



European Association of Urology



## Platinum Priority – Editorial and Reply from Authors

Referring to the article published on pp. 606–614 of this issue

# The Promise and Challenges of Randomized Controlled Trials for Surgical Interventions

Karim A. Touijer\*

Urology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, Department of Urology, Weill Medical College of Cornell University, New York, NY, USA

At a number of panel discussions at scientific meetings over recent months, urologists have debated whether partial nephrectomy for renal cortical tumors confers a survival benefit over radical nephrectomy. Proponents of both views put forward intelligent, valid points but almost always came short of a conclusion. What has emerged from these discussions is an important question: Can data from retrospective analyses, with their inherent potential for selection bias, provide stronger evidence than that obtained from a randomized controlled trial closed prior to meeting the target accrual numbers?

Randomized controlled clinical trials (RCTs) are powerful tools, generating the highest level of evidence to determine whether a cause-and-effect relationship exists between a health care intervention and a given outcome. However, the relevance and exactitude of an RCT's findings are intimately tied to the rigor with which it is designed, executed, and analyzed.

Undoubtedly, surgical RCTs are difficult to conduct. The challenges include:

- Poor accrual, which leads to underpowered studies
- Refusal of randomization by patients because they may already have chosen their surgeon for his or her qualifications or have a preference for a given approach
- Blinding of surgeons, patients, and, to a lesser degree, the party assessing the measured outcome, which can be impractical
- The difficulty of controlling for the disparities in skill and experience between surgeons and centers.

Consolidated Standards of Reporting Trials (CONSORT) guidelines [1,2], issued in 1996 and most recently updated in 2010, provide a framework for trialists to publish their results with transparency, providing the critical reader with answers about why the study was initiated, how the research was conducted, and how the results were analyzed. The CONSORT guidelines include a checklist of items that should be included in clinical trial reports, ranging from how participants were allocated to interventions to the generalizability or external validity of the trial findings.

A critical assessment of the quality of reporting of RCTs in urologic literature between 1996 to 2004 showed that less than half of the 152 RCTs assessed conformed to the CONSORT guidelines with regard to key methodological criteria, such as justification of the sample size, a single primary outcome, effect-size estimates for secondary outcome variables, and a description of the implementation of randomization [3].

In this issue of *European Urology*, Porpiglia and colleagues report the results of a single-surgeon surgical RCT comparing the recovery of continence at 3 mo between two groups, 60 patients each, treated by laparoscopic radical prostatectomy with or without robotic assistance [4]. The authors conclude that robot-assisted laparoscopic radical prostatectomy provided better functional results with regard to recovery of potency and continence.

The report performs relatively well on the CONSORT checklist but has considerable deficiencies, such as the lack of effect-size estimates for secondary end points and underpowered subset analyses (eg, the finding of potency is based on a comparison of 35 patients in each arm, with only 14 vs 11 men undergoing bilateral intrafascial

DOI of original article: <http://dx.doi.org/10.1016/j.eururo.2012.07.007>.

\* Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10065, USA. Tel. +1 646 422 4486 or +1 212 988 0768.

E-mail address: [touijera@mskcc.org](mailto:touijera@mskcc.org).

preservation in the robotic and laparoscopic groups, respectively). Along with the failure to report 95% confidence intervals, such inconsistencies lead to imprecision in their conclusions.

Porpiglia and colleagues, however, are to be congratulated for conducting an excellent single-surgeon quality-assurance trial. Although the concept that an outcome or performance can often be improved simply by measuring the outcome and providing feedback is well recognized [5–7], Porpiglia et al. took this concept to another level of sophistication. Initially, a surgeon suspects from personal experience that there is a 25% difference in recovery of urinary continence at 3 mo favoring robotic over laparoscopic prostatectomy. Then the surgeon endeavors to scientifically test this hypothesis through an RCT comparing the two approaches. Unfortunately, the authors did not elaborate on the implications of these results for their practice.

The generalizability of this trial's findings is limited. Often, studies comparing the outcome of two surgical techniques are merely a comparison of surgeons' performances, unless conducted on a larger scale and designed specifically to account for such variables. Several studies have shown a wide variability of complication rate, and functional and oncologic outcomes among surgeons performing radical prostatectomy [8,9]. The magnitude of the differences between surgeons is so important that its impact on a comparative study outcome would dwarf that of any potential difference associated with the surgical approach.

