

Open vs Robotic Radical Cystectomy: what's the evidence?

Presenter: Justin Collins


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Potential of minimally invasive surgery


- Less bleeding
- Less postoperative pain
- Shorter hospital stay
- Quicker return to normal life
- Less external and internal scarring
- Better cosmetic outcome

? Equivocal or better surgical outcomes

Open Cystectomy



Robotic cystectomy



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Important outcome measures of Radical Cystectomy


- **Oncological**
- Functional
- Complications
- Learning curve
- Cost

Indications for Robotic-assisted Radical Cystectomy

- Same guidelines and indications as open surgery
- Complete bilateral pelvic lymph node dissection
- Minimize positive margin risk
- Extracorporeal Urinary diversion usually done through small (7 - 10cm) midline incision. Neobladder to urethra anastomosis done robotically.
- Intracorporeal Urinary diversion done with totally laparoscopic approach

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Rep

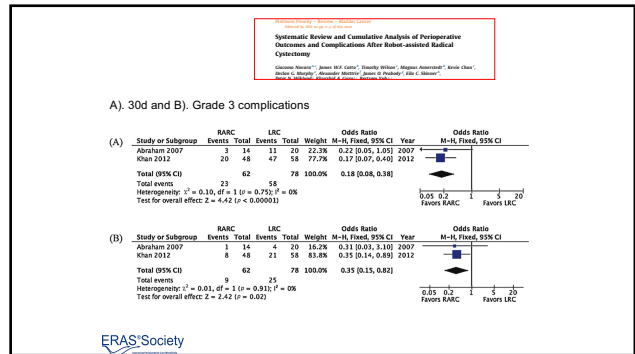
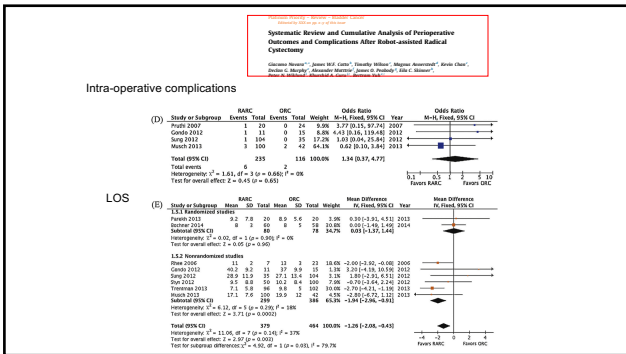
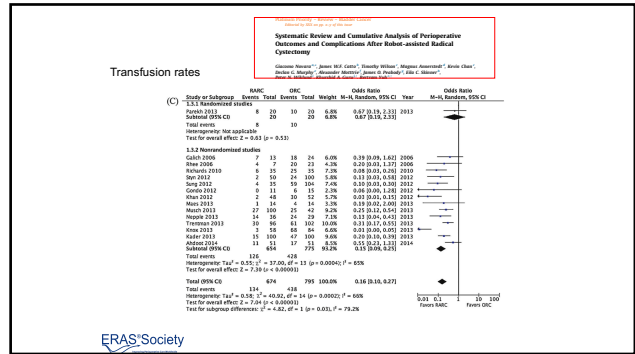
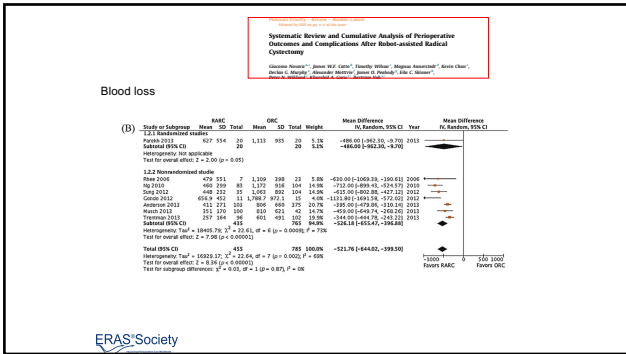


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Potential of a RARC approach



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Early recurrences following Radical Cystectomy

- Often occurs early
- Average presentation 10-15 months after RC
- 80% within the first 2 years
- Poor prognostic indicator
- Hypothesized potential negative effects of RARC
 - Pneumoperitoneum
 - Insufflation
 - Inadequate Lymph Node dissection

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

Daniel P. Nguyen^{1,2,3,4}, Bashir Al Hussein Al Awamih⁵, Xian Wu⁶, Padraic O'Malley⁷, Igor M. Inoyatov⁸, Abimbola Ayangbesan⁹, Bishop M. Faltus¹⁰, Paul J. Christos¹¹, Douglas S. Scherr¹²

Table 3 - Multivariate Cox regression analysis of variables associated with recurrence after radical cystectomy

| Variable | OR | 95% CI | P value |
|----------------------------|-----------|-----------|---------|
| Age (continuous) | 1.01 | 0.99-1.04 | 0.7 |
| Race (white) | 1.11 | 0.91-1.36 | 0.37 |
| Clinical stage | Reference | - | - |
| T1 | 0.33 | 0.12-0.93 | 0.037 |
| T2 | 0.41 | 0.15-1.14 | 0.08 |
| T3 | 0.39 | 0.19-0.84 | 0.02 |
| T4 | 0.44 | 0.15-1.36 | 0.2 |
| Tumor size | Reference | - | - |
| ORC | Reference | - | - |
| RARC | 0.78 | 0.59-1.03 | 0.2 |
| Perioperative chemotherapy | 3.27 | 2.01-5.32 | <0.0001 |
| Pathway type | Reference | - | - |
| Open | 2.20 | 0.69-6.96 | 0.2 |
| Robotic | 1.00 | 1.00-1.00 | 0.02 |
| Year | 1.00 | 1.00-1.00 | 0.02 |
| Year | 1.00 | 1.00-1.00 | 0.02 |

