Robot-assisted radical prostatectomy, an update of the current evidence

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SUMMARY

Robot-assisted radical prostatectomy has become standard-of-care in most centres of excellence in the treatment of prostate cancer. Recent literature shows a reduced complication risk, reduced transfusion need, shorter hospitalisation and functional and oncological benefit in comparison with open radical prostatectomy. Long term follow-up data and large randomised clinical trails are currently lacking.

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INTRODUCTION

Prostate cancer is the most common cause of malignancy in men in Europe.[1] Radical prostatectomy (RP) remains the standard-of-care treatment for surgically fit patients with localised prostate cancer, with a proven benefit compared to watchful waiting.[2] In recent years, we have witnessed a shift from open radical prostatectomy (ORP) to minimally invasive techniques, and particularly to robot-assisted radical prostatectomy (RARP).[3] In this review we aim to summarise the benefits of this relatively new technique on the basis of recent literature.

ONCOLOGICAL OUTCOME

When performing a prostatectomy a surgeon strives for negative surgical margins, because patients with positive surgical margins have an increased risk of relapse and biochemical recurrence.[4,5] Recent non-randomised studies report a clearly reduced incidence of positive surgical margins with RARP in comparison to ORP.[6–9] A recent cohort study by *Pearce et al.* (2016) also reports a reduced risk of positive surgical margins (OR 0.88; 95% CI 0.83-0.93, P<0.01) and more importantly a reduced use of postoperative radiation therapy (OR 0.71; 95% CI 0.63-0.80, P<0.01).[10] The experience of the surgeon is a factor that should be taken into account, independent of the technique. Additional randomised trials are necessary to confirm the oncological benefit of RARP with long term follow-up. Recently there has been a shift from androgen deprivation therapy (ADT) or ADT combined with radiotherapy (RT) to surgery for locally-advanced prostate cancer (LAPC), albeit in highly selected patients. Current evidence for surgery on LAPC is based on either retrospective or small prospective case series. Although there is limited evidence, prostatectomy should be considered as a part of a multimodal treatment for LAPC combined with an extended pelvic lymphadenectomy and postoperative RT and ADT. RARP and ORP can both be considered, depending on the experience of the surgeon and the extent of the disease.

FUNCTIONAL OUTCOME

The primary goal with prostate cancer surgery is an optimal oncological result with a minimal negative impact on a functional level. The main functional disorders after surgery are urinary incontinence and erectile dysfunction. *Haglind et al.* (2015) demonstrated no significant difference in urinary incontinence or erectile dysfunction between RARP (n=778) and ORP (n=1,847) in a prospective non-randomised study with a follow-up of twelve months after surgery.[11] Similarly, no difference was observed in a systematic review by *Ficarra et al.* (2009) comparing RARP with ORP, with the available data available at the time, including seven prospec-

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tive non-randomised studies, two retrospective studies comparing contemporary series of patients and one retrospective study using historical series as control.[12] However a more recent non-randomised population study comparing RARP (n=933) with ORP (n=1,505) reports an improved recovery of erectile function at six and twelve months postoperatively, and an improved recovery of urinary incontinence at six months, but a similar outcome at twelve months postoperatively in patients treated with RARP.[13] This latest study shows a functional benefit in the short term with RARP but long term data is currently lacking.

COMPLICATIONS

Clear arguments in favour of RARP are found in the level of perioperative and postoperative complications. Quoc-Dien *Trinh et al.* (2012) showed a lower transfusion need with RARP patients (OR 0.34; 95% CI, 0.28-0.40), a reduced risk of intraoperative complications (OR 0.47; 95% CI 0.31-0.71) and a reduced risk of postoperative complications (OR 0.86; 95% CI 0.77-0.96) in a patient population of 19.462 patients (61.1% RALP, 38.0% ORP).[14] These postoperative complications are situated on the cardiac, respiratory and the vascular field and are significantly less frequent with RARP in comparison to ORP. The authors suggest that these benefits can be explained by the minimally invasive nature of RARP, which causes a minimal immunological and metabolic acute phase response. In a recent cohort study of 629.593 patients *Leow et al.* (2016) found a 32% less complication risk with RARP in comparison to ORP.[15] The cohort study by *Pearce et al.* (2016) reports a reduced 30-day mortality with RARP in comparison to ORP (OR 0.28; 95% CI 0.13-0.60, P<0.01).[10]

