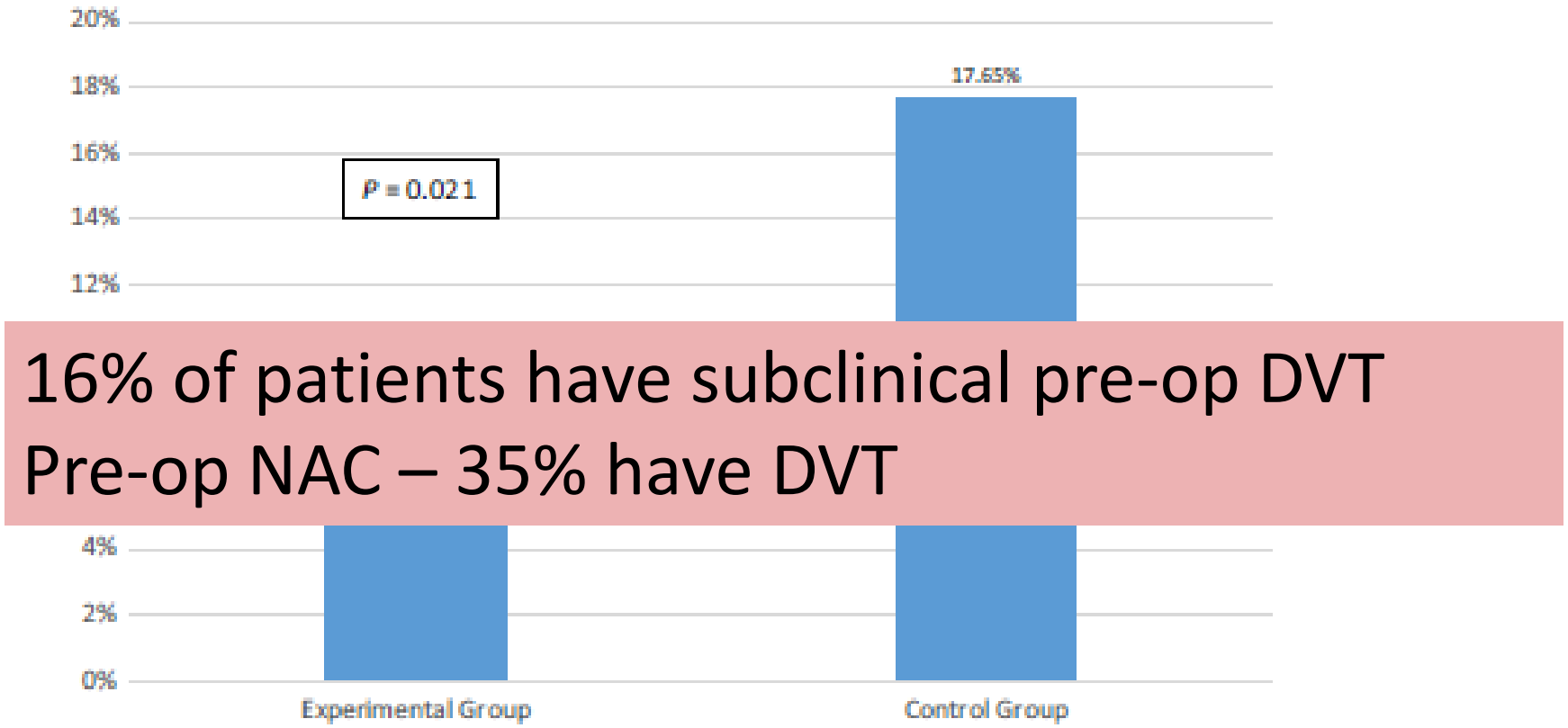
Khaleel S et al. J. Urol. 2021

Post op VTE prophylaxis



Schomburg J, et al. Urol. Oncol. 2018; Schomburg J, et al. Urology 2018

Post op VTE prophylaxis



16% of patients have subclinical pre-op DVT

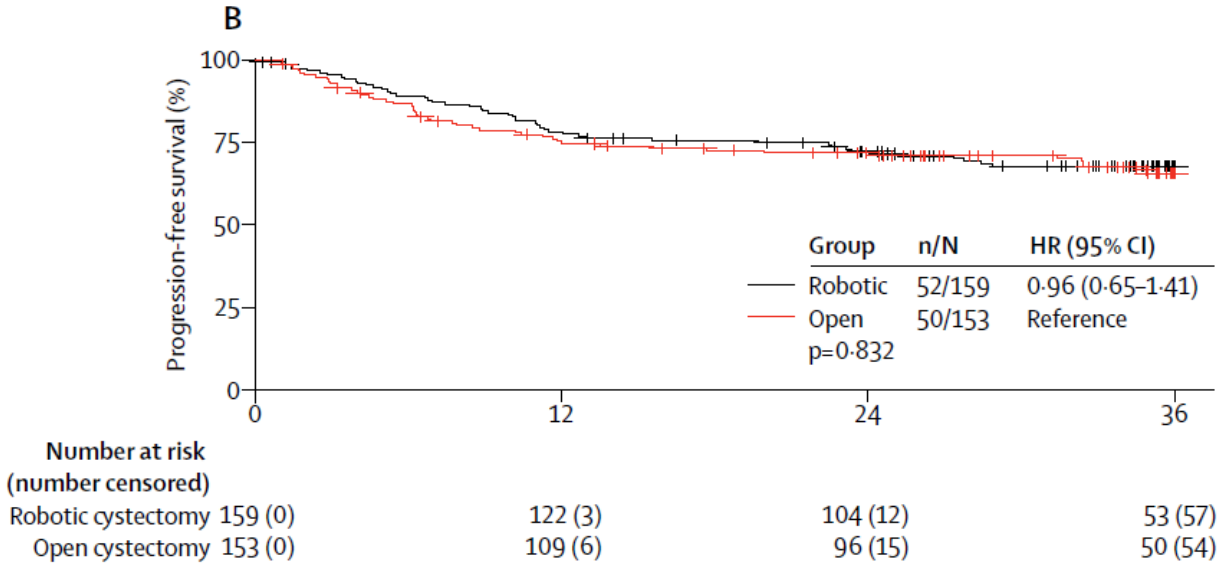
Pre-op NAC – 35% have DVT

Schomburg J, et al. Urol. Oncol. 2018; Schomburg J, et al. Urology 2018

Robot-assisted radical cystectomy versus open radical cystectomy in patients with bladder cancer (RAZOR): an open-label, randomised, phase 3, non-inferiority trial

Dipen J Parekh, Isildinha M Reis, Erik P Castle, Mark L Gonzalgo, Michael E Woods, Robert S Svatek, Alon Z Weizer, Badrinath R Konety, Mathew Tollefson, Tracey L Krupski, Norm D Smith, Ahmad Shabsigh, Daniel A Barocas, Marcus L Quek, Atreya Dash, Adam S Kibel, Lynn Shemanski, Raj S Pruthi, Jeffrey Scott Montgomery, Christopher J Weight, David S Sharp, Sam S Chang, Michael S Cookson, Gopal N Gupta, Alex Gorbonos, Edward M Uchio, Eila Skinner, Vivek Venkatramani, Nachiketh Soodana-Prakash, Kerri Kendrick, Joseph A Smith Jr, Ian M Thompson

- LOS
- EBL
- OR time
- Complications – no different



Combined experience with intracorporeal conduits (IRCC)

- Advantage:
  - Less EBL
  - Decreased transfusion
- LOS 8d vs 9d
- Complications equivalent

Ahmad H, et al, Eur. Urol 2013

Combined experience with intracorporeal conduits (IRCC)

- Advantage:
  - Less EBL
  - Decreased transfusion
- LOS 8d vs 9d
- Complications equivalent

Multivariable analysis – type of diversion (EC vs. IC)
- no effect on complications or mortality

