DR. STEFANIA ZAMBONI (Orcid ID : 0000-0002-6244-4120)
DR. FRANCESCO SORIA (Orcid ID : 0000-0001-8443-8453)
DR. MOHAMMAD M ABUFARAJ (Orcid ID : 0000-0002-6603-6319)
DR. DAVID D'ANDREA (Orcid ID : 0000-0003-1625-1077)
MR. WEI SHEN TAN (Orcid ID : 0000-0002-6119-4043)
DR. GIUSEPPE SIMONE (Orcid ID : 0000-0002-4868-9025)
DR. ATIQULLAH AZIZ (Orcid ID : 0000-0002-3114-9604)
DR. GUILLAUME PLOUSSARD (Orcid ID : 0000-0002-6004-2152)
DR. MARCO MOSCHINI (Orcid ID : 0000-0002-3084-2458)

Article type : Original Article

Article Category: Robotics and Laparoscopy

Differences in utilization-trend and time changes of peri-operative outcomes of robotic and open radical cystectomy between American and European selected centers: an international multicenter collaboration

Stefania Zamboni[1,2], Francesco Soria[3,4], Romain Mathieu[3,5], Evanguelos Xylinas[6], Mohammad Abufaraj[3,7], David D`Andrea[3], Wei Shen Tan[8,9], John D. Kelly[8,9], Giuseppe Simone[10], Michele Gallucci[10], Anoop Meraney[11], Suprita Krishna[12], Badrinath R. Konety[12], Alessandro Antonelli[2], Claudio Simeone[2], Philipp Baumeister[1], Agostino Mattei[1], Alberto Briganti[13], Andrea Gallina[13], Francesco Montorsi[13], Michael Rink[14], Atiqullah Aziz[15], Pierre I. Karakiewicz[16], Morgan Rouprêt[17], Anthony Koupparis[18], Douglas S Scherr[19], Guillaume Ploussard[20], Prasanna Sooriakumaran[9,21], Shahrokh F. Shariat[3,19,22], Marco Moschini[3,1]

On behalf of the European Association of Urology - Young Academic Urologists (EAU-YAU), Urothelial carcinoma working group
On behalf of the EAU Research Foundation

[1] Klinik für Urologie, Luzerner Kantonsspital, Lucerne, Switzerland

[2] Urology Unit, ASST Spedali Civili, Brescia, Italy; Department of Medical and Surgical Specialties, Radiological Science and Public Health, University of Brescia, Italy
[3] Department of Urology, Comprehensive Cancer Center, Medical University of Vienna, Vienna General Hospital, Vienna, Austria;
[4] Division of Urology, Department of Surgical Sciences, University of Studies of Torino, Turin, Italy
[5] Department of Urology, Rennes University Hospital, Rennes, France
[6] Department of Urology Bichat Hospital, Paris Descartes University, Paris, France
[7] Division of Urology, Department of Special Surgery, Jordan University Hospital, The

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/bju.14791
This article is protected by copyright. All rights reserved.

Accepted Article

University of Jordan, Amman, Jordan
[8] Division of Surgery and Intervention Science, University College London, London, UK; Department of Urology, University College London Hospital, London, UK.
[9] Department of Uro-oncology, University College London Hospital NHS Foundation Trust.
[10] "Regina Elena" National Cancer Institute, Department of Urology, Rome, Italy.
[11] Urology Division, Hartford Healthcare Medical Group, Hartford, USA.
[12] Department of Urology, University of Minnesota, Minneapolis, MN
[13] Department of Urology, Urological Research Institute, San Raffaele Scientific Institute, Milan, Italy
[14] Department of Urology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.
[15]Department of Urology, University Medical Center Rostock, Rostock, Germany
[16] Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Centre, Montreal, Quebec, Canada
[17] Sorbonne Université, GRC n°5, ONCOTYPE-URO, AP-HP, Hôpital Pitié-Salpêtrière, F-75013 PARIS, France
[18] Bristol Urological Institute, North Bristol NHS Trust, Southmead Hospital, Bristol, UK
[19] Department of Urology, Weill Cornell Medical College, New York-Presbyterian Hospital, New York, NY, USA
[20] Department of Urology, La croix du sud, Toulouse, France
[21]Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden
[22] Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX.

Corresponding author:
Stefania Zamboni M.D.
Department of Urology, Luzerner Kantonsspital, Lucerne, Switzerland
Email: stefania.zamboni@libero.it

Running head: changing trends in use of robot-assisted radical cystectomy

Keywords: time trend, bladder cancer, radical cystectomy, robotic, RARC, RC

No disclosures or conflict of interest.

This article is protected by copyright. All rights reserved.

Accepted Article

Abstract

Objectives: To compare utilization trends and time-changes in perioperative outcomes of robot assisted radical cystectomy (RARC) in American (AC) and European centers (EC).

Materials and methods: retrospective evaluation of 2,401 patients treated with open radical cystectomy (ORC) and RARC for bladder cancer at 12 AC and EC between 2006 and 2018. Kruskal-Wallis and Chi-square test evaluated differences between continuous and categorical variables.