Table 4 - Distribution of locations among patients with recurrence and secondary urethral carcinoma within 2 yr after open (ORC) and robot-assisted radical cystectomy (RARC)

| Variable | ORC | RARC |
|------------------------------|-----------|--------------|
| Any recurrence | 3379 (42) | 57 (15) (36) |
| Local recurrence | 1088 (28) | 26 (16) (36) |
| Quintessential bed | 11 (2) | 14 (38) |
| PDE template | 6 (6) | 12 (30) |
| Disease recurrence | 2673 (36) | 43 (87) (29) |
| Lymph | 9 (28) | 34 (100) |
| Liver | 8 (25) | 10 (27) |
| Bladder | 8 (25) | 76 (182) |
| Extravesical lymph node | 4 (12) | 30 (77) |
| Peritoneal carcinomatosis | 2 (6) | 9 (23) |
| Other (ovary, adrenal) | 7 (21) | 0 |
| Secondary urethral carcinoma | 0 | 4 |
| Upper urinary tract | 0 | 1 (3) |
| Urethra | 0 | 1 (3) |

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Letter to the Editor

Re: Daniel P. Nguyen, Bashir Al Hussein Al Awamih, Xian Wu, et al. Recurrence Patterns After Open and Robot-assisted Radical Cystectomy for Bladder Cancer. Eur Urol. In press. <http://dx.doi.org.proxy.kib.ki.se/10.1016/j.euro.2015.02.003>

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| Recurrence type | ORC, n/n (%) | RARC, n/n (%) | Rate ratio (95% CI) | p value |
|---|--------------|---------------|---------------------|---------|
| Number of distant recurrences as denominator | | | | |
| Extrapelvic LN recurrence | 4/26 (15) | 10/43 (23) | 0.66 (0.15–2.29) | 0.51 |
| Peritoneal carcinomatosis | 2/26 (8) | 9/43 (21) | 0.37 (0.04–1.78) | 0.20 |
| Number of patients in treatment arm as denominator | | | | |
| Extrapelvic LN recurrence | 4/65 (6) | 10/147 (7) | 0.90 (0.21–3.14) | 0.89 |
| Peritoneal carcinomatosis | 2/65 (3) | 9/147(6) | 0.50 (0.05–2.43) | 0.40 |

CI = confidence interval; LN = lymph node; ORC = open radical cystectomy; RARC = robot-assisted radical cystectomy.

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

Daniel P. Nguyen^{1,2,3,*}, Bashir Al Hussein Al Awamih^{1,2}, Xian Wu¹, Padraic O'Malley³, Igor M. Inayotov¹, Abimbola Ayangbesan³, Bishoy M. Fattas³, Paul J. Christos¹, Douglas S. Scherr¹

Table 2. Distribution of locations among patients with recurrence and secondary surgical interventions within 2 yr after open (ORC) and robot-assisted radical cystectomy (RARC).

| Variable | ORC | RARC |
|--|-----------|-----------|
| Any recurrence ^a | 5379 (42) | 5176 (32) |
| Local recurrence ^b | 1565 (12) | 2476 (15) |
| Quadrant node ^c | 8 (4) | 12 (1) |
| Other recurrences ^c | 2673 (30) | 4974 (29) |
| None | 9792 | 14781 |
| Local | 9 (10) | 10 (2) |
| Extrapelvic lymph node | 4 (15) | 10 (2) |
| Peritoneal carcinomatosis ^c | 3 (10) | 10 (2) |
| Other (breast, adrenal) | 3 (12) | 0 |
| Upper urinary tract | 0 | 1 (7) |
| Unknown | 0 | 1 (7) |

ORC = open radical cystectomy; RARC = robot-assisted radical cystectomy; LN = lymph node; ORC = open radical cystectomy; RARC = robot-assisted radical cystectomy.

Table 3. Multivariable Cox regression analysis of variables associated with recurrence after radical cystectomy.

| Variable | HR | 95% CI | p value |
|---------------------------|-----------|------------|---------|
| Age (continuous) | 1.01 | 0.99–1.04 | 0.2 |
| Primary node | 0.11 | 0.03–0.39 | 0.03 |
| Time to recurrence | Reference | < | < |
| LN ^d status | 0.11 | 0.01–1.99 | 0.03 |
| T1 | 0.45 | 0.15–1.34 | 0.08 |
| T2 | 0.95 | 0.35–2.64 | 0.22 |
| T3 | 2.39 | 0.78–7.68 | 0.14 |
| T4 | 0.44 | 0.13–1.68 | 0.22 |
| Time to recurrence | Reference | < | < |
| ORC | 1.1 | 0.65–1.86 | 0.71 |
| ERCC ^e | 0.78 | 0.50–1.21 | 0.2 |
| Preoperative chemotherapy | 5.57 | 2.63–11.82 | <0.0001 |
| Pathologic stage | Reference | < | < |
| ISUP ^f grade | 1.28 | 0.64–2.56 | 0.1 |
| T1 | 1.28 | 0.64–2.56 | 0.1 |
| T2 | 1.38 | 1.03–1.84 | 0.04 |
| T3 | 4.52 | 2.26–9.03 | <0.0001 |
| T4 | 1.82 | 1.03–3.28 | 0.04 |
| ISUP ^f grade | Reference | < | < |
| M1N ^g | 1.19 | 0.81–1.76 | 0.2 |
| M2N ^g | 1.83 | 1.16–2.89 | 0.01 |
| Neoadjuvant chemotherapy | 1.03 | 0.71–1.51 | 0.88 |
| Preoperative lymph node | 1.18 | 0.69–2.01 | 0.55 |

HR = hazard ratio; CI = confidence interval; ORC = open radical cystectomy; RARC = robot-assisted radical cystectomy.

