

# Open versus robotic radical cystectomy: Results from the 3-year follow-up of the RAZOR trial

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## SUMMARY

The RAZOR (robotic-assisted radical cystectomy [RARC] versus open-radical cystectomy [ORC] in patients with bladder cancer) trial was a multi-center, open-label, randomized, phase 3, noninferiority study that recruited patients between July 2011 and November 2014. Initial results of the 2-year follow-up were published earlier.<sup>[1]</sup> The inclusion criteria were age  $\geq 18$  years, biopsy-proven clinical Stage T1–T4, N0–N1, M0 bladder cancer, and refractory carcinoma *in situ*. Pregnant women, those with prior open abdominal or pelvic surgery and conditions precluding pneumoperitoneum were excluded from the study. Three hundred and fifty patients were randomized. After excluding those who did not have surgery and/or protocol violations, 150 patients in RARC and 152 patients in ORC were included for per-protocol analysis. Progression-free survival (PFS) at 2 years was the primary outcome. PFS at 2 years was 72.3% (95% confidence interval [CI] 64.3–78.8) in RARC and 71.6% (95% CI 63.6–78.2) in ORC showing oncological noninferiority of RARC.<sup>[1]</sup> RARC had lesser estimated blood loss, blood transfusions, and hospital stay. The operative time was higher in RARC (median minutes: 428 [interquartile range (IQR) 322–509] vs. 361 [IQR 281–450]). All urinary diversions were extracorporeal. There was no difference in surgical margins, lymph node yield, and perioperative and postoperative complications. There was also no difference in the quality of life.<sup>[1]</sup>

In the present study,<sup>[2]</sup> the authors update the 3-year follow-up data. In addition to PFS, they report the overall survival (OS) and recurrence rate. They also report the factors affecting PFS, OS, and recurrence.

At 3 years, there was no difference in PFS ( $P = 0.756$ ) and OS ( $P = 0.432$ ). The estimated PFS was 68.4% (95% CI 60.1–75.3) and 65.4% (95% CI 56.8–72.7), and OS was 73.9% (95% CI 65.5–80.5) and 68.5% (95% CI 59.8–75.7), in RARC and ORC, respectively.<sup>[2]</sup>

There was no statistically significant difference in the cumulative recurrence rates ( $P = 0.802$ ). The recurrence rate was 26% and 26.3% in RARC and ORC, respectively. Furthermore, there was no difference in the type or location of recurrence.<sup>[2]</sup>

On multivariate analysis, age  $>70$  years (hazard ratio [HR] 95% CI for PFS 1.62 [1.06–2.76]  $P = 0.027$  and for OS 1.99 [1.22–3.25]  $P = 0.006$ ), poor performance status (Eastern Co-operative Oncology Group 2–3) (HR 95% CI for PFS 3.32 [1.22–9.08]  $P = 0.019$  and for OS 3.67 [1.33–10.15]  $P = 0.012$ ), and occurrence of major complications (Clavien-Dindo 3 and above) (HR 95% CI for PFS 1.71 [1.06–2.76]  $P = 0.027$  and for OS 1.84 [1.10–3.09]  $P = 0.021$ ) predicted worse PFS and OS. Greater pathological stage and positive surgical margins predicted higher recurrence and worse PFS and OS.<sup>[2]</sup>

The surgical approach, extent of lymphadenectomy, blood transfusions, and perioperative chemotherapy were not significant predictors of PFS and OS.<sup>[2]</sup>

The authors concluded the oncological equivalence of RARC with ORC for bladder cancer.

As acknowledged by the authors, the study was not powered to detect OS and cumulative recurrence (the study was powered for noninferiority of 2-year PFS between the two groups). However, the study provides high-level prospective data regarding the oncological efficacy of RARC.

## COMMENTS

RAZOR was the first multicentered randomized controlled trial (RCT) comparing the oncological outcomes of RARC and ORC. Similar to the results from the RAZOR trial, a recent review that included five RCTs (including RAZOR) concluded that ORC and RARC had similar outcomes for recurrence, major complications, quality of life, and positive surgical margins.<sup>[3]</sup> The rates of blood transfusion and length of hospital stay were lesser in RARC.

Initial apprehensions about RARC included unusual sites of recurrence and peritoneal carcinomatosis possibly

due to pneumoperitoneum, lack of tactile feedback and cutting through the tumor, and resultant dissemination and aerosolization.<sup>[4]</sup> However, in the present study, there were no differences in the pattern of recurrences between the ORC and RARC.

The benefits of minimally invasive surgery in terms of lesser postoperative complications and better quality of life were not seen in the RARC group. Critics have pointed out that extracorporeal urinary diversion negates the “true” minimally invasive nature of RARC. However, at the time the study was designed, RARC and intracorporeal diversion were still emerging and performed only in few centers. Studies such as iROC (Robotic-assisted radical cystectomy with intracorporeal diversion versus open radical cystectomy) may throw more light on this aspect.<sup>[5]</sup> Furthermore, the operating time was longer in RARC. This may be due to the way time was calculated. In this study, operating time was calculated from room-in to room-out as opposed to other studies which calculated time as skin incision to closure.<sup>[1]</sup>

Future superiority trials addressing cost analysis and looking into specific groups that may benefit (for factors such as age, stage, and body habitus) may add evidence regarding the true value of RARC and aid in careful patient selection.

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