Editorial

Will long term oncologic follow-up make the case for robotic assisted radical cystectomy?

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The use of robot-assisted radical cystectomy (RARC) has increased steadily over the last 15 years (1). The impetus for adopting minimally invasive surgery is based on decreased perioperative morbidity and length of stay compared to the gold standard, open radical cystectomy (ORC). However, the most important aspect in cancer surgery adoption is oncological outcome and, until recently, there has been a paucity of prospective randomized controlled trails (RCTs) comparing RARC and ORC. Following their initial publication that pertained to perioperative outcomes (2), Bochner *et al.* report the oncological outcomes of a single-center, prospective RCT which included 118 patients with median follow-up of 5 years (3). In this study, the authors did not find a significant difference in recurrence-free, cancer-specific and overall survival between RARC and ORC.

Patients were randomized with allocation concealment to either RARC or ORC with pelvic lymphadenectomy and open/extracorporeal urinary diversion between 2010 and 2013. Baseline characteristics, including age and use of neoadjuvant chemotherapy were similar in both groups. Patients with cT4 disease were excluded from the analysis, however the pathologic staging included those with pT4 disease (6.9% in ORC and 8.3% in RARC) and was distributed equally.

Bochner *et al.* reported similar oncological outcomes between both groups of patients; there were no significant differences in disease-specific or recurrence-free survival (P=0.4 for both), as well as all-cause mortality (P=0.8). In their analysis, disease recurrence was subdivided into local, abdominal, or distal. When comparing patterns of recurrence in that distribution there were no significant differences between open and robotic cases. However, when pelvic and abdominal recurrences were grouped as "locoregional" recurrences, the ORC group had a significantly lower rate of recurrence in this distribution (sHR: 0.34; 95% CI: 0.12–0.93; P=0.035). Conversely, while not statistically significant, the ORC group had a higher rate of distant metastases (sHR: 2.21; 95% CI: 0.96–5.12; P=0.064). It is important to keep in mind that the trial was designed and powered to assess complication rates between RARC and ORC, therefore the oncological outcomes are secondary and should be interpreted with caution.

Previous studies have often suggested that 2 years is sufficient to detect >80% of recurrences (4). This study distinguishes itself based on the relatively long-term follow-up (median 4.9 years) as it includes recurrence data from patients past the 2-year follow-up mark. Oftentimes, patients with advanced disease preferentially undergo ORC due to the complexity of the procedure. The study of interest maintained a balance in disease stage between both groups, however, the entire cohort is skewed towards lower stage disease. This distribution does not reflect the national or their own institutional trends as noted by the authors themselves, which further limits what can be deduced about recurrence and survival in those with advanced disease opting to undergo RARC.

These results are comparable to other important retrospective and prospective studies; including a study

that included 2,187 patients from 17 countries by the International Robotic Cystectomy Consortium (IRCC) (5) and the Randomized Open versus Robotic Cystectomy (RAZOR) phase 3, non-inferiority trial that analyzed 302 patients from 15 academic centers across the U.S (6). The IRCC found recurrence free, cancer-specific, and overall survival to be 67%, 75%, and 50%, respectively with a median follow-up of 5.6 years. At the 2-year endpoint of the RAZOR trial, progression-free survival in the RARC group compared with ORC (72.3% *vs.* 71.6%; $P_{noninferiority}$=0.001) was also similar. In line with the aforementioned studies, the study by Bochner *et al.* reports a risk of recurrence of 36% and 41% at 5 years for RARC and ORC, respectively (difference: –5.2%; 95% CI: –25% to 14%).

Positive surgical margin (PSM) rate for RARC relative to ORC was 6% *vs.* 5% (P=0.59) in the RAZOR trial compared to 3.6% *vs.* 4.8% in the Bochner *et al.* study. Additionally, the IRCC reported PSM in 8% of their population. Given that PSM may correlate with higher stage disease, the higher rate observed in the IRCC and RAZOR data may be reflective of the larger percentage of pT4 disease in that cohort (9% in IRCC and 8–11% in RAZOR). In addition, the heterogeneity of PSM rates in RARC may indeed be attributable to the learning curve and the added difficulty of lack of tactile feedback during RARC (7).

In contrast to the Bochner *et al.* study, the RAZOR trial found no significant difference in local or distal recurrence between RARC and ORC (4% *vs.* 3%; P=0.54, and 22% *vs.* 23%, respectively). The definition of local recurrence in the RAZOR trial included recurrence in the cystectomy bed, pelvic lymphadenectomy template or abdominal wall/port site, whereas bowel recurrence and peritoneal carcinomatosis were considered distal recurrences. In the RAZOR trial, there were no significant differences found in rates of peritoneal carcinomatosis (two in RARC, one in ORC) and abdominal wall recurrence (one case in the ORC group and none in the RARC). Interestingly, Bochner *et al.* note an uncommon pattern of recurrence only in the RARC group with five cases involving the abdominal wall, excluding port sites, and three with rectosigmoid invasion. This rate is higher than previously published RARC (8,9) and ORC series (10). The cause of uncommon recurrence patterns has been proposed to be attributable to pneumoperitoneum, tumor spillage, and inadequate resection (11) or may simply be explained by tumor stage (12). Albeit the difference in methodology and reporting of recurrence patterns, the incidence of atypical recurrences is low, and in each of the aforementioned studies remains comparable to the comparative ORC group.

While this recent analysis serves as a valuable contribution to the cache of randomized trials comparing RARC and ORC, it has several limitations; the long-term oncologic outcome data is underpowered to detect differences in overall recurrence trends and does not represent advanced stage cystectomy. Additionally, both this and the RAZOR trial perform exclusively extracorporeal urinary diversion, despite the growing interest in intracorporeal diversion in most high-volume centers (13). Furthermore, while the prescription of chemotherapy was similar between both groups, it was not standard and its use may obviate differences in post-surgical risk of recurrence.

The question that robotic approach might provide better oncological outcomes still remains under investigation. However, certain perioperative aspects have been reproduced in the literature, such as its positive impact on length of stay and post-operative blood loss. Of note, the adoption of enhanced recovery after surgery protocols may further narrow the margin between both techniques. Bochner *et al.* have made a substantial contribution in providing long term, randomized prospective follow up data to show no difference in RARC *vs.* ORC oncologic outcomes; such studies are crucial in advancing our understanding on the safety of RARC in order to provide the best patient care.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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