Results: Overall, 49.5% of patients underwent RARC and 51.5% ORC. RARC became the most commonly performed procedure in contemporary patients with an increase from 29% in 2006-2008 to 54% in 2015-2018 ($p<0.001$). In AC, the use of RARC was higher than ORC since 2006 and remained stable over time whereas in EC its use increased exponentially from 2% to 50%. In both groups RARC patients had less advanced T stages ($p<0.001$), ASA scores ($p<0.05$), lower blood loss ($p=0.001$) and shorter length of stay ($p<0.05$). No differences were found in early complications. Early readmissions- and reoperations-rates were worse for patients treated with RARC in EC. However, when contemporary patients only were considered, the statistical significances were lost.

Conclusion: Our study reveals that the use of RARC has constantly increased since its introduction, overtaking ORC in the most contemporary series. While RARC was more frequently performed than ORC since the beginning in AC and remained substantially stable over time, its use exponentially increased in the EC. The different trend in use and time-changes of peri-operative outcome between AC and EC can be attributed to the earlier introduction and spread of RARC in AC compared to the European ones.

Introduction

Bladder cancer (BCa) is the ninth most common cancer worldwide and the 13th in term of yearly mortality from cancer [1],[2] . Open radical cystectomy (ORC) with bilateral pelvic lymph node dissection (PLND) is the standard surgical approach for treating very high-risk non-muscle invasive and non-metastatic, muscle invasive urothelial BCa [3]. Despite application of enhanced recovery programs [4], this complex procedure remains associated with high rates of peri-operative morbidity, readmission and mortality [5]. Growing literature supports the use of robotic assisted radical cystectomy (RARC) that has shown reduced blood loss, need of transfusions

This article is protected by copyright. All rights reserved.

and length of hospitalization compared to ORC [6],[7],[8],[9],[10],[11],[12],[13]. Whereas the difference in oncological outcome between ORC and RARC has been cause of debate for a long time [10],[14] the results of the RAZOR trial [15] support the hypothesis that RARC is non-inferior to ORC considering 2-year progression-free survival rates. Even though debate regarding benefit of RARC is still open, its use has become more common, especially in referral centers, but sparse data exist regarding its actual diffusion and its trend of utilization in contemporary patients. Therefore, the aim of this study is to compare utilization trends and time-changes in perioperative outcomes of ORC and RARC through a large multicenter collaboration.

Material and Methods

A retrospective analysis of institutional databases was carried out. We collected data from 2,401 patients treated with radical cystectomy and PLND for BCa at 12 North American and European institutions between 2006 and 2018. All the centers involved in our study, were high-volume centers, were equipped with the daVinci robotic system, performed both robotic and open cystectomy and consequently had the chance to choose between one of the two procedures. Although expertise in their field, surgeons who performed RARC and those who performed ORC were different. Centers were anonymized and data were divided into two groups depending on the location of the center (American or European). All preoperative, intraoperative and post-operative data were collected. Patients' characteristics included age at surgery, year of surgery, American Society of Anesthesiologists (ASA) score, neoadjuvant chemotherapy (NAC), prior abdominal surgery defined as abdominal or pelvic surgery performed for any reason and prior pelvic radiotherapy. Intraoperative features included technique used for surgery list in RARC, ORC, blood loss (ml), operation

This article is protected by copyright. All rights reserved.

Accepted Article

time (min) and type of urinary diversion. Pathological features included pathological tumor status (pT according to 6th edition TNM classification) [16], pathological grade evaluated according to WHO grading 2004, lymph node invasion (LNI), total number of lymph nodes (LN) removed and number of positive nodes. Post-operative features included 30-day complications, readmission and re-operation.

Endpoint definition

The first endpoint was to report the prevalence of patients treated with RARC and ORC across time. The secondary endpoint was to report temporal trends in perioperative outcomes according to the usage of RARC or ORC in American (AC) and European centers (EC) in order to assess possible differences in trend between the two locations.

Statistical analysis

Frequencies and proportions were used to describe categorical variables according to RARC and ORC use. Means, median and interquartile range (IQR) described continuous variables. The Kruskal-Wallis test and Chi-square test evaluated differences between continuous and categorical variables, respectively. Statistical significance was considered at $p<0.05$. Statistical analysis was performed using STATA 14.0® (Stata Corp., College Station, TX, USA).

Accepted Article

This article is protected by copyright. All rights reserved.

Results

Baseline characteristic

Patient characteristics are reported in **Table 1.** Of the 2,401 patients who underwent radical cystectomy for BCa, 1,189 (49.5%) were treated with RARC and 1,212 (50.5%) with ORC. 71% of patients treated in AC and 42% of those treated in the European ones were treated with RARC. In both AC and EC patients treated with RARC had less comorbidities (AC: ASA $\leq$ 2, 39.4% in RARC and 27% in ORC, p=0.04, EC: ASA$\leq$ 2, 73% in RARC and 47.7% in ORC, p<0.001) and had less advanced cancers with lower pT stages (AC: pT stage $\leq$ 2, 60 % in RARC and 50% of patients treated with ORC, p<0.001, EC: pT stage $\leq$ 2, 63% in RARC and 57% of patients treated with ORC, p<0.001).

Moreover, in EC, patients who underwent RARC had lower rates of LNI (RARC vs ORC 26% vs 35%, p<0.001) and were younger (median age 66 years [IQR: 59-71] for RARC vs 70 years [IQR:59-71] for ORC, p=0.001).