Long-term Oncologic Outcomes Following Robot-assisted Radical Cystectomy: Results from the International Robotic Cystectomy Consortium

Syed Johar Raza¹, Timothy Wilson², James O. Peabody³, Peter Wilkman⁴, Douglas S. Scherr¹, Ali Al-Daghamin¹, Shiva Dhalaj¹, Muhammad Shamim Khan¹, Prokar Dasgupta⁵, Alex Mottrie⁶, Mani Menon⁷, Bertram Yuh⁸, Lee Richstone⁹, Matthias Saar⁹, Michael Stoeckle⁹, Abolfazl Hasselini⁹, Jihad Kouk¹, James L. Mohler¹, Koon-Ho Rha¹, Gregory Wilding¹, Khursheed A. Guru¹



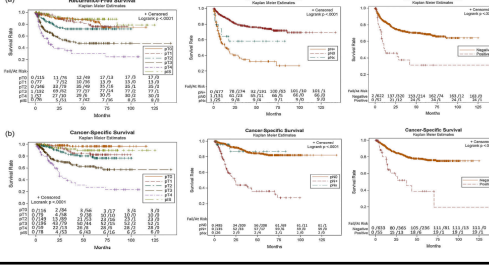
Table 3. Univariable and Multivariable analysis of factors associated with recurrence-free, cancer-specific, and overall survival.

| Variable | Univariable | | | Multivariable | | |
|---|--------------|---------------------|---------|---------------|---------------------|---------|
| | Hazard ratio | Confidence interval | p value | Hazard ratio | Confidence interval | p value |
| Proportional hazard model for recurrence-free survival | | | | | | |
| Age | 1.01 | (1.00–1.01) | 0.2 | 1.00 | (0.98–1.02) | 0.8 |
| Gender (male vs female) | 0.82 | (0.58–1.17) | 0.24 | 0.74 | (0.50–1.11) | 0.1 |
| pT stage (≥2 vs ≤2) | 3.74 | (2.79–5.08) | <0.001 | 2.12 | (1.45–3.13) | <0.0002 |
| LN (positive vs negative) | 1.13 | (1.10–1.17) | <0.001 | 1.08 | (1.02–1.13) | <0.001 |
| Margins (positive vs negative) | 2.06 | (1.93–2.20) | <0.001 | 2.16 | (1.27–3.68) | 0.005 |
| Adjuvant chemotherapy (yes vs no) | 4.00 | (3.74–4.26) | <0.001 | 3.20 | (2.28–4.60) | <0.001 |
| Histology (TCC vs variant) | 0.79 | (0.51–1.17) | 0.1 | 0.55 | (0.37–0.80) | <0.002 |
| Proportional hazard model for cancer-specific survival | | | | | | |
| Age | 1.01 | (1.00–1.01) | 0.09 | 1.02 | (1.00–1.04) | 0.03 |
| Gender (male vs female) | 0.84 | (0.52–1.27) | 0.4 | 0.83 | (0.52–1.31) | 0.5 |
| pT stage (≥2 vs ≤2) | 4.87 | (3.34–7.08) | <0.001 | 4.78 | (2.91–7.86) | <0.001 |
| LN (positive vs negative) | 1.12 | (1.04–1.21) | <0.001 | 1.11 | (1.01–1.21) | <0.001 |
| Margins (positive vs negative) | 3.62 | (0.18–4.55) | <0.001 | 1.52 | (0.91–2.52) | 0.2 |
| Adjuvant chemotherapy (yes vs no) | 1.28 | (0.98–1.68) | <0.001 | 1.23 | (0.71–1.93) | 0.4 |
| Histology (TCC vs variant) | 1.36 | (0.92–2.00) | 0.1 | 1.07 | (0.70–1.63) | 0.7 |
| Proportional hazard model for overall survival | | | | | | |
| Age | 1.02 | (1.01–1.03) | 0.002 | 1.02 | (1.01–1.04) | 0.002 |
| Gender (male vs female) | 1.06 | (0.80–1.41) | 0.7 | 1.13 | (0.78–1.62) | 0.5 |
| pT stage (≥2 vs ≤2) | 3.40 | (2.70–4.27) | <0.001 | 3.60 | (2.08–6.19) | <0.001 |
| LN (positive vs negative) | 1.10 | (1.01–1.18) | <0.001 | 1.07 | (1.02–1.12) | <0.003 |
| Margins (positive vs negative) | 2.41 | (1.98–3.09) | <0.001 | 1.51 | (0.96–2.39) | 0.07 |
| Adjuvant chemotherapy (yes vs no) | 2.31 | (1.78–2.98) | <0.001 | 1.12 | (0.60–1.93) | 0.5 |
| Histology (TCC vs variant) | 1.05 | (0.75–1.39) | 0.7 | 0.82 | (0.61–1.11) | 0.2 |

LN = lymph node; TCC = transitional cell carcinoma.

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| Variable | Result |
|---|------------|
| Follow-up, mo, median (IQR) | 67 (18–84) |
| Local recurrence, yes, n (%) | 79 (11) |
| Metastatic recurrence, yes, n (%) | 154 (22) |
| Time to recurrence, mo, median (IQR) | 24 (8–60) |
| Survival status, alive, n (%) | 383 (55) |
| Time to cancer-specific death, mo, median (IQR) | 14 (8–28) |
| Time to non-cancer-specific death, mo, median (IQR) | 10 (4–33) |
| Time to death, mo, median (IQR) | 15 (7–33) |
| 5-yr survival, % | |
| Recurrence-free | 67 |
| Cancer-specific | 75 |
| Overall | 50 |

IQR = interquartile range. * Includes combined local and metastatic recurrences.