When a trial is designed to randomize patients to receive one of two surgical approaches, all performed by the same surgeon, the misconception is that it compares the surgical approaches, while, in fact, it compares only the performance of the surgeon with one or the other technique.

**Conflicts of interest:** The author has nothing to disclose.

## References

- [1] Schulz KF, Altman D, Moher D, CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c332.
- [2] Moher D, Hopewell S, Schulz KF, et al., CONSORT Group. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trial. *BMJ* 2010;340:c869.
- [3] Scales Jr CD, Norris RD, Keitz SA, et al. A critical assessment of the quality of reporting of randomized, controlled trials in the urology literature. *J Urol* 2007;177:1090–4, discussion 1094–5.
- [4] Porpiglia F, Morra I, Lucci Chiarissi M, et al. Randomised controlled trial comparing laparoscopic and robot-assisted radical prostatectomy. *Eur Urol* 2013;63:606–14.
- [5] Mazzola C, Savage C, Ahallal Y, et al. Nodal counts during pelvic lymph node dissection for prostate cancer: an objective indicator of quality under the influence of very subjective factors. *BJU Int* 2012;109:1323–8.
- [6] Touijer K, Kuroiwa K, Saranchuk JW, et al. Quality improvement in laparoscopic radical prostatectomy for pT2 prostate cancer: impact of video documentation review on positive surgical margin. *J Urol* 2005;173:765–8.
- [7] Touijer K, Kuroiwa K, Vickers A, et al. Impact of a multidisciplinary continuous quality improvement program on the positive surgical margin rate after laparoscopic radical prostatectomy. *Eur Urol* 2006;49:853–8.
- [8] Begg CB, Riedel ER, Bach PB, et al. Variations in morbidity after radical prostatectomy. *N Engl J Med* 2002;346:1138–44.
- [9] Vickers A, Savage C, Bianco F, et al. Cancer control and functional outcomes after radical prostatectomy as markers of surgical quality: analysis of heterogeneity between surgeons at a single cancer center. *Eur Urol* 2011;59:317–22.

<http://dx.doi.org/10.1016/j.eururo.2012.08.018>

## Platinum Priority

**Reply from Authors re: Karim A. Touijer. The Promise and Challenges of Randomized Controlled Trials for Surgical Interventions. *Eur Urol* 2013;63:615–6**

***Randomised Controlled Clinical Trials in a Surgical Setting: Always the Best?***

**Francesco Porpiglia<sup>\*</sup>, Cristian Fiori**

Division of Urology, "San Luigi Gonzaga" Hospital-Orbassano (Turin), University of Turin, Turin, Italy

We all agree that randomised controlled trials (RCTs) represent the most powerful tool in the hands of researchers, and data from these studies offer results with a high level of

evidence. The difficulties of performing RCTs were well described by Touijer in his interesting editorial comment [1], and these difficulties could explain the low number of RCTs in the urologic literature. The efforts to adhere to Consolidated Standards of Reporting Trials guidelines [2,3] make things even more difficult for clinicians.

Fortunately, we only partially experienced these difficulties in completing our study [4]. Only 2 of 129 patients (1.5%) refused study inclusion. This percentage is surprisingly low and most likely related to the minimally invasive approaches offered to the patients (pure and robot-assisted laparoscopy). Most of our patients were referred to our institution because of our experience in minimally invasive techniques, regardless of the technique we use.

Because the most experienced surgeon in laparoscopic and robotic surgery performed all of the procedures, we overcame the difficulties of controlling for disparities in skill and experience between surgeons.

However, we deemed blinding the procedure to the clinician and the patients as an insurmountable obstacle

DOIs of original articles: <http://dx.doi.org/10.1016/j.eururo.2012.07.007>, <http://dx.doi.org/10.1016/j.eururo.2012.08.018>.

<sup>\*</sup> Corresponding author. Division of Urology, Department of Clinical and Biological Sciences, University of Turin "San Luigi" Hospital, Regione Gonzole 10, 10043 Orbassano (Turin), Turin, Italy. Tel. +39 0119026557; Fax: +39 0119026244.

E-mail address: [porpiglia@libero.it](mailto:porpiglia@libero.it) (F. Porpiglia).