Temporal trend in the use of RARC

Figure 1 depicts temporal trends according to the type of cystectomy in overall population, in AC and EC. We observed an increase in rate of use of RARC over time in the overall population (RARC vs. ORC 2006-2008: 29% vs. 71%, 2009-2011: 37% vs. 63%, 2012-2014: 38% vs. 62%, 2015-2018: 54% vs 46% p<0.001). As regards AC the use of RARC was greater than ORC since 2006 and remained essentially stable over time (RARC vs. ORC 2006-2008: 80% vs. 20%, 2009-2011: 74% vs. 26%, 2012-2014: 61% vs. 40%, 2015-2018: 77% vs 23% p<0.001). On the contrary, in EC the use of RARC increased exponentially from 2% in 2006-2008 to 50% in 2015-2018 (p<0.001).

This article is protected by copyright. All rights reserved.

Accepted Article

Accepted Article

Perioperative outcomes

Table 2 reports a summary of perioperative outcomes according type of cystectomy. In both AC and EC, patients treated with RARC had significantly lower blood loss (AC: median 400 ml [IQR:287-650] for RARC and 600 ml [IQR: 400-1000] for ORC, p=0.001, EC: 300 ml [IQR: 200-500] for RARC and 500 ml [IQR: 300-800] for ORC, p=0.001) and shorter length of stay (AC: median 7 days [IQR:6-10] for RARC vs 8 days [IQR: 7-12] for ORC, p=0.001, EC: 10 days [IQR: 8-14] for RARC vs 15 days [IQR: 9-22] for ORC. P=0.001) compared to those treated with ORC. Duration of surgery was significantly lower for RARC in patients treated in AC (RARC vs ORC: 400 min [IQR: 330-483] vs 418 min [IQR: 362-521], p=0.01) whereas was significantly higher in patients treated in those European (RARC vs ORC: 335 min [IQR: 278-390] vs 310 min [IQR: 258-360], p=0.001).

In contrast to those treated in AC, patients treated with RARC in EC underwent more likely neobladder (p<0.001) and had higher median number of LN removed (p=0.001). **Figure 2** and **Figure 3** show intraoperative outcomes of RARC vs ORC according year of surgery.

No significant differences were found in < 30 days complications, readmissions and re-operation in patients treated in AC (all p>0.05). On the other hand, patients treated with RARC in EC were more likely to be readmitted within 30 days (p=0.001) and re-operated (p=0.002) compared those treated with ORC. **Figure 4** reports early post-operative outcomes in AC and EC of RARC vs ORC according year of surgery.

This article is protected by copyright. All rights reserved.

Accepted Article

Discussion

According to international guidelines [3],[17], ORC with bilateral PLND remains the gold standard treatment for very high risk non-muscle invasive BCa and non-metastatic, muscle invasive BCa. However, since the introduction of RARC in 2003 [18], many institutions equipped with robotic system have begun to perform this procedure. In our multicenter study, we evaluated the trend in RARC use in 12 European and American tertiary referral centers.

We found that since its introduction, RARC has been widely adopted. Overall, we observed an initial slow but gradual increase in the use of RARC in the first 6 years (from 29% to 37%), followed by a rapid and substantial increase which progressed into RARC being more commonly used than ORC in most contemporary series. In the most recent period of our study (2015-2018), RARC has become the most performed procedure with a 54% of cystectomies being performed using this approach in the centers involved in our study. While in American institutions RARC was more frequently performed than ORC since 2006 and remained substantially stable over time, in EC the use of RARC increased exponentially, with a relevant growth from 2% in 2006-2008 to 50% in 2015-2018. The important different trend between the two groups of centers can be attributed to the earlier introduction of RARC in the American ones.

The same explanation could be provided for the results we have found in post-operative outcomes. No significant differences were found in early complications rates between RARC and ORC in both American and European centers similarly to results recently reported by Soria et al [19]. Moreover, in EC, rates of early re-

This article is protected by copyright. All rights reserved.

admissions and re-operations were worse for patients treated with RARC whereas no significant differences were found between the two procedures in patients treated in AC. However, when the analyses were performed just on contemporary patients (2015-2018 group) the significant differences found in EC were lost and, as shown in figure 4, RARC's rates of re-admissions and re-operations decreased substantially after the first triennium, concurrently to the increase in the use of RARC in Europe.

Even though RARC has spread significantly and some of the centers involved in our study have performed RARC for over a decade, we found pathologic characteristics of patients submitted to RARC were globally less severe, with less advanced disease than patients undergoing ORC. In both AC and EC, patients treated with RARC had lower pT stages and ASA scores. In addition, in EC only, patients submitted to RARC had also higher LNI rates. These differences indicated a probable selection bias where RARC was reserved for patients affected by organ confined disease or less advanced cancers and this could probably be related to a more cautious approach in patient selection in first few years of adoption of this technical approach, especially during the learning curve.

Considering peri-operative outcomes, the median number of LN removed was significantly higher in RARC (p=0.001) for EC (but not for the Americans). Our findings confirm those from Hu et al. [20] who reported that RARC was associated with greater lymph node yield compared to ORC, with 41.5% versus 34.9% having $\geq$ 10 lymph nodes removed (p=0.03). This difference could be attributed to the relevant difficulty in performing RARC, which represents the most challenging robotic procedure, usually approached only by surgeons with previous extensive experience in

This article is protected by copyright. All rights reserved.

Accepted Article

radical prostatectomy and pelvic lymphadenectomy. Conversely, the open procedure, is performed by almost all the urologists. Moreover, the technical advantages provided by robotic surgery such as magnification of images could help to perform a more accurate PLND.