Long-term Oncologic Outcomes Following Robot-assisted Radical Cystectomy: Results from the International Robotic Cystectomy Consortium

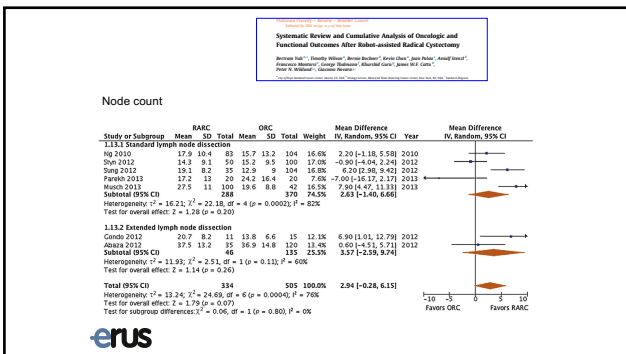
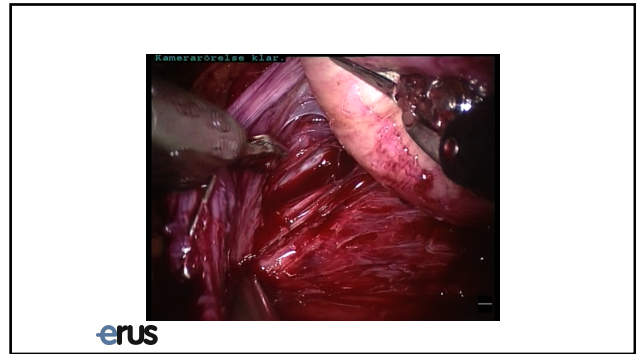
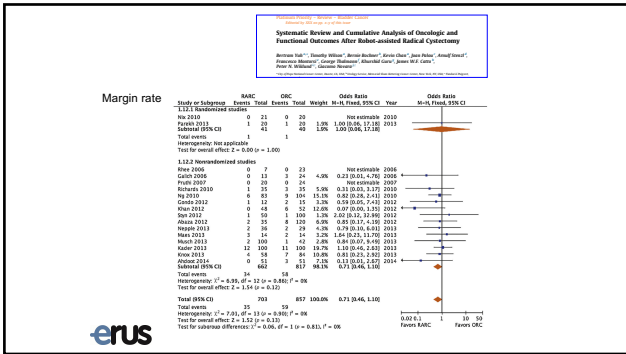
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Table 4 - Comparison of long-term oncologic outcomes among historical open and robot-assisted radical cystectomy series.

| Study | Number | Duration | Follow-up, mo, mean (range) | OC disease, % | Non-TCC, % | PLN yield | Neoadjuvant chemotherapy, % | RFS, % | CSS, % | OS, % |
|---------------------------|--------|-----------|-----------------------------|-----------------|------------|-----------|-----------------------------|----------|--------|-------|
| Choenis et al. 2008 [6] | 2720/0 | 1970–2000 | 66 (0–410) | 74 | 64 | NR | 20 | NR | 56 | NR |
| Stenz et al. 2001 [5] | 1054/0 | 1971–1997 | 120 (1–336) | 63 ^c | 0 | NR | 23 | 5 | 68 | NR |
| Hautmann et al. 2012 [16] | 1100/0 | 1986–2009 | 38 (0–282) | 67 ^d | 0 | 18 | 18 | Excluded | 70 | 58 |
| Shariat et al. 2006 [19] | 888/0 | 1984–2003 | 39 (0.4–183) | 57 | 0 | 20 | 23 | 5 | 58 | 66 |
| Xifreas et al. 2010 [10] | 175/R | 2004–2011 | 37 (21–53) | 65 | 4 | 19 | 17 | 23 | 63 | 66 |
| Yuh et al. 2014 [9] | 162/R | 2004–2010 | 52 (NR) | 67 | 0 | 28 | 22 | 23 | 74 | 80 |
| Raza et al. 2014 [8] | 99/R | 2005–2009 | 40 (12.7–70.8) | 49 | NR | 21 | 30 | 6 | 53 | 68 |
| Current study | 702/R | 2003–2009 | 67 (18–84) | 62 | 32 | 16 | 21 | 15 | 67 | 75 |

CSS = cancer-specific survival; NR = not reported; OC = open radical cystectomy; OC = organ confined; OS = overall survival; PLN = pelvic lymph node; R = robot-assisted radical cystectomy; RFS = recurrence-free survival; TCC = transitional cell carcinoma. * Median. ^c Includes pT3a as organ confined. ^d Includes pT3a as organ confined.



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Platinum Priority – Brief Correspondence
Editorial by Nicholas Rajanbenra and Manish 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. Collins¹, Abolfazl Hoesseini², Christofer Adding³, Tommy Nyberg⁴, Anthony Koupparis⁵, Edward Rowe⁶, Matthew Perry⁸, Rami Issa⁹, Martin C. Schumacher⁷, Carl Wijburg¹⁰, Abdullah E. Canda¹¹, Melvin D. Balbay¹², Karel Decastecker¹³, Christian Schwentner¹⁴, Arnulf Stenzl¹⁵, Sebastian Edeling¹⁶, Saša Pokupic¹⁷, Fredrik D'Hondt¹⁸, Alexander Mottrie¹⁹, Peter N. Wiklund¹⁹

