available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Editorial and Reply from Authors

Referring to the article published on pp. 768–774 of this issue

"A Robot Saved My Life": Is It a Myth?

Anders Bjartell

Department of Urology, Skåne University Hospital, Malmö, Lund University, Lund, Sweden

Outcomes of robot-assisted radical prostatectomy (RARP) have been reported in several papers, although it has been only about a decade since the method was introduced. No long-term follow-up data for RARP are available for comparison with open radical prostatectomy (ORP).

Sweden is a country with a high incidence and an extremely high mortality rate for prostate cancer (PCa) [1]. One of the first European centers at which RARP was introduced is at Karolinska University Hospital in Stockholm, Sweden. In the current issue of *European Urology*, Sooriakumaran and collaborators at this center present medium-term oncologic outcomes of RARP with a biochemical recurrence–free survival (BRFS) of 84.8% at a median follow-up of 6.3 yr, and they concluded that there were "satisfactory" outcomes for this procedure [2].

The authors report clinical outcomes from a case series of 904 patients who underwent RARP as monotherapy for PCa from January 2002 to December 2006 at a single high-volume center. Cox univariable and multivariable regression analyses were used to determine BRFS estimates and predictors of biochemical recurrence (BCR) as defined by confirmed prostate-specific antigen (PSA) relapse of $\geq$0.2 ng/ml [2]. Preoperative PSA >10, postoperative Gleason sum $\geq$4 + 3, pathologic T3 disease, positive surgical margin status (SMS), and lower surgeon volume were found to be associated with increased risk of BCR. Unfortunately, the authors did not have access to lymph node status or tumor volume, which is a weakness that may have confounded the reported outcome data. The authors also admit that this lack of access is an important limitation of their study.

The authors are to be congratulated, as this study represents the largest sample size thus far to report oncologic outcomes of RARP with $\geq$5 yr follow-up. Looking at other recent studies, Suardi et al. [3] reported BRFS after RARP at an overall rate after 7 yr of 81.0%, but the population studied comprised only 184 patients. Larger studies already exist but have shorter follow-up times. Menon et al. [4] reported an overall BRFS of 86.4% for a large series of 1384 patients with a median follow-up of 5.2 yr and a median time to BCR of 20.4 mo, which is shorter than the 27.7 mo reported by Sooriakumaran et al. [2]. Comparing this study with contemporary RARP series reveals that other studies generally are performed on more favorable patient populations [5]. Patel et al. published a multi-institutional study from seven centers with a total of 6169 RARP patients and found a positive SMS rate of 15.7% [6], compared with the 16.2% rate reported in a recent meta-analysis of 62 389 cases of RARP [7]. Although differences exist among study populations, the rate of BRFS does not seem to differ among recent studies.

Another important question to be answered is whether we can show any advantages of RARP compared with OPR. In a recent study, Dorin et al. reported on 2487 patients who underwent ORP, and they found a 10-yr PSA relapse rate of 8%, 17%, and 24% in D'Amico low-, intermediate-, and high-risk patients, respectively, at a median follow-up of 7.2 yr [8]. This finding is comparable with the report from Sooriakumaran et al. with 8%, 15%, and 36%, respectively, and the studies were also similar in terms of rates of pT3 and positive SMS. We conclude that it is difficult to show any advantage for RARP compared with ORP regarding BCR.

Additional studies to compare RARP and OPR are ongoing at many centers and in Sweden [9]. The Laparoscopic Prostatectomy Robot Open (LAPPRO) trial is a prospective nonrandomized trial comparing RARP and ORP in aspects of short- and long-term functional and oncologic outcome, cost effectiveness, and quality of life, supplying new knowledge to support future decisions in treatment strategies for PCa. Although the primary end point is urinary leakage 1 yr after surgery, several secondary end points of major importance will also be explored. The study started in September 2008, with accrual continuing to

DOI of original article: http://dx.doi.org/10.1016/j.eururo.2012.05.024
E-mail address: anders.bjartell@med.lu.se.

November 2011; analysis will be performed on a cohort of 700 men in the ORP group and 1400 men in the RARP group. This is an excellent opportunity for subsequent studies in which we can compare the oncologic outcomes of RARP performed at high-volume centers like those in Stockholm with other Swedish centers. The findings will provide a nationwide picture of the overall oncologic outcome of RARP. Perhaps we already know the answer—that RARP should be performed only at high-volume centers by very experienced surgeons to obtain the very best outcome, an idea that has been discussed in several publications.

Sooriakumaran and coworkers reported on variables to predict PSA relapse. Besides well-established factors shown in previous studies, the authors also reported surgeon volume to be a determinant of BCR, which is in contrast to a large study on ORP [10]. However, other studies clearly show the importance of surgeon volume for both BCR rate and positive SMS, which is quite understandable. It is urgent that additional studies on learning curve issues be performed and that secure training programs be developed to educate the next generation of robot-assisted surgeons.