In our study, intraoperative blood loss was lower in RARC for both AC an EC, in accordance to the findings from several retrospective studies [6],[7],[8],[9],[10],[11],[12],[13] and the RAZOR trial [15]. On the other hand, estimated blood loss slightly decreased in ORC across time, in concordance with previous literature [21],[22] probably for technical improvement that occurred in ORC surgery or to the introduction of haemostatic devices and agents. Length of hospitalization was shorter for RARC in both groups, as in comparative retrospective and prospective studies [6],[7],[8],[9],[10],[11],[12],[13] and in the meta-analysis by Tan et al [23]. Moreover, the length of stay for both RARC and ORC was lower for patients treated in AC compared to those treated in EC, probably as a consequence of differences in healthcare systems.

This study is not without limitations. First of all, it is a retrospective study and data should be interpreted in this context. Second, every patient included in our study was treated in a tertiary referral center, therefore our findings might not be applicable to patients who underwent RC in smaller, lower-volume centers. Third, no data regarding intra- or extra-corporeal technique for urinary diversion were available. Fourth, the cause of readmissions and type of complications (medical or surgical) were not available for analyses. Fifth, the name of the surgeon for each procedure was not available. Consequently, we did not have the chance to analyze the learning curve

This article is protected by copyright. All rights reserved.

Accepted Article

and its relationship with peri-operative outcomes. Moreover, our study was unable to adjust for length of hospitalization, readmission and mortality to Charlson Comorbidity Index, specific comorbidities, laboratory values and type of urinary diversion that could influence results of these outcomes.

Conclusion

Our study reveals that the use of RARC has constantly increased since its introduction, overtaking ORC in the most contemporary series. While RARC was more frequently performed than ORC since the beginning in AC and remained substantially stable over time, its use exponentially increased in the EC. Early readmissions- and reoperations-rates were worse for patients treated with RARC in EC. However, when contemporary patients only were considered, the statistical significances were lost. The differences in time-changes of perioperative outcome between AC and EC can be attributed to the earlier introduction and spread of RARC in AC compared to the European ones.

Accepted Article

This article is protected by copyright. All rights reserved.

Accepted Article

Figure Legend

Figure 1- Time trend in use of open radical cystectomy (ORC) and robotic radical cystectomy (RARC) with bilateral pelvic lymph node dissection (PLND) for bladder cancer (BCa) in overall population and separately in American and European centers.

Figure 2 - Time trend in median blood loss (ml) and operation time (days) of open radical cystectomy (ORC) and robotic radical cystectomy (RARC) with pelvic lymph node dissection (PLND) for bladder cancer (BCa) in American and European centers.

Figure 3 - Time trend in median number of lymph node removed and length of stay (days) of open radical cystectomy (ORC) and robotic radical cystectomy (RARC) with pelvic lymph node dissection (PLND) for bladder cancer (BCa) in American and European centers.

Figure 4 - Time trend in rates of < 30 days complications, readmission and re-operation
of open radical cystectomy (ORC) and robotic radical cystectomy (RARC) with pelvic lymph node dissection (PLND) for bladder cancer (BCa) in American and European centers.

Acknowledgments
No disclosures or conflict of interest.

This article is protected by copyright. All rights reserved.