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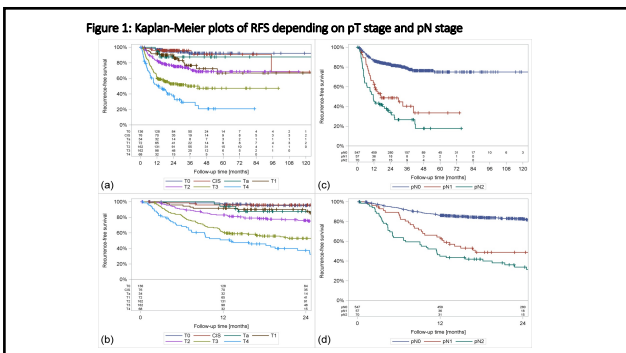


Table 2: Distribution of recurrence locations in first 24 months

| Variable | Overall | Urinary diversion type | |
|--|------------|------------------------|------------|
| | | Ileal Conduit | Neobladder |
| Any recurrence, n (%) | 173 (24.1) | 133 (27.8) | 40 (17.0) |
| Local recurrence, n (%) | 72 (10.0) | 56 (11.7) | 16 (6.8) |
| Cystectomy bed | 22 (3.1) | 19 (4.0) | 3 (1.3) |
| Distal ureteric | 3 (0.4) | 2 (0.4) | 1 (0.4) |
| Urethral | 3 (0.4) | 2 (0.4) | 1 (0.4) |
| Pelvic LN | 48 (6.7) | 36 (7.5) | 12 (5.1) |
| Distant recurrences, n (%) | 118 (16.5) | 89 (18.6) | 29 (12.3) |
| Lung | 39 (5.4) | 31 (6.5) | 8 (3.4) |
| Liver | 35 (4.9) | 24 (5.0) | 11 (4.7) |
| Bone | 41 (5.7) | 30 (6.3) | 11 (4.7) |
| Brain | 6 (0.8) | 5 (1.0) | 1 (0.4) |
| Adrenal | 4 (0.6) | 3 (0.6) | 1 (0.4) |
| Pancreas | 2 (0.3) | 2 (0.4) | 0 (0.0) |
| Extrapelvic LN | 1 (0.1) | 1 (0.2) | 0 (0.0) |
| Peritoneal carcinomatosis | 44 (6.1) | 35 (7.3) | 9 (3.8) |
| Port site | 5 (0.7) | 4 (0.8) | 1 (0.4) |
| Skin | 2 (0.3) | 1 (0.2) | 1 (0.4) |
| Muscle | 1 (0.1) | 0 (0.0) | 1 (0.4) |
| Secondary urothelial carcinoma, n (%) | 1 (0.1) | 0 (0.0) | 1 (0.4) |
| Upper urinary tract | 2 (0.3) | 1 (0.2) | 1 (0.4) |
| Presenting with local and distant recurrences, n (%) | 31 (4.3) | 25 (5.2) | 6 (2.6) |

NAC administration in RARC patients: Upstaging and downstaging of pathological stage and association with oncological outcomes

| Variable | No. | No change to staging | Upstaged (any pT stage) | Upstaged to pT4 disease | Downstaged (any pT stage) | Downstaged to pT0 | P value |
|---|-----|----------------------|-------------------------|-------------------------|---------------------------|-------------------|---------|
| All patients (%) Missing = 11 | 706 | 210 (29.75) | 230 (32.58) | 55 (7.79) | 266 (37.68) | 134 (18.98) | |
| Patients receiving NAC (%) Missing = 28 | 174 | 40 (22.99) | 33 (18.97) | 7 (4.02) | 101 (58.05) | 62 (35.63) | <0.0001 |
| Patients not receiving NAC (%) Missing = 28 | 515 | 163 (31.65) | 193 (37.48) | 47 (9.13) | 159 (30.87) | 58 (13.21) | <0.0001 |
| PSM rate (%) Missing = 0 | 34 | 8 (23.53) | 25 (73.53) | 13 (38.24) | 1 (2.94) | 0 (0) | <0.0001 |
| Negative surgical margin rate (%) Missing = 11 | 672 | 202 (30.06) | 205 (30.51) | 42 (6.25) | 265 (39.43) | 134 (19.94) | <0.0001 |

PSM = positive surgical margin NAC = neoadjuvant chemotherapy

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Meta-analysis of open vs robotic cystectomy

Table 1. Characteristics of included studies.

| First author and reference | Recruitment | Country | Primary end point | Number of patients, OR/ RARC |
|----------------------------|------------------------|---------|----------------------------|------------------------------|
| Nix et al. 2010 [16] | April 2008- Jan 2009 | USA | Lymph node yield | 20/ 21 |
| Parakh et al. 2013 [14] | July 2009- June 2011 | USA | Feasibility study | 20/ 20 |
| Bochner et al. 2015 [17] | March 2010- March 2013 | USA | Perioperative complication | 58/ 60 |
| Khan et al. 2016 [15] | March 2009- July 2012 | UK | Perioperative outcomes | 20/ 20 |

- Small sample size (40-118 patients/ study)
- Single centre
- Feasibility studies OR Closed before planned recruitment
- Learning curve effect

Tan et al. PLOS One 2016

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

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Summary
Background: Radical cystectomy is the surgical standard for invasive bladder cancer. Robot-assisted cystectomy has been proposed to provide similar oncological outcomes with lower morbidity. We aimed to compare progression-free survival in patients with bladder cancer treated with open cystectomy and robot-assisted cystectomy.