What, then, is the most important outcome measure in studies on RARP? The answer is perhaps whether the disease is lethal or not lethal. As we know from several studies, positive SMS does not always correspond to BCR, and BCR does not always translate to PCa-specific death. The median time to BCR was 2.3 yr in this study. The rate of positive surgical margins was 21.6%, and the overall BRFS was as high as 84.8%; these findings indicate that small foci of tumor in the surgical margin will not necessarily cause BCR within the next few years of follow-up. Kaplan-Meier estimates of PCa-specific and other-cause mortality at a follow-up of 10 yr were 2.0% and 5.9%, respectively, in this study. It is quite clear that follow-up is too short to make any kind of conclusions from these figures. The long-term consequences of focal positive SMS in RARP is one of the key issues to be investigated in future studies.

Unfortunately, the importance of retroperitoneal lymph node dissection (RPLND) in combination with RARP in high-risk patients was never addressed in the study by Sooriakumaran et al. [2]. The authors were not able to report lymph node status, which may indicate that they followed a selected cohort. No patients received adjuvant treatment, and only 6.4% high-risk patients were included, which makes it understandable why the results are quite favorable and may not be representative of a less homogenous group of patients. We must also be aware of the fact that this is a population of men who may not always benefit from this treatment and whose outcome is expected to be excellent.

Although RARP monotherapy is an excellent choice for curative treatment in many patients, it is at least as important to focus on combined treatments offered to men with locally advanced PCa. Studies comparing RARP and extended RPLND in combination with external-beam radiation therapy and/or pharmacologic treatments are urgently needed in this group of patients.

What can we expect in the next few years? We have only just begun to put together our experiences of RARP as a lifesaving procedure. RARP will probably continue to increase compared with ORP despite the increasing costs. Although the present study may add another small piece of knowledge with regard to outcome after RARP, we need to gain more information from future studies before we can tailor the best treatment, avoid overtreatment, and improve the survival rate in men with locally advanced PCa using a better model for personalized outcome prediction. However, do we need additional studies of this kind? There is still an unmet need to identify the optimal treatment for men with more advanced PCa, as previously mentioned. Such studies are perhaps more urgent than contemporary studies, including this one by Sooriakumaran et al., that deal with men who rarely will die from PCa.

Conflicts of interest: The author has nothing to disclose.

References

[1] Center MM, Jemal A, Lortet-Tieulent J, et al. International variation in prostate cancer incidence and mortality rates. Eur Urol 2012; 61:1079–92.

[2] Sooriakumaran P, Haendler L, Nyberg T, et al. Biochemical recurrence after robot-assisted radical prostatectomy in a European single-centre cohort with a minimum follow-up time of 5 years. Eur Urol 2012;62:768–74.

[3] Suardi N, Ficarra V, Willemsen P, et al. Long-term biochemical recurrence rates after robot assisted radical prostatectomy: analysis of a single-center series of patients with a minimum follow-up of 5 years. Urology 2011;79:133–8.

[4] Menon M, Bhandari M, Gupta N, et al. Biochemical recurrence following robot-assisted radical prostatectomy: analysis of 1384 patients with a median 5-year follow-up. Eur Urol 2010; 58:838–46.

[5] Tewari AK, Srivastava A, Mudaliar K, et al. Anatomical retro-apical technique of synchronous (posterior and anterior) urethral transection: a novel approach for ameliorating apical margin positivity during robotic radical prostatectomy. BJU Int 2010; 106:1364–73.

[6] Patel VR, Coelho RF, Rocco B, et al. Positive surgical margins after robotic assisted radical prostatectomy: a multi-institutional study. J Urol 2011;186:511–6.

[7] Tewari A, Sooriakumaran P, Bloch DA, Seshadri-Kreaden U, Hebert AE, Wiklund P. Positive surgical margin and perioperative complication rates of primary surgical treatments for prostate cancer: a systematic review and meta-analysis comparing retropubic, laparoscopic, and robotic prostatectomy. Eur Urol 2012;62:1–15.

[8] Dorin RP, Daneshmand S, Lassoff MA, Cai J, Skinner DG, Lieskovsky G. Long-term outcomes of open radical retropubic prostatectomy for clinically localized prostate cancer in the prostate-specific antigen era. Urology 2012;79:626–31.

[9] Thorsteinsdottir T, Stranne J, Carlsson S, et al. LAPPRO: a prospective multicentre comparative study of robot-assisted laparoscopic and retropubic radical prostatectomy for prostate cancer. Scand J Urol Nephrol 2011;45:102–12.

[10] Barocas DA, Salem S, Kordan Y, et al. Robotic assisted laparoscopic prostatectomy versus radical retropubic prostatectomy for clinically localized prostate cancer: comparison of short term biochemical recurrence-free survival. J Urol 2010;183:990–6.

http://dx.doi.org/10.1016/j.eururo.2012.06.051