Ahmad H, et al, Eur. Urol 2013

Research

JAMA | Original Investigation

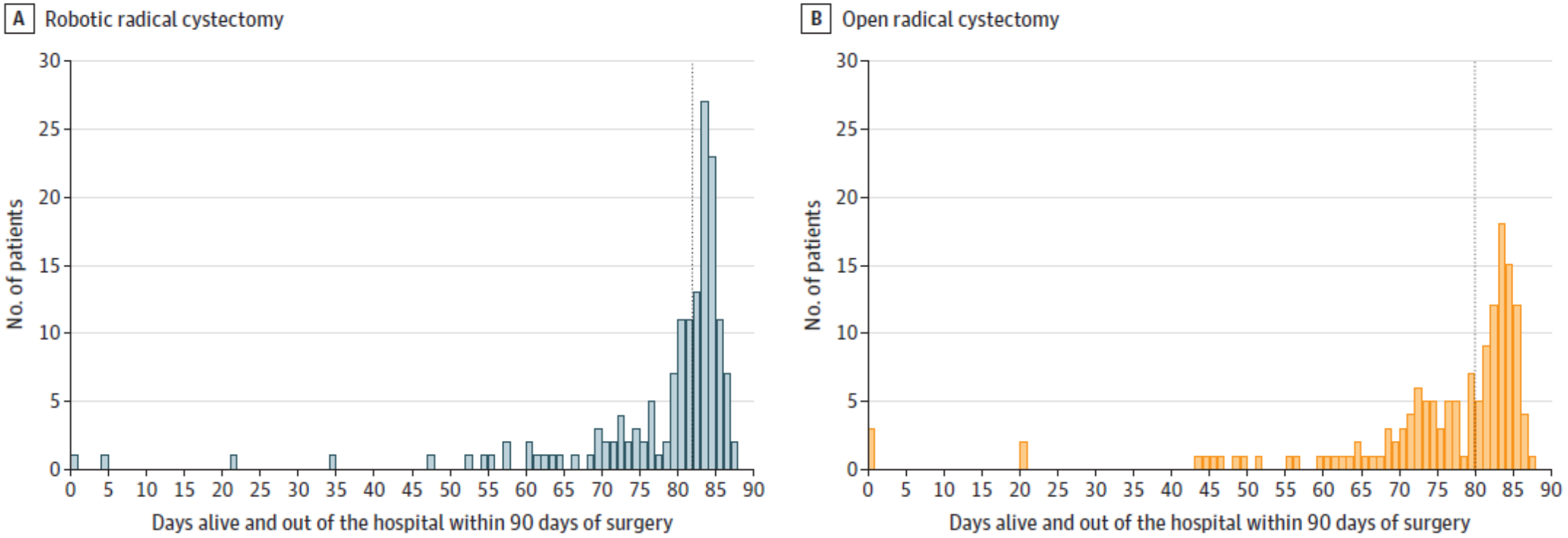
Effect of Robot-Assisted Radical Cystectomy With Intracorporeal Urinary Diversion vs Open Radical Cystectomy on 90-Day Morbidity and Mortality Among Patients With Bladder Cancer

A Randomized Clinical Trial

James W. F. Catto, PhD; Pramit Khetrapal, PhD; Federico Ricciardi, PhD; Gareth Ambler, PhD; Norman R. Williams, PhD; Tarek Al-Hammouri, MBChB; Muhammad Shamim Khan, MB, BS; Ramesh Thurairaja, MD; Rajesh Nair, MSc; Andrew Feber, PhD; Simon Dixon, PhD; Senthil Nathan, MPhil; Tim Briggs, BSc; Ashwin Sridhar, MSc; Imran Ahmad, PhD; Jaimin Bhatt, MBChB; Philip Charlesworth, DM; Christopher Blick, DM; Marcus G. Cumberbatch, PhD; Syed A. Hussain, MD; Sanjeev Kotwal, MD; Anthony Koupparis, MD; John McGrath, MD; Aidan P. Noon, MD; Edward Rowe, MD; Nikhil Vasdev, DSc; Vishwanath Hanchanale, MSc; Daryl Hagan, MSc; Chris Brew-Graves, MSc; John D. Kelly, MD; for the iROC Study Team

LOS difference = 1.11 days

Figure 2. Distribution of Days Alive and Out of the Hospital Within 90 Days of Surgery According to Group