Methods: The RAZOR study is a randomised, open-label, non-inferiority, phase 3 trial done in 15 medical centres in the USA. Eligible participants (aged ≥18 years) had biopsy-proven clinical stage T1-T4, N0-N1, M0 bladder cancer or refractory carcinoma in situ. Individuals who had previously had open abdominal or pelvic surgery, or who had any pre-existing health conditions that would preclude safe initiation or maintenance of pneumoperitoneum were excluded. Patients were centrally assigned (1:1) via a web-based system, with block randomisation by institution, stratified by type of urinary diversion, clinical T stage, and Eastern Cooperative Oncology Group performance status, to receive robot-assisted radical cystectomy or open radical cystectomy with extracorporeal urinary diversion. Treatment allocation was only masked from pathologists. The primary endpoint was 2-year progression-free survival, with non-inferiority established if the lower bound of the one-sided 97.5% CI for the treatment difference (robotic cystectomy minus open cystectomy) was greater than -15 percentage points. The primary analysis was done in the per-protocol population. Safety was assessed in the same population. This trial is registered with ClinicalTrials.gov, number NCT01557676.

| | Robotic cystectomy (n=150) | Open cystectomy (n=152) |
|--------------------------------------|----------------------------|-------------------------|
| Median age, years (range) | 70 (43-90) | 67 (37-85) |
| Sex | | |
| Men | 126 (84%) | 128 (84%) |
| Women | 24 (16%) | 24 (16%) |
| Body mass index (kg/m ²) | | |
| Median (IQR) | 27.8 (25.0-30.8) | 28.2 (24.9-31.7) |
| <25 | 38 (25%) | 39 (26%) |
| 25-29.9 | 60 (40%) | 64 (42%) |
| ≥30 | 52 (35%) | 49 (32%) |
| ECOG performance status | | |
| 0 | 117 (78%) | 109 (72%) |
| 1 | 29 (19%) | 39 (26%) |
| 2-3 | 4 (3%) | 4 (3%) |
| Clinical and TURBT stage* | | |
| Tis | 6 (4%) | 6 (4%) |
| Ta | 1 (1%) | 4 (3%) |
| T1 | 41 (27%) | 41 (27%) |
| T2 | 82 (55%) | 81 (53%) |
| T3 | 16 (11%) | 16 (11%) |
| T4 | 4 (3%) | 4 (3%) |

| | 62 (41%) | 70 (46%) |
|--|--------------|--------------|
| Neoadjuvant chemotherapy† | 41 (27%) | 55 (36%) |
| Adjuvant chemotherapy† | 25 (17%) | 17 (11%) |
| Urinary diversion procedure‡ | | |
| Neobladder | 35 (24%) | 30 (20%) |
| Ileal conduit | 113 (75%) | 122 (80%) |
| Continent cutaneous reservoir | 1 (1%) | — |
| Baseline haemoglobin (g/dL), mean (SD) | 13.05 (1.87) | 12.81 (1.87) |

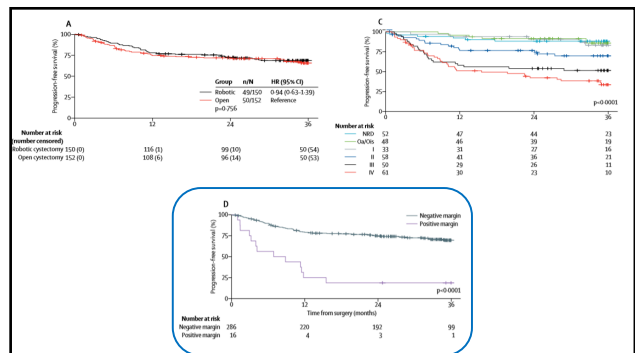
Data are n (%), unless otherwise specified. ECOG—Eastern Cooperative Oncology Group; TURBT—transurethral resection of bladder tumour. *Staging according to American Joint Committee on Cancer staging for bladder cancer 7th edition. †Data on chemotherapy use and type of chemotherapy were not available for two patients in the open cystectomy group, and data on chemotherapy type was not available for one patient in the robotic cystectomy group. ‡Five patients in the robotic cystectomy group and two in the open cystectomy group received neoadjuvant and adjuvant chemotherapy. †Three patients in the robotic cystectomy group had ileal conduit instead of the planned neobladder urinary diversion, one patient had neobladder instead of ileal conduit urinary diversion, and one patient had continent cutaneous reservoir instead of the planned ileal conduit urinary diversion. Nine patients in the open cystectomy group had ileal conduit instead of the planned neobladder urinary diversion, and one patient had neobladder instead of the planned ileal conduit urinary diversion.

Table 1: Baseline patient characteristics of the per-protocol population

| | Robotic cystectomy | Open cystectomy | Difference (95% CI) | p value* |
|---|----------------------|----------------------|---------------------|----------|
| Per-protocol analysis set | | | | |
| Patients with disease progression within 2 years of surgery | 41/150 (27%) | 42/152 (28%) | — | — |
| 2-year progression free survival (95% CI) | 72.3% (64.3 to 78.8) | 71.6% (63.6 to 78.2) | 0.7% (-9.6 to 10.9) | 0.001 |
| Patients with disease progression (total events)† | 49/150 (33%) | 50/152 (33%) | — | — |
| Modified intention-to-treat analysis set | | | | |
| Patients with disease progression within 2 years of surgery | 43/150 (29%) | 42/152 (27%) | — | — |
| 2-year progression free survival (95% CI) | 72.3% (64.5 to 78.6) | 71.8% (63.8 to 78.3) | 0.5% (-9.7 to 10.6) | 0.001 |
| Patients with disease progression (total events)† | 52/150 (35%) | 50/152 (33%) | — | — |

Data are % (95% CI) or n/N (%), unless otherwise specified. *One-sided p value for non-inferiority. †Total events that had occurred by the data cutoff.