Accepted Article

References

[1] Antoni S, Ferlay J, Soerjomataram I, Znaor A, Jemal A, Bray F. Bladder Cancer Incidence and Mortality: A Global Overview and Recent Trends. Eur Urol 2017;71:96–108. doi:10.1016/j.eururo.2016.06.010.
[2] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin 2018;68:7–30. doi:10.3322/caac.21442.
[3] Alfred Witjes J, Lebret T, Compérat EM, Cowan NC, De Santis M, Bruins HM, et al. Updated 2016 EAU Guidelines on Muscle-invasive and Metastatic Bladder Cancer. Eur Urol 2017;71:462–75. doi:10.1016/j.eururo.2016.06.020.
[4] Collins JW, Patel H, Adding C, Annerstedt M, Dasgupta P, Khan SM, et al. Enhanced Recovery After Robot-assisted Radical Cystectomy: EAU Robotic Urology Section Scientific Working Group Consensus View. Eur Urol 2016;70:649–60. doi:10.1016/j.eururo.2016.05.020.
[5] Moschini M, Simone G, Stenzl A, Gill IS, Catto J. Critical Review of Outcomes from Radical Cystectomy: Can Complications from Radical Cystectomy Be Reduced by Surgical Volume and Robotic Surgery? Eur Urol Focus 2016;2:19–29. doi:10.1016/j.euf.2016.03.001.
[6] Bochner BH, Dalbagni G, Sjoberg DD, Silberstein J, Keren Paz GE, Donat SM, et al. Comparing Open Radical Cystectomy and Robot-assisted Laparoscopic Radical Cystectomy: A Randomized Clinical Trial. Eur Urol 2015;67:1042–50. doi:10.1016/j.eururo.2014.11.043.
[7] Hanna N, Leow JJ, Sun M, Friedlander DF, Seisen T, Abdollah F, et al. Comparative effectiveness of robot-assisted vs. open radical cystectomy. Urol Oncol 2018;36:88.e1-88.e9. doi:10.1016/j.urolonc.2017.09.018.
[8] Nix J, Smith A, Kurpad R, Nielsen ME, Wallen EM, Pruthi RS. Prospective randomized controlled trial of robotic versus open radical cystectomy for bladder cancer: perioperative and pathologic results. Eur Urol 2010;57:196–201. doi:10.1016/j.eururo.2009.10.024.
[9] Hussein AA, May PR, Jing Z, Ahmed YE, Wijburg CJ, Canda AE, et al. Outcomes of Intracorporeal Urinary Diversion after Robot-Assisted Radical Cystectomy: Results from the International Robotic Cystectomy Consortium. J Urol 2018;199:1302–11. doi:10.1016/j.juro.2017.12.045.
[10] Challacombe BJ, Bochner BH, Dasgupta P, Gill I, Guru K, Herr H, et al. The Role of Laparoscopic and Robotic Cystectomy in the Management of Muscle-Invasive Bladder Cancer With Special Emphasis on Cancer Control and Complications. European Urology 2011;60:767–75. doi:10.1016/j.eururo.2011.05.012.
[11] Yu H, Hevelone ND, Lipsitz SR, Kowalczyk KJ, Nguyen PL, Choueiri TK, et al. Comparative analysis of outcomes and costs following open radical cystectomy versus robot-assisted laparoscopic radical cystectomy: results from the US Nationwide Inpatient Sample. Eur Urol 2012;61:1239–44. doi:10.1016/j.eururo.2012.03.032.
[12] Styn NR, Montgomery JS, Wood DP, Hafez KS, Lee CT, Tallman C, et al. Matched comparison of robotic-assisted and open radical cystectomy. Urology 2012;79:1303–8. doi:10.1016/j.urology.2012.01.055.
[13] Ng CK, Kauffman EC, Lee M-M, Otto BJ, Portnoff A, Ehrlich JR, et al. A comparison of postoperative complications in open versus robotic cystectomy. Eur Urol 2010;57:274–81. doi:10.1016/j.eururo.2009.06.001.
[14] Martin AD, Nunez RN, Pacelli A, Woods ME, Davis R, Thomas R, et al. Robot-assisted radical cystectomy: intermediate survival results at a mean follow-up of 25 months. BJU Int 2010;105:1706–9. doi:10.1111/j.1464-410X.2009.09042.x.

This article is protected by copyright. All rights reserved.

[15] Parekh DJ, Reis IM, Castle EP, Gonzalgo ML, Woods ME, Svatek RS, et al. Robot-assisted radical cystectomy versus open radical cystectomy in patients with bladder cancer (RAZOR): an open-label, randomised, phase 3, non-inferiority trial. Lancet 2018;391:2525–36. doi:10.1016/S0140-6736(18)30996-6.
[16] AJCC Cancer Staging Manual | Frederick L, Greene | Springer n.d. https://www.springer.com/us/book/9781475736564 (accessed October 3, 2018).
[17] Chang SS, Bochner BH, Chou R, Dreicer R, Kamat AM, Lerner SP, et al. Treatment of Non-Metastatic Muscle-Invasive Bladder Cancer: AUA/ASCO/ASTRO/SUO Guideline. J Urol 2017;198:552–9. doi:10.1016/j.juro.2017.04.086.
[18] Menon M, Hemal AK, Tewari A, Shrivastava A, Shoma AM, El-Tabey NA, et al. Nerve-sparing robot-assisted radical cystoprostatectomy and urinary diversion. BJU Int 2003;92:232–6.
[19] Soria F, Moschini M, D'andrea D, Abufaraj M, Foerster B, Mathiéu R, et al. Comparative Effectiveness in Perioperative Outcomes of Robotic versus Open Radical Cystectomy: Results from a Multicenter Contemporary Retrospective Cohort Study. Eur Urol Focus 2018. doi:10.1016/j.euf.2018.11.002.
[20] Hu JC, Chughtai B, O'Malley P, Halpern JA, Mao J, Scherr DS, et al. Perioperative Outcomes, Health Care Costs, and Survival After Robotic-assisted Versus Open Radical Cystectomy: A National Comparative Effectiveness Study. European Urology 2016;70:195–202. doi:10.1016/j.eururo.2016.03.028.
[21] Linder BJ, Frank I, Cheville JC, Tollefson MK, Thompson RH, Tarrell RF, et al. The impact of perioperative blood transfusion on cancer recurrence and survival following radical cystectomy. Eur Urol 2013;63:839–45. doi:10.1016/j.eururo.2013.01.004.
[22] Moschini M, Bianchi M, Gandaglia G, Cucchiara V, Luzzago S, Pellucchi F, et al. The Impact of Perioperative Blood Transfusion on Survival of Bladder Cancer Patients Submitted to Radical Cystectomy: Role of Anemia Status. Eur Urol Focus 2016;2:86–91. doi:10.1016/j.euf.2015.03.002.
[23] Tan WS, Khetrapal P, Tan WP, Rodney S, Chau M, Kelly JD. Robotic Assisted Radical Cystectomy with Extracorporeal Urinary Diversion Does Not Show a Benefit over Open Radical Cystectomy: A Systematic Review and Meta-Analysis of Randomised Controlled Trials. PLoS ONE 2016;11:e0166221. doi:10.1371/journal.pone.0166221.

Accepted Article

This article is protected by copyright. All rights reserved.

