Editorial

Early or delayed radiotherapy after prostatectomy—who really benefits?

Henk van der Poel[1], Marie-Anne van Stam[2]

[1]Department of Urology, Netherlands Cancer Institute, Amsterdam, The Netherlands; [2]Department of Urology, University Medical Centre Utrecht, Utrecht, The Netherlands

Correspondence to: Henk van der Poel. Department of Urology, Netherlands Cancer Institute, Amsterdam, The Netherlands. Email: h.vd.poel@nki.nl.

Provenance: This is a Guest Editorial commissioned by Editorial Board Member Dr. Xiongbing Zu, MD, PhD (Department of Urology, Xiangya Hospital, Central South University, Changsha, China).

Comment on: Gandaglia G, Briganti A, Clarke N, *et al*. Adjuvant and Salvage Radiotherapy after Radical Prostatectomy in Prostate Cancer Patients. Eur Urol 2017. [Epub ahead of print].

Submitted Mar 06, 2017. Accepted for publication Mar 07, 2017.
doi: 10.21037/tau.2017.03.68
View this article at: http://dx.doi.org/10.21037/tau.2017.03.68

The review by Gandaglia *et al*. (1) clearly shows that we are in the process of drawing a roadmap towards the use of postprostatectomy radiotherapy. The outline is clear: we know that some patients benefit from the combination of surgery and radiotherapy, and we know that these patients have an increased risk of side effects. However, at this moment, the roadmap also shows a lot of gaps; we don't have clear evidence which patients will really benefit, and there is no clarity about the optimal treatment delivery. The by Gandaglia *et al*. (1) drawn roadmap reveals many of these gaps, and provides a good starting point for future studies.

Any cancer treatment should balance oncological and functional outcomes. Early adjuvant radiotherapy in men with increased risk of locally remnant disease was shown to improve clinical progression free survival in 3 and overall survival in 1 RCT even at relatively doses of radiotherapy without additional androgen ablation. Scrutinizing the control groups in these 3 trials is important to understand the clinical value of these findings at today's standards. As correctly remarked by the authors of the systematic review, not all men in the control group with PSA recurrence did receive salvage radiotherapy and if so, relatively later at higher PSA levels than currently performed. A recent retrospective analysis suggested that compared to early adjuvant radiotherapy, early salvage radiotherapy may be similarly effective to control metastases-free survival at 8 years (2). The role of pelvic radiotherapy in the salvage setting remains undetermined and data from the RTOG05-34 trial on this topic are to be awaited.

Interestingly, several retrospective series have suggested a benefit of pelvic radiotherapy in men with proven nodal metastases after prostatectomy (3-6). The poor description of patient selection and method of radiotherapy used prohibits any conclusions on the use of radiotherapy in men with pN1 disease.

Still some recent clinical findings need to be considered. Although, as correctly noted by the authors, 68Ga-PSMA-PET may perform better at higher PSA values. A recent systematic review found positive 68Ga-PSMA PET scans in 42% of men with a PSA between 0–0.2 (7). This is well below the generally assumed optimal threshold of 0.5 for a favorable outcome of salvage radiotherapy (8). However, a positive 68Ga-PSMA-PET scan will almost certainly alter the decision to perform salvage radiotherapy to the prostatic fossa. Considering the toxicity of any additional local treatment after prostatectomy (increased risk of urinary, sexual, and bowel problems) (9); up to 58% 3-year incontinence after SRT (10), and the paucity of data on an overall survival benefit, a 68Ga-PSMA-PET scan should be strongly considered in all men with a rising PSA after prostatectomy. This is supported by the recent retrospective observation that despite local salvage radiotherapy 43% of men with Gleason 9–10 cancers develop metastases and 54% of men have biochemical recurrence overall (11).

The decision on additional radiotherapy after prostatectomy should be a well balanced one weighing a possible survival benefit versus earlier toxicity, in particular when an early use of radiotherapy is considered. In the near

future 68Ga-PSMA-PET scanning will have to prove itself as a good road sign how to continue.

Acknowledgements

None.

Footnote

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

References

1. Gandaglia G, Briganti A, Clarke N, et al. Adjuvant and Salvage Radiotherapy after Radical Prostatectomy in Prostate Cancer Patients. Eur Urol 2017. [Epub ahead of print].
2. Fossati N, Karnes RJ, Boorjian SA, et al. Long-term Impact of Adjuvant Versus Early Salvage Radiation Therapy in pT3N0 Prostate Cancer Patients Treated with Radical Prostatectomy: Results from a Multi-institutional Series. Eur Urol 2016. pii: S0302-2838(16)30433-X.
3. Abdollah F, Suardi N, Cozzarini C, et al. Selecting the optimal candidate for adjuvant radiotherapy after radical prostatectomy for prostate cancer: a long-term survival analysis. Eur Urol 2013;63:998-1008.
4. Nini A, Gandaglia G, Fossati N, et al. Patterns of Clinical Recurrence of Node-positive Prostate Cancer and Impact on Long-term Survival. Eur Urol 2015;68:777-84.
5. Tilki D, Preisser F, Tennstedt P, et al. Adjuvant radiation therapy is associated with better oncological outcome compared with salvage radiation therapy in patients with pN1 prostate cancer treated with radical prostatectomy. BJU Int 2017;119:717-23.
6. Rusthoven CG, Jones BL, Flaig TW, et al. Improved Survival With Prostate Radiation in Addition to Androgen Deprivation Therapy for Men With Newly Diagnosed Metastatic Prostate Cancer. J Clin Oncol 2016;34:2835-42.
7. Perera M, Papa N, Christidis D, et al. Sensitivity, Specificity, and Predictors of Positive ⁶⁸Ga-Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer: A Systematic Review and Meta-analysis. Eur Urol 2016;70:926-37.
8. Cornford P, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part II: Treatment of Relapsing, Metastatic, and Castration-Resistant Prostate Cancer. Eur Urol 2017;71:630-42.
9. van Stam MA, Aaronson NK, Pos FJ, et al. The Effect of Salvage Radiotherapy and its Timing on the Health-related Quality of Life of Prostate Cancer Patients. Eur Urol 2016;70:751-7.
10. Zaffuto E, Gandaglia G, Fossati N, et al. Early Postoperative Radiotherapy is Associated with Worse Functional Outcomes in Patients with Prostate Cancer. J Urol 2017;197:669-75.
11. Stish BJ, Pisansky TM, Harmsen WS, et al. Improved Metastasis-Free and Survival Outcomes With Early Salvage Radiotherapy in Men With Detectable Prostate-Specific Antigen After Prostatectomy for Prostate Cancer. J Clin Oncol 2016. [Epub ahead of print].

Cite this article as: van der Poel H, van Stam MA. Early or delayed radiotherapy after prostatectomy—who really benefits? Transl Androl Urol 2017;6(3):593-594. doi: 10.21037/tau.2017.03.68

