

# Understanding the roles of randomized trials for robotic prostatectomy

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*Comment on:* Yaxley JW, Coughlin GD, Chambers SK, *et al.* Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: early outcomes from a randomised controlled phase 3 study. *Lancet* 2016;388:1057-66.

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The long-standing debate on the relative benefits of robotic surgery reached a milestone this July with the publication of early results from the first randomized trial comparing open versus robotic radical prostatectomy. In their study, “Robot-assisted Laparoscopic Prostatectomy Versus Open Radical Retropubic Prostatectomy: Early Outcomes from a Randomized Controlled Phase 3 Study”, Yaxley *et al.* randomized 326 men at their institution to receive either radical retropubic prostatectomy (RRP) or robot-assisted laparoscopic prostatectomy (RALP) (1). Men were compared based on functional outcomes including urinary and sexual function (as measured by validated survey instruments, EPIC and IIEF) and oncologic outcomes including positive margin status and imaging or biochemical recurrence (at 24 weeks—not reported in the current paper). There was no significant difference in urinary and quality of life outcomes at 12 weeks post-operatively. In terms of oncologic outcomes the authors found a non-significant trend towards more positive surgical margins in the robotic surgical group.

The authors should be commended for executing the first randomized trial comparing open versus robotic prostatectomy, which comes on the heels of a similar trial evaluating robotic versus open radical cystectomy (2). Similar to a good body of observational research showing little definitive oncologic or quality of life benefit for robotic prostatectomy over traditional open prostatectomy (3-6), despite higher costs (7) the findings suggest that

widespread adoption of this expensive surgical technique (now the dominant mode for surgical removal of the prostate in the developed world) may be unwarranted.

While a randomized trial provides a high level of evidence, we feel it is important to highlight some general strengths and weaknesses of this trial in particular as well as surgical trials more generally. First, there is the question of blinding: in a trial comparing open versus robotic surgery, blinding is impossible. Patients, caregivers and outcomes assessors are all aware of allocation. While this does not necessarily prejudice the results it may open the door to biases in outcomes assessment and reporting.

Second, a trial is only valid if the interventions in the study are similar to those used in community practice. For trials of medications this is trivial, but for surgical trials this may be a significant issue. Specifically, are the surgeons within the trial similar to those in the community? When a trial of robotic versus open radical cystectomy was performed at a large oncology center—critics rightly wondered whether the results of very high volume surgical oncologists (who had performed literally thousands of the procedure) would be generalizable to community practice (8). The same issues are evident in this trial. Surgical trials in other fields (e.g., randomized comparisons of carotid endarterectomy versus stenting) have employed credentialing procedures to ensure a comparative baseline level of skill—however even this does not necessarily entail that trial surgeons or interventionists are similar to those in

community practice (9-11).

In this trial the robotic surgeon had an experience of 200 robotic prostatectomies at the start of this trial, while the open surgeon had performed over 1,500. By the end of the trial this had increased to over 1,000 for the robotic surgeon and over 2,000 for the open surgeon. Setting aside the question of whether head-to-head comparison of surgeons with a 5-fold differential in initial experience is warranted, such high volumes may not be similar to typical community urologists. Many series from the United States suggest a typical community hospital volume of around 10/year for open and around 40–50/year for robotic prostatectomies (12). In light of the well-known volume outcomes effect for prostatectomy (13) results of the high-volume surgeons in this trial may not be transferrable to usual practice.

Another issue with the above trial is the short follow-up. Data suggest that recovery of sexual function may take up to 1 year (14). The 3-month follow-up in this trial thus may be too short to fully realize the benefits of robotic prostatectomy, especially when 25% of the cohort lacked even that follow-up.

Ultimately, any trial comparing surgical techniques depends on surgeon expertise; a head-to-head comparison of two surgeons is therefore intrinsically limited. Intuitively, as the number of surgeons increase, differences in outcomes may become more attributable to general aspects of one approach or another rather than individual differences in surgeon skill or experience. Yaxley *et al.* report that the decision to employ only two surgeons was made to “limit surgical heterogeneity”. But we would argue that this is the wrong approach. What most readers want to know is whether one technique (in the hands of a typical surgeon) is generally better than another. There is evidence for tremendous variability in robotic prostatectomy (15). By including a large number of surgeons and comparing differences on average between typical surgeons, the influence of outliers can be reduced and more generalizable statements about differences in techniques can be made.

While randomized controlled trials limit certain types of biases and reduce spurious associations, it is important to understand that surgical trials carry their own limitations. In addition to randomized prospective trials, observational and population-based research may provide key, generalizable insights into treatment trends, patterns of care, and effectiveness for typical patients treated by typical doctors. Ultimately, what patients, surgeons, hospitals and insurers want to know is how one approach is generally different

than another. For this information, we wonder whether a 2-surgeon randomized trial can significantly move the dial when the vast majority of surgeries in are already performed robotically.

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## Footnote

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

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