Table 2: Analysis of progression-free survival



| | Robotic cystectomy (n=150) | Open cystectomy (n=152) | Difference (95% CI) | p value |
|---------------------------------------|----------------------------|-------------------------|---------------------|---------|
| <i>(Continued from previous page)</i> | | | | |
| Lymph node dissection† | | | | |
| Extended | 76/149 (51%)§ | 84/152 (55%) | -4.3 (-15.5 to 7.0) | 0.46 |
| Standard | 73/149 (49%) | 68/152 (45%) | - | - |
| Lymph nodes removed, mean (SD) | 23.3 (12.5) | 25.7 (14.5) | - | 0.13 |
| Positive surgical margin | 9 (6%) | 7 (5%)¶ | 1.4 (-3.7 to 6.5) | 0.59 |
| Positive bladder margin | 6 (4%) | 5 (3%) | 0.7 (-3.5 to 4.9) | 0.74 |
| Positive urethral margin | 3 (2%) | 4 (3%) | -0.6 (-4.0 to 2.8) | 1.00 |

Data are n (%) or median (IQR), unless specified otherwise. †Graded according to the Clavien-Dindo classification. ‡Staging according to American Joint Committee on Cancer staging for bladder cancer 7th edition. §Standard lymph node dissection included all potential lymph-node-bearing tissue with the lateral limit of the genitofemoral nerve, the distal limit of Cooper's ligament to include the lymph node of Cloquet, the proximal limit of the crossing of the ureter over the common iliac vessels, the medial limit of the bladder to include the tissue medial to the hypogastric artery, and the posterior limit of the floor of the obturator fossa with circumferential mobilisation of the external iliac artery and vein. For extended lymph node dissection the upper limit of the dissection was extended superiorly to the aortic bifurcation. ¶Some patients did not have lymph node dissection. ¶¶Two patients had positive bladder and urethral margins.

Table 3: Perioperative and pathological outcomes in the per-protocol population

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EAU
European Association of Urology

Platinum Priority – Bladder Cancer
Editorial by Robert Pickard on pp. 622–623 of this issue

A Single-centre Early Phase Randomised Controlled Three-arm Trial of Open, Robotic, and Laparoscopic Radical Cystectomy (CORAL)

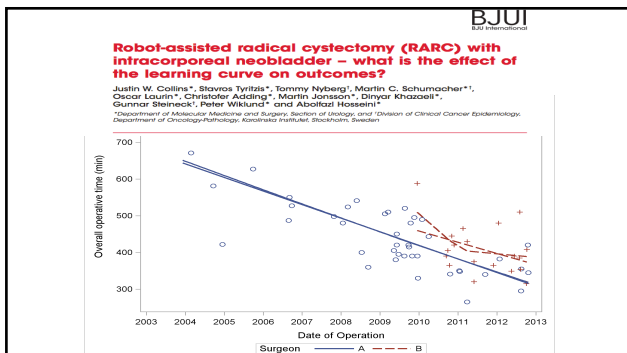
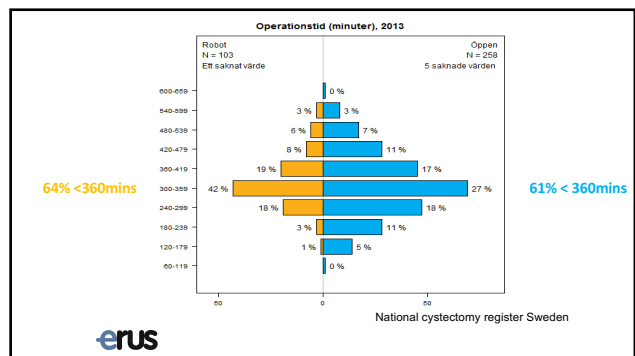
Muhammad Shamim Khan^{a,b,*}, Christine Gan^a, Kamran Ahmed^a, Ahmad Fahim Ismail^a, Jane Watkins^a, Jennifer A. Summers^a, Janet L. Peacock^a, Peter Rimington^a, Prokar Dasgupta^{a,b}

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Table 6 – Secondary outcome measures

| | ORC (n = 20) | RARC (n = 20) | LRC (n = 19) | |
|--|--------------|---------------|--------------|--------------------------------|
| Perioperative outcomes | | | | |
| Operative time, min, mean (SD) | 293 (66) | 389 (98) | 301 (51) | p < 0.001 |
| | | | ORC vs RARC | 96.4 (-49.6 to -42; p < 0.001) |
| | | | RARC vs LRC | 87.7 (34.1 to 142; p < 0.001) |
| | | | ORC vs LRC | -7.8 (-62 to 46; p = 0.9) |
| Estimated blood loss, ml, mean (SD) | 808 (329) | 585 (618) | 460 (485) | p = 0.070 |
| Time to flatus, d, mean (SD) | 3.2 (1.6) | 3.6 (2.5) | 2.9 (1.1) | p = 0.23 |
| Time to oral solids, d, mean (SD) | 7.5 (5.7) | 4.0 (4.0) | 4.0 (4.4) | p = 0.030 |
| | | | ORC vs RARC | 3.5 (0.75-4.25; p = 0.049) |
| | | | RARC vs LRC | 0.0 (-0.25 to 0.25; p = 0.5) |
| | | | ORC vs LRC | 3.5 (1.0-4.0; p = 0.01) |
| Length of stay, d, mean (SD) | 14.4 (5.9) | 11.9 (6.2) | 9.7 (3.6) | p = 0.031 |
| | | | ORC vs RARC | 2.45 (-1.40 to 6.30; p = 0.3) |
| | | | RARC vs LRC | 2.16 (-1.73 to 6.06; p = 0.4) |
| | | | ORC vs LRC | 4.61 (0.72-8.51; p = 0.005) |
| Pathologic outcomes, n/h (%) | | | | |
| Positive resection margins | 2/20 (10) | 3/20 (15) | 1/19 (5) | p = 0.9 |
| Oncologic outcomes at 12 mo ^a , n/h (%) | | | | |
| Recurrence | 2/19 (11) | 5/19 (26) | 3/18 (17) | p = 0.5 |
| Overall mortality | 0/19 (0) | 1/20 (5) | 3/18 (17) | p = 0.1 |
| Disease-specific mortality | 0/19 (0) | 0/20 (0) | 2/18 (11) | p = 0.1 |