HOSPITALISATION

Another important advantage is the significant shorter hospital stay after RARP. *Alemozaffar et al.* (2014) report an average of 1.8 days for RARP and 2.9 days for ORP in a cohort study of 903 patients.[3] This shorter hospital stay is also described by Quoc-Dien *Trinh et al.* (2012) where ORP has a significantly longer hospital stay >2 days compared with RARP (OR: 0:28; 95% CI 0.26-0.3, P<0.001). *Leow et al.* (2016) also report a prolonged hospital stay in RARP patients compared to ORP patients (OR 0.28; P<0.001). A prolonged hospital stay was defined as a stay exceeding the median of the entire cohort.[15]

TRANSFUSION

Schmitges et al. (2012) found that the transfusion need has dropped since the introduction of minimally invasive surgery in a group of 119,966 patients in the United States (US) between 1998 and 2007.[16] They found a doubling of transfusion need from 5.1% in RARP patients to 11.4% in ORP patients. *Soubra et al.* (2015) describe similar results in a patient population of 28,854 patients between 1992-2009, also in the US.[17] They report a clear reduction in transfusion need since the introduction of RARP. Their logistic regression model shows a reduced transfusion need in high volume centres (ORP and RARP) (OR 0.606; 95% CI 0.507-0.724, P<0.0001) and an even lower transfusion need in centres (low and high volume centres) when using RARP instead of ORP (OR 0.207; 95% CI, 0.162-0.265, P<0.0001). *Alemozaffar et al.* (2014) report a similar reduction of an 83% less transfusion need with RARP in their cohort study comparing RARP (n=282) with ORP (n=621).[3] This reduction of transfusion need was also reported by *Leow et al.* (2016) with RARP (n=73.131) in comparison to ORP (n=23.804) (OR 0.33; P=0.02).

TRANSFUSION-RELATED IMMUNE MODULATION

It has been shown that blood transfusions cause substantial changes to the anti-inflammatory and pro-inflammatory environment of the recipient. This phenomenon is called transfusion-related immune modulation (TRIM). Laboratory and animal experiments show that stored blood and old erythrocytes may have tumour-promoting effects.[18] In colorectal cancer, there is a known association between perioperative blood transfusion and an increased risk of cancer recurrence.[19] *Soubra et al.* also report an association between blood transfusions and cancer-specific survival (OR 1.699; 95% CI, 1.294-2.230, P<0.0001) and overall survival (OR 1.1166; 95% CI 1.043-1.303, P<0.0069) in prostate cancer.[17] These findings need to be confirmed in large randomised trials but already provide an additional argument in favour of RARP because of the previously described reduced need of transfusions. Awareness of this issue is important in making individualised decisions on transfusion in patients undergoing prostate cancer surgery.

CONCLUSION

The current issue with robotic assisted laparoscopic surgery is primarily the limited follow-up data com-

KEY MESSAGES FOR CLINICAL PRACTICE

1 Pros:
- **Functional benefit[13]**
- **Oncological benefit[6–10,17,18]**
- **Reduced complication risk[10,14,15]**
- **Shorter hospitalisation[3,14]**
- **Reduced blood transfusion need[16–18]**

2 Cons:
- **Higher cost**

3 Future:
- **Long term follow-up data**
- **Large randomised clinical trails**

pared with open surgery and particularly long term oncological follow-up data that is readily available in open surgery. Experience of the surgeon remains an important factor, independent of the technique, but large randomised clinical trials are currently lacking. The public debate focuses primarily on the cost of robot-assisted laparoscopic surgery, which consists of the purchase price of the device and the cost of disposables (limited reusable instruments that are used for each procedure). On the other hand, we report the above-described advantages at oncological level (reduced positive surgical margins and less use of postoperative RT), the advantages at functional level, reduced risk of complications, reduced transfusion need and a shorter length of hospital stay.

