



# Does robotic radical cystectomy impede oncological outcome in bladder cancer patients?

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*Comment on:* Bochner BH, Dalbagni G, Marzouk KH, *et al.* Randomized Trial Comparing Open Radical Cystectomy and Robot-assisted Laparoscopic Radical Cystectomy: Oncologic Outcomes. *Eur Urol* 2018;74:465-71.

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In recent years, new surgical procedures have expanded the urological treatment spectrum. In addition to a number of new developments in urological endoscopy, such as fluorescence-assisted transurethral resection of bladder tumours or improved laser systems, these include minimally invasive surgical techniques in “major” uro-oncologic surgery. In particular, the use of robot-assisted methods is becoming more important, as they play an important role in patient awareness, not least because of offensive marketing.

If new procedures are implemented in medical routine, the quality of patient care must not decrease. It must be shown that the new methods are also at least equivalent, but reasonably superior, to established methods even outside of clinical studies.

In this context, Bochner and his colleagues set up a prospective randomized trial comparing traditional open radical cystectomy (ORC) to robot-assisted radical cystectomy (RARC). The primary outcome of this trial was overall 90-d grade 2–5 complications defined by a modified Clavien system (1). Results of this trial which enrolled 118 patients (60 RARC, 58 ORC) focussing on the primary outcome as well as on a number of further relevant perioperative outcomes have been published in 2014 and 2015 (2,3). In summary, neither 90-d grade 2–5 complication rate nor other relevant perioperative parameters (margin status, lymph node yield, quality of life, differed comparing ORC and RARC. Though, the authors observed a lower transfusion rate and less wound complications in RARC patients while OR time was longer

and costs were higher for RARC patients. While this level I evidence as well as the results from a number of other prospective and retrospective analysis (4-9) clearly showed that perioperative patients’ safety is not impeded by RARC, there is still an ongoing debate on oncological outcomes of RARC as compared to ORC. In particular, this debate has been fuelled by recent controversial reports regarding differences in recurrence patterns comparing ORC to RARC and a higher rate of early recurrence comparing ORC to laparoscopic radical cystectomy (10-12). Therefore, the oncological follow-up data reported by Bochner *et al.* in this recent post-hoc analysis of their prospective randomized trial is of major importance.

## Summary of the study results

A total of 118 patients have been included in this analysis (60 RARC, 58 ORC). Baseline characteristics of both groups were balanced, though more male patients were included in the RARC group and pathological pT0 stage was more frequent in the RARC group (probably more complete responses following neoadjuvant chemotherapy). The authors did not observe any relevant difference in oncological outcomes comparing ORC and RARC patients after a median follow-up time of 4.9 years. Recurrence-free survival as well as bladder-cancer-specific and all-cause mortality were similar. Regarding recurrence pattern, ORC patients trended to develop more distant recurrences, while local/regional recurrences seemed to be more frequent in

RARC patients. However, acknowledging giving limitations of their secondary analysis (the trial was not powered to detect differences regarding oncological outcomes or differences in recurrence pattern) the authors draw conclusions carefully and state that “*The secondary outcomes from our randomized trial did not definitively demonstrate differences in cancer outcomes in patients treated with ORC or RARC*” and “*The wide CIs (confidence intervals) around the difference in recurrence risk preclude us from making conclusions regarding oncologic equivalence of the surgical modalities.*”

So, given his careful conclusions, do we need still to fear that, in the long run of oncological outcome, we may harm our patients by offering them a modern surgical approach to radical cystectomy? I do not think so.

### Oncological survival data

While indeed the data presented by Bochner *et al.* may be impeded by given limitations as study design and a selected patient population (e.g., few patients with extravesical disease, a rather high rate of patients treated with neoadjuvant chemotherapy), their results are supported by a number of further studies focussing on oncological outcomes in RARC patients. For example, in the RAZOR (RARC versus ORC in patients with bladder cancer) trial, no differences in 2-year progression-free survival rate comparing ORC and RARC patients (RARC 72.3%, ORC 71.6%) was observed indicating non-inferiority of the robotic approach. In addition, a number of retrospective analysis support these findings as well (13-15). In fact, these results are not unexpected, as RARC has already been shown to be safe regarding perioperative predictors of oncological outcomes as lymph node yield and margin status. In my opinion, integrating radical cystectomy in a multimodal approach with consequent perioperative systemic therapy (neoadjuvant and adjuvant chemotherapy) is more relevant for the patient outcome than the surgical approach. Accordingly, research efforts now should focus on this field (immunotherapy, radiation therapy, small molecules, combinatorial treatments).

### Recurrence pattern

The second important issue is whether the surgical approach may trigger the pattern of recurrence in relapsing patients. Indeed, Bochner *et al.* report that in RARC patients, local/regional relapse was observed more frequently while distant metastases were more frequent

in ORC patients. There are other studies, which report differences in metastatic pattern or unexpected metastatic pattern triggered by the surgical as well. For example, Albisinni *et al.* report on unexpected metastatic sites (scapula, corpora cavernosa and axillary lymph nodes) in recurrent patients following laparoscopic radical cystectomy and Nguyen *et al.* observed extrapelvic lymphatic and peritoneal metastases more frequently in RARC patients (23% vs. 15%, 21% vs. 8%) (10,11). However, in my opinion, these differences are more likely to be triggered rather by tumor biology than by the surgical approach as reported in a follow-up study in a follow-up study on 310 RARC patients by Nguyen *et al.* as well (16). Further, from the oncologist’s perspective, in the end it does not really matter for the patient where but that he relapses following curative intended radical cystectomy. Nevertheless, from a scientific perspective these findings deserve a closer look not only including surgical but also biological factors.

### Conclusions

In summary, the study of Bochner *et al.* underlines that we may offer RARC to our patients not only without impeding perioperative but also oncological safety. Neither progression-free nor cancer-specific survival is impaired by RARC and findings regarding differences in pattern of relapse between ORC and RARC are, in my opinion, only of minor relevance for the patient.

Nevertheless, prospective scientific evaluation of RARC following strict documentation of perioperative and follow-up date is further of major importance and therefore mandatory, as there still remain unanswered question, e.g., long-term functional outcomes depending on the technique of diversion or long-term complications.

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### Footnote

*Conflicts of Interest:* The author has no conflicts of interest to declare.

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