Accepted Article

Table 1- Baseline characteristics of patients treated with open radical cystectomy (ORC) and robotic radical cystectomy (RARC) with pelvic lymph node dissection (PLND) for clinical non-metastatic bladder cancer (BCa) in American and European centers.

	American centers				**European centers**			
Variable	**Overall (n=651,100%)**	**RARC (n=459, 71%)**	**ORC (n=192, 29%)**	**p value**	**Overall (n=1,750, 100%)**	**RARC (n=730, 42%)**	**ORC (n=1,020, 58%)**	**p value**
Age								
Mean	67	67	68	0.2	67	65	69	0.001
Median (IQR)	68 (61-76)	68 (60-74)	70 (61-76)		68 (61-74)	66(59-71)	70 (59-71)	
Gender								
Male	525 (81%)	155 (81%)	370 (81%)	0.9	1,405 (80%)	585 (80%)	820 (80%)	0.9
Female	126 (19%)	37 (19%)	89 (19%)		345 (20%)	145 (20%)	200 (20%)	
BMI								
Mean	27	28	27	0.4	26	27	26	0.02
Median (IQR)	27 (24-30)	27 (24-30)	27 (24-31)		26 (23-29)	26 (23-29)	26 (23-28)	
ASA score								
1	2 (0.3%)	2 (0.4%)	0 (0.0%)	0.04	93 (7.8%)	83 (13%)	10 (1.7%)	<0.001
2	225 (35%)	177 (39%)	48 (27%)		642 (54%)	381 (60%)	261 (46%)	
3	384 (60%)	262 (57%)	122 (69%)		417 (35%)	158 (25%)	259 (46%)	
4	24 (4.0%)	17 (4.0%)	7 (4.0%)		43 (3.6%)	10 (1.6%)	33 (5.9%)	
Prior therapy								
No	448 (72%)	329 (75%)	119 (66%)	<0.001	1,328 (77%)	438 (61%)	890 (88%)	<0.001
NAC	139 (22%)	79 (18%)	60 (33%)		393 (23%)	276 (38%)	117 (12%)	
RT	32 (5.0%)	3 (0.6%)	0 (0.0%)		9 (0.5%)	7 (1.0%)	2 (0.2%)	
NAC+RT	3 (0.5%)	30 (6.8%)	2 (1.1%)		2 (0.1%)	2 (0.3%)	0 (0.0%)	
pT								
pT0-1	294 (45%)	233 (51%)	61 (32%)	<0.001	781 (45%)	368 (51%)	413 (41%)	<0.001
pT2	97 (15%)	62 (14%)	25 (18%)		250 (14%)	87 (12%)	163 (16%)	
pT3-4	256 (40%)	162 (35%)	94 (50%)		707 (41%)	271 (27%)	436 (43%)	
LNI	135 (22%)	88 (21%)	47 (25%)	0.2	408 (31%)	137 (26%)	271 (35%)	<0.001

RARC=robot assisted radical cystectomy, ORC=open radical cystectomy, IQR=interquartile range, MBI=body mass index, ASA=American society od anesthesiologist, NAC=neoadjuvant chemotherapy, RT=radiotherapy, LN=lymph node invasion

This article is protected by copyright. All rights reserved.

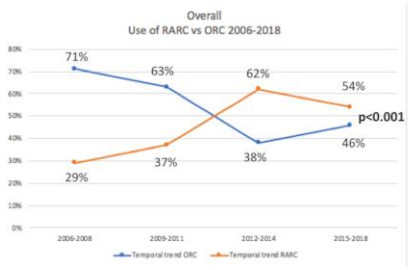
Table 2- Peri-operative outcomes in patients treated with open radical cystectomy (ORC) and robotic radical cystectomy (RARC) with pelvic lymph node dissection (PLND) for clinical non-metastatic bladder cancer (BCa) in American and European centers.

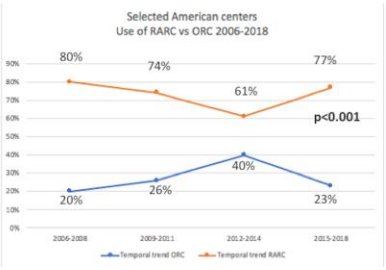
	American centers				**European centers**			
	Overall (N=651, 100%)	**RARC (N=459, 71%)**	**ORC (N=192, 29%)**	**p value**	**Overall (N=1,750,100%)**	**RARC (N=730, 42%)**	**ORC (N=1,020, 58%)**	**p value**
Urinary diversion								
Neobladder	108 (20%)	94 (22%)	14 (14%)		508 (40%)	311 (48%)	197 (32%)	
Ileal conduit	353 (66%)	275 (64%)	78 (77%)	0.1	577 (45%)	318 (49%)	259 (41%)	<0.001
Pouch	63 (12%)	55 (12%)	8 (8.0%)		30 (2.3%)	16 (2.3%)	14 (3.0%)	
UCS	3 (1.0%)	3 (1.0%)	0 (0.0%)		159 (12%)	4 (0.6%)	155 (25%)	
Other	4 (1.0%)	3 (1.0%)	1 (1.0%)		1 (0.07%)	1 (0.1%)	0 (0.0%)	
Operation time, min								
Mean	428	421	445	0.01	336	341	330	0.001
Median (IQR)	406 (333-507)	400 (330-483)	418 (362-521)		330 (270-380)	335 (278-390)	310 (258-360)	
Blood loss, ml								
Mean	603	523	801	0.001	529	437	617	0.001
Median, IQR	500 (300-750)	400 (287-650)	600 (400-1000)		400 (200-650)	300 (200-500)	500 (300-800)	
Length of stay, days								
Mean	10	9	10	0.001	15	13	17	0.001
Median	8 (6-11)	7 (6-10)	8 (7-12)		12 (9-18)	10 (8-14)	15 (9-22)	
Number of LN removed								
Mean	21	21	21	0.6	16	19	14	0.001
Median	19 (13-27)	19 (13-27)	19 (13-27)		15 (9-22)	16 (11-25)	13 (8-20)	
Complications <30 days	260 (68%)	158 (69%)	102 (67%)	0.7	711 (43%)	313 (44%)	398 (42%)	0.4
Readmission <30 days	110 (29%)	74 (32%)	36 (23%)	0.07	123 (8.0%)	64 (11.0%)	59 (6.0%)	0.001
Reoperation <30 days	26 (6.0%)	16 (7.0%)	10 (7.0%)	0.9	42 (4.0%)	29 (6.0%	13 (2.0%)	0.002