REFERENCES

1. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. Eur J Cancer. 2013;49:1374–1403.

2. Bill-Axelson A, Holmberg L, Ruutu M, et al. Radical prostatectomy versus watchful waiting in early prostate cancer. N Engl J Med. 2005;352:1977–84.

3. Alemozaffar M, Sanda M, Yecies D, et al. Kenfield SA. Benchmarks for operative outcomes of robotic and open radical prostatectomy: Results from the health professionals follow-up study. Eur Urol. 2015;67:432–8.

4. Pfitzenmaier J, Pahernik S, Tremmel T, et al. Positive surgical margins after radical prostatectomy: do they have an impact on biochemical or clinical progression? BJU Int. 2008;102:1413–8.

5. Yossepowitch O, Briganti A, Eastham JA, et al. Positive surgical margins after radical prostatectomy: A systematic review and contemporary update. Eur Urol. 2014;65:303–13.

6. Hu JC, Gandaglia G, Karakiewicz PI, et al. Comparative effectiveness of robot-assisted versus open radical prostatectomy cancer control. Eur Urol. 2014;66:666–72.

7. Sooriakumaran P, Srivastava A, Shariat SF, et al. A Multinational, Multi-institutional Study Comparing Positive Surgical Margin Rates Among 22393 Open, Laparoscopic, and Robot-assisted Radical Prostatectomy Patients. Eur Urol. 2013;66:1–7.

8. Thompson JE, Egger S, Böhm M, et al. Superior quality of life and improved surgical margins are achievable with robotic radical prostatectomy after a long learning curve: A prospective single-surgeon study of 1552 consecutive cases. Eur Urol. 2014;65:521–31.

9. Tewari A, Sooriakumaran P, Bloch DA, et al. 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.

10. Pearce SM, Pariser JJ, Karrison T, et al. Comparison of Perioperative and Early Oncologic Outcomes between Open and Robotic Assisted Laparoscopic Prostatectomy in a Contemporary Population Based Cohort. J Urol. 2016;196:76–81.

11. Haglind E, Carlsson S, Stranne J, et al. Urinary Incontinence and Erectile Dysfunction After Robotic Versus Open Radical Prostatectomy: A Prospective, Controlled, Nonrandomised Trial. Eur Urol. 2015;68:216–25.

12. Ficarra V, Novara G, Artibani W, et al. Retropubic, Laparoscopic, and Robot-Assisted Radical Prostatectomy: A Systematic Review and Cumulative Analysis of Comparative Studies. Eur Urol. 2009;55:1037–63.

13. O'Neil B, Koyama T, Alvarez J, et al. The Comparative Harms of Open and Robotic Prostatectomy in Population-Based Samples. J Urol, 2015;195:321–9.

14. Trinh Q-D, Sammon J, Sun M, et al. Perioperative Outcomes of Robot-Assisted Radical Prostatectomy Compared With Open Radical Prostatectomy: Results From the Nationwide Inpatient Sample. Eur Urol. 2012;61:679–85.

15. Leow JL, Chang SL, Meyer CP, et al. Robot-assisted Versus Open Radical Prostatectomy: A Contemporary Analysis of an All-payer Discharge Database. Eur Urol. 2016;70(5):837-845.

16. Schmitges J, Sun M, Abdollah F, et al. Blood transfusions in radical prostatectomy: A contemporary population-based analysis. Urology. 2012;79:332–8.

17. Soubra A, Zabell JR, Adejoro O, et al. Effect of perioperative blood transfusion on mortality for major urologic malignancies. Clin Genitourin Cancer. 2015;13:e173–81.

18. Cata JP, Wang H, Gottumukkala V, et al. Inflammatory response, immunosuppression, and cancer recurrence after perioperative blood transfusions. Br J Anaesth. 2013;110:690–701.

19. Parrott NR, Lennard TW, Taylor RM, et al. Effect of perioperative blood transfusion on recurrence of colorectal cancer. Br J Surg. 1986;73:970–3.