LRC = laparoscopic radical cystectomy; ORC = open radical cystectomy; RARC = robot-assisted radical cystectomy.
^a Time to oral solids, d; data presented with median and interquartile range.
^b 12-mo recurrence, n = 2 were lost to follow-up, n = 1 died before 12 months therefore not analysed for 12-month recurrence. 12-mo overall mortality: 2 participants were lost to follow-up; 12-mo disease-specific mortality: 2 participants were lost to follow-up and 2 died from other disease but were still included in the analysis.



Oncological conclusions

- RARC results in comparable PSM rates and EPLND counts
- The evidence to support an association between RARC and unusual recurrence patterns is poor
- Early recurrences following RARC are associated with pathological non-organ confined TCC, positive lymph nodes and PSM's
- Early recurrence rates and patterns following totally intracorporeal RARC are similar to published open radical cystectomy series
- Increasing NAC administration rates would likely further improve oncological outcomes

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Better outcomes for RARC compared to ORC

- Surgical technique- Tan et al. BJU 2016, Kethrapal et al. Curr Urol Reports 2017
- Enhanced recovery- Collins et al. Eur Urol 2016, Tan et al. BJU 2017, Tan et al. Urologia 2017
- Equivocal oncological outcomes- Collins et al. Eur Urol 2015, Tan et al. Urol Onc 2016
- Shorter length of stay- Collins et al. BJU 2016, Tan et al. BJU 2017, Tan et al. Eur Urol Focus 2016
- Lower complication rate- Tan et al. BJU 2017, Tan et al. Eur Urol Focus 2016
- Better tolerated by physiologically unfit patients- Lamb et al. Urol Onc 2016
- Better tolerated by preoperative anaemic patients- Tan et al. J Endourol 2017
- Potentiated the effect of enhanced recovery- Tan et al. BJU 2017

Sources of emerging evidence

- RACE study is a comparative effectiveness study (Netherlands).
- iROC (UK)



A phase III multicentre randomised controlled trial to compare the efficacy of Robotically Assisted Radical Cystectomy (RARC) and intracorporeal urinary diversion with Open Radical Cystectomy (ORC) in patients with bladder cancer.

Chief Investigator: Professor James Catto
Co-Investigator: Professor John Kelly
Coordinating Centre: Surgical & Interventional Trials Unit (SITU),

The need for iROC.

- ORC is considered standard of care for definitive treatment of bladder cancer.
- eRARC and ORC have been compared in previous RCTs.
- iRARC has never been compared with either eRARC or ORC under trial setting.
- On the basis of current evidence, NHS England concluded there was 'no evidence of sufficient quality on which to support robotic cystectomy'



Study Objectives

Primary Objective:

- To compare the number of days alive and out of hospital within 90 days from surgery in patients undergoing iRARC and ORC.

Secondary Objective:

- To assess recovery and complications in patients undergoing iRARC and ORC.

UCL - Surgical & Interventional Trials Unit (SITU)



Fitness Tracker

- To be worn by patient 7 days at a time at:
 - Before cystectomy (Baseline)
 - Post-operative day 5
 - 5 weeks appointment
 - 3 months appointment
 - 6 months appointment
 - 1 year appointment
- Patients to post tracker back to UCL using pre-stamped addressed envelopes
 - If patient still in hospital at day 12 post-operatively, collect from patient and post.



Please advise subjects not to cut straps



Conclusions



- RARC appears at least equivalent to ORC oncological and complication outcomes
- RARC improves patient recovery time
- RCTs are awaited to confirm (or refute) current evidence
- Digital (robotic) surgery will likely aid learning curves and improve patient outcomes



University College
London Hospitals
NHS Foundation Trust

Table of Assessments

| Visit | Screening/Assessments (at start of trial) | Adherence / Targets (%) | | Follow-up | | |
|---|--|----------------------------|---------------------------|--------------------------|--------------------------|--------------------------|
| | | Baseline (Day 0) | Post-operative (Day 9) | Visit 2 (12-14 weeks) | Visit 3 (24-26 weeks) | Visit 5 (52-54 weeks) |
| Informed Consent & Randomisation | X | | | | | |
| Demographic Data, Medical History, Medication | X | | | | | |
| Physical examination, Vitals Signs | X | | | | | |
| Consent for surgery assessment | X | | | | | |
| Eligibility for ORC setting | X | | | | | |
| Randomisation | X | | | X | X | X |
| Pre-operative laboratory blood samples | X | X | | | X | X |
| Consent collected for translational research | X | X | | X | X | |
| Chemical-DNA assessment | | | X | X | X | X |
| Adverse Events | | X | X | X | X | X |
| Biopsy Site | | X | | | | |
| Tumour Sample | | X | | | | |
| Post-operative assessment | | X | | | | |
| Operative Follow-up | | | | X | X | X |
| OS Data | | X | | X | X | X |
| TOX Data | | X | | X | X | X |
| OS Data (CR & QOL-ASAS) | | X | | X | X | X |
| OS Data (CR & QOL-ASAS) | | X | | X | X | X |
| OS Data (CR & QOL-ASAS) | | X | | X | X | X |
| OS Data (CR & QOL-ASAS) | | X | | X | X | X |
| OS Data (CR & QOL-ASAS) | | X | | X | X | X |