Catto J et al. JAMA 2022

Complications

Complications	No. (%) Robotic cystectomy (n = 161)	Open cystectomy (n = 156)	Difference, % (95% CI)
Clavien-Dindo grade[a]	n = 151	n = 150	
No complications	59 (39.1)	50 (33.3)	5.7 (-5.1 to 16.6)
I	26 (17.2)	21 (14.0)	3.2 (-5.0 to 11.4)
II	41 (27.2)	46 (30.7)	-3.5 (-13.8 to 6.7)
III	0	1 (0.7)	
IIIa	8 (5.3)	14 (9.3)	-4.0 (-9.9 to 1.8)
IIIb	9 (6.0)	11 (7.3)	-1.4 (-7.0 to 4.3)
IV	0	0	
IVa	5 (3.3)	4 (2.7)	0.6 (-3.2 to 4.5)
IVb	0	0	
V	3 (2.0)	3 (2.0)	-0.0 (-3.2 to 3.1)

Catto J et al. JAMA 2022

QOL outcomes

Variable	At 5 weeks	12 weeks	≥26 weeks
EQ 5D-5L	Different	Not different	Not different*
EORTC QLQ-BLM-30	Not different	Not different	Not different
WHODAS 2.0	Different	Different	Not different
Physical activity (steps)	Not different	Not different	Not different
Strength and stamina	Different	Different	Not different

* Clinically meaningful difference is -0.08. The value in this trial was -0.07

Catto J et al. JAMA 2022

Health Related Quality of Life of Patients with Bladder Cancer in the RAZOR Trial: A Multi-Institutional Randomized Trial Comparing Robot versus Open Radical Cystectomy

Maria F. Becerra, Vivek Venkatramani, Isildinha M. Reis, Nachiketh Soodana-Prakash, Sanoj Punnen, Mark L. Gonzalgo, Shyamal Raolji, Erik P. Castle, Michael E. Woods, Robert S. Svatek, Alon Z. Weizer, Badrinath R. Konety, Mathew Tollefson, Tracey L. Krupski, Norm D. Smith, Ahmad Shabsigh, Daniel A. Barocas, Marcus L. Quek, Atreya Dash and Dipen J. Parekh*

Variable	3 months FACT BL score	6 months FACT BL score	Statistical
Robot vs open	0.28	1.27	No difference

Conclusions: Our data suggests lack of significant differences in the health related quality of life in robotic and open cystectomies. As robotic procedures become more widespread it is important to discuss this finding during counseling.

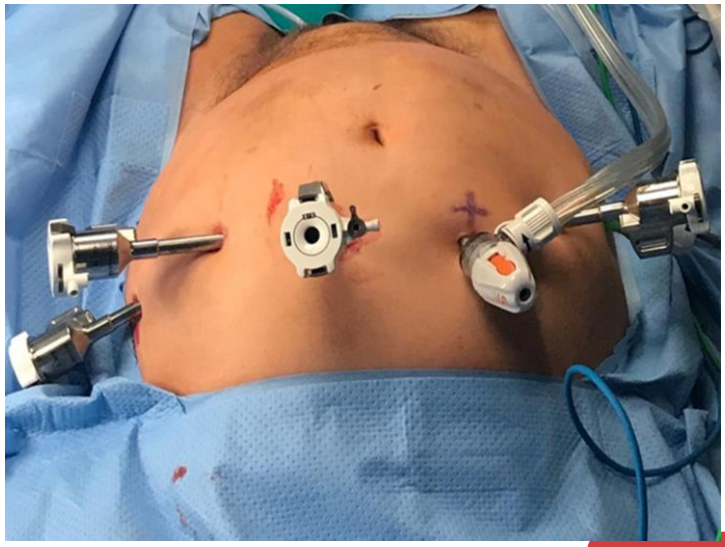
Comparison of trials

RAZOR

- OR Time 428 vs 361
- LOS 6 vs 7 days
- Complications no different
- QOL no different

iROC

- OR Time 295 vs. 270
- LOS 7 vs 8 days
- Complications no different
- QOL different at 5 weeks



Take home points

- Patient selection is key
- Bowel prep not needed – ERAS and nutrition important
- Get to it quickly!
- Technical completeness of surgery important, lymphadenectomy
- Younger patients who are willing to self cath – better candidates for neobladder
- Robot unclear advantage
- Watch for metabolic derangements during followup