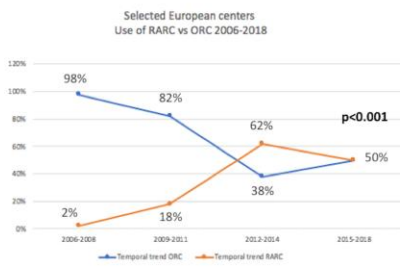
ORC= Open radical cystectomy, RARC= Robot-Assisted radical cystectomy, UCS=ureterocutaneostomy, IQR = interquartile range, LN=lymphnodes

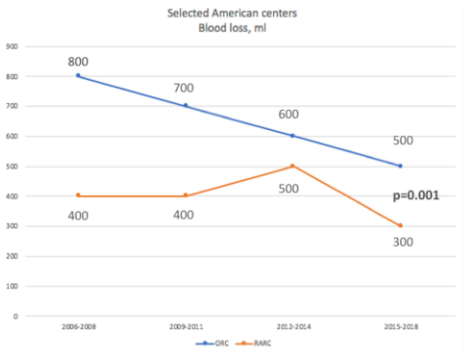
This article is protected by copyright. All rights reserved.

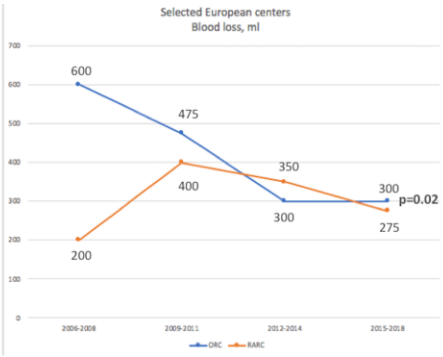
Accepted Article



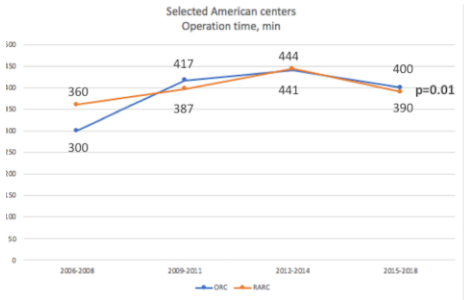


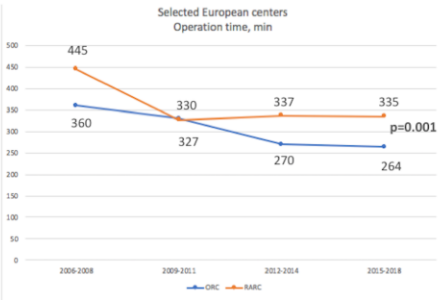






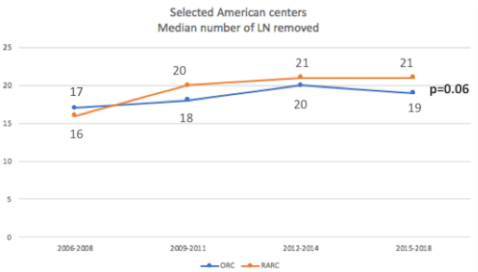
Blood loss - Selected American centers	
RARC vs ORC time trend	P=0.001
RARC time trend	p=0.02
ORC time trend	p=0.001
RARC vs ORC Contemporary patients	p=0.001
Blood loss - Selected European centers	
RARC vs ORC time trend	P=0.02
RARC time trend	p=0.02
ORC time trend	p=0.1
RARC vs ORC Contemporary patients	p=0.001
Operation time - Selected American centers	
RARC vs ORC time trend	P=0.01
RARC time trend	p=0.001
ORC time trend	p=0.001
RARC vs ORC Contemporary patients	p=0.02
Operation time- Selected European centers	
RARC vs ORC time trend	P=0.001
RARC time trend	p=0.3
ORC time trend	p=0.01
RARC vs ORC Contemporary patients	p=0.001

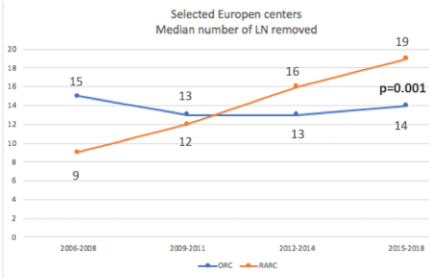




This article is protected by copyright. All rights reserved.

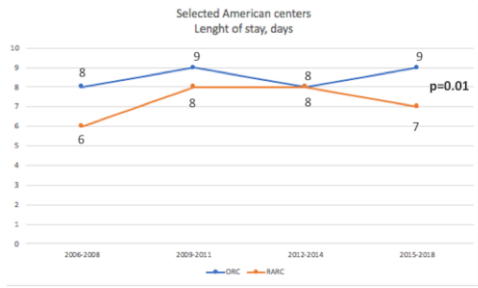
Accepted Article

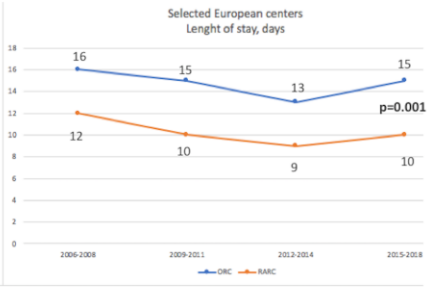




Number of LN - Selected American centers	
RARC vs ORC time trend	P=0.06
RARC time trend	p=0.01
ORC time trend	p=0.4
RARC vs ORC Contemporary patients	p=0.3

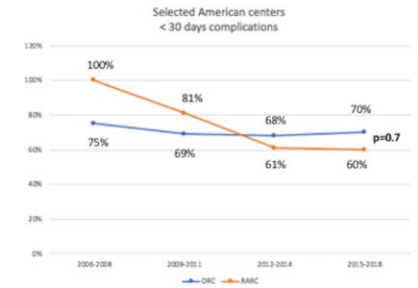
Number of LN - Selected European centers	
RARC vs ORC time trend	P=0.001
RARC time trend	p=0.01
ORC time trend	p=0.07
RARC vs ORC Contemporary patients	p=0.001

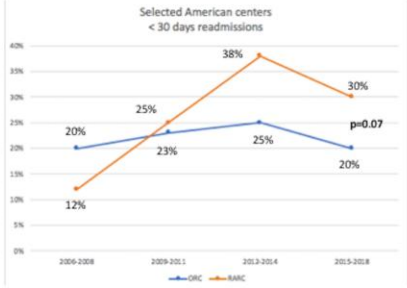


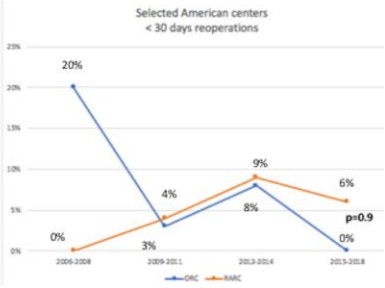


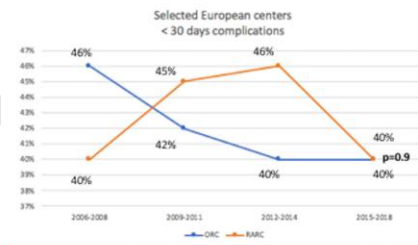
Lenght of stay - Selected American centers	
RARC vs ORC time trend	P=0.01
RARC time trend	p=0.001
ORC time trend	p=0.001
RARC vs ORC Contemporary patients	p=0.02

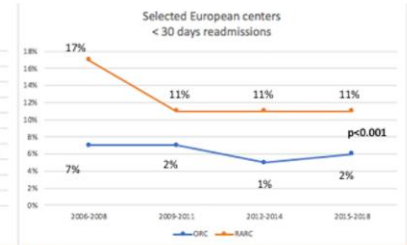
Lenght of stay -Selected European centers	
RARC vs ORC time trend	P=0.001
RARC time trend	p=0.3
ORC time trend	p=0.01
RARC vs ORC Contemporary patients	p=0.001

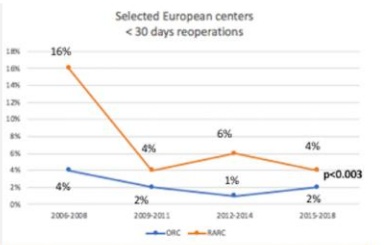












< 30 days complications - Selected American centers	
RARC vs ORC time trend	p=0.7
RARC time trend	p=0.9
ORC time trend	p=0.1
RARC vs ORC Contemporary patients	p=0.4

< 30 days readmissions - Selected American centers	
RARC vs ORC time trend	p=0.07
RARC time trend	p=0.02
ORC time trend	p=0.09
RARC vs ORC Contemporary patients	p=0.4

< 30 days reoperations - Selected American centers	
RARC vs ORC time trend	P=0.9
RARC time trend	p=0.5
ORC time trend	p=03
RARC vs ORC Contemporary patients	p=0.3

<30 days complications - Selected European centers	
RARC vs ORC time trend	p=0.3
RARC time trend	p=0.5
ORC time trend	p=0.5
RARC vs ORC Contemporary patients	p=0.9

< 30 days readmissions - Selected European centers	
RARC vs ORC time trend	p<0.001
RARC time trend	p=0.9
ORC time trend	p=0.6
RARC vs ORC Contemporary patients	p=0.06

< 30 days reoperations - Selected European centers	
RARC vs ORC time trend	p=0.003
RARC time trend	p=0.5
ORC time trend	p=0.3
RARC vs ORC Contemporary patients	p=0.2

This article is protected by copyright. All rights reserved.