

Editorial: Sequelae of Prostate Cancer Therapy: Avoidance Strategies and Management Options

Clemens M. Rosenbaum^{1*†}, Felix Campos-Juanatey^{2†} and Luis A. Kluth^{3†} for the Trauma Reconstructive Urology Working Party of the European Association of Urology Young Academic

¹ Department of Urology, Asklepios Hospital Barmbek, Hamburg, Germany, ² Department of Urology, Marqués de Valdecilla University Hospital, Santander, Spain, ³ Department of Urology, University Hospital Frankfurt, Goethe University Frankfurt, Frankfurt, Germany

Keywords: urinary incontinence, prostate neoplasia, erectile dysfunction, urethral stricture, radiation, prostatectomy, focal therapy

Editorial on the Research Topic

Sequelae of Prostate Cancer Therapy: Avoidance Strategies and Management Options

OPEN ACCESS

Edited and reviewed by:

Cozzarini Cesare, San Raffaele Hospital (IRCCS), Italy

*Correspondence:

Clemens M. Rosenbaum c.rosenbaum@asklepios.com

[†]Member of the Trauma and Reconstructive Urology Working Party of the European Association of Urology (EAU) Young Academic Urologists (YAU)

Specialty section:

This article was submitted to Genitourinary Surgery, a section of the journal Frontiers in Surgery

Received: 06 January 2022 Accepted: 07 February 2022 Published: 06 April 2022

Citation:

Rosenbaum CM, Campos-Juanatey F and Kluth LA (2022) Editorial: Sequelae of Prostate Cancer Therapy: Avoidance Strategies and Management Options. Front. Surg. 9:849669. doi: 10.3389/fsurg.2022.849669 Prostate cancer is the most common malignancy among men in the Western world (1). More than 80% of patients with clinically localized prostate cancer will undergo definite treatment (2). Most common treatment options are radical prostatectomy and radiotherapy, focal therapies such as high-intensity focused ultrasound (HIFU) or cryoablation being increasingly used. All of them come along with different patterns of early and late side effects (3). Given excellent survival rates at 10 years (4), urologists have to face a relevant number of patients who present with one of these prostate cancer treatment related sequelae.

The goal of our Research Topic "Sequelae of Prostate Cancer Therapy: Avoidance Strategies and Management Options" was therefore to provide readers, researchers and physicians a comprehensive overview of strategies to prevent consequences of prostate cancer therapies and future perspectives of management of sequelae of prostate cancer treatments.

One of the most common side effects of prostate cancer treatment is urinary incontinence (5). Prostatectomy has worse effects on urinary incontinence compared to radiation therapy (5). Rahnama'i et al. illustrate the current knowledge of how to avoid urinary incontinence during radical prostatectomy. Besides surgical factors, patient characteristics as higher body mass index, older age, pre-existing lower urinary tract symptoms, neurological disease and functional bladder changes, have been identified to negatively impact continence (6). Lately, sarcopenia, defined as low skeletal muscle volume, has been increasingly recognized as a potential risk factor for worse outcome in oncologic patients. However, Angerer et al. were able to show that it has no influence on post-prostatectomy continence rates. As treatment of post-prostatectomy caused urinary incontinence, the artificial urinary sphincter has been considered the gold standard for several decades. Rahnama'i et al. demonstrated in their review several alternative surgical procedures that challenge the artificial urinary sphincter (6).

Another common consequence of prostate cancer treatment is erectile dysfunction (5). Sparing neurovascular bundles during surgery is the most important factor to maintain erectile function. Besides nerve-sparing surgery, methods for penile rehabilitation after radical prostatectomy and radiation therapy are focus of current research. Nicolai et al. give an overview about pathophysiology and treatment of erectile dysfunction following

radical prostatectomy. In addition, Schoentgen et al. are able to show in their systematic review, that sexual rehabilitation prior to radical prostatectomy may result in better erectile recovery.

For both urinary incontinence and erectile dysfunction, tissue engineering could help to overcome the current borders of treatment. Autologous stem cell transplantation is one of the most promising approaches. Adamowicz et al. describe a tissue engineering approach, mode of vascular and neuro-regeneration and stem cell safety. They are able to illustrate the unquestionable potential of tissue engineering to improve outcome of prostate cancer treatment related sequelae (Adamowicz et al.).

Furthermore, bladder outlet obstruction is a common problem not only after radical prostatectomy but also after radiation therapy.

The review "Contemporary Management of Vesico-Urethral Anastomotic Stenosis After Radical Prostatectomy" gives an overview about pathophysiology and treatment of vesicourethral anastomotic stenosis. The authors demonstrate endourological procedures should still remain as an initial treatment. However, in refractory stenoses, open or robotic reconstruction is a viable option with high success rates (Rosenbaum et al.). In contrast to vesicourethral anastomotic stenosis after radical prostatectomy, radiation induced membranous urethral strictures may occur years after therapy. Waterloos et al. illustrate that management of radiation induced urethral strictures can be challenging. Poor vascularized tissue and the proximity of the sphincter can impair functional outcomes (Waterloos et al.).

Devasted bladder outlet or radiogenic chronic cystitis are rare complications after prostate cancer treatments, but can have a huge impact on quality of life. Hoeh et al. provide an overview about treatment options in these patients, in which urinary diversion may also be discussed as a definite treatment.

Most of the aforementioned problems result of surgery or radiation. Focal therapy aims to selectively treat the part of the prostate that harbors significant prostate cancer while preserving the rest of the gland. Aim of this therapeutic approach is to retain the oncological benefit of active treatment while minimizing side-effects. Most common complications of focal therapy are urinary tract infections, acute urinary retention, dysuria and haematuria, however, urinary incontinence is rare. In the salvage setting, after external beam radiation therapy, focal therapy has a significantly higher rate of severe complications. Rakauskas et al. give a comprehensive overview.

Finally, all type of treatment inherit the risk of recurrence. After radical prostatectomy, the role and timing of radiation therapy remains highly controversial (7-9). Zattoni et al. give a comprehensive overview about the currently ongoing discussion. Still, about 40% of patients develop biochemical recurrence within 10 years after primary therapy (10). Limited sensitivity and specificity of conventional imaging methods, such as computed tomography and magnetic resonance imaging has led to efforts in developing better modalities. Lately PSMA-PET/CT has been introduced as such. Initially promising results have been confirmed. Leitsmann et al. are able to demonstrate that mesorectal lymph node metastases detected by PSMA-PET/CT seem to be a relevant localization of tumor recurrence after active therapy. They may serve as index lesion in the treatment of recurrent prostate cancer.

Prostate Cancer remains one of the major parts of Urology. Primary treatment of prostate cancer and management of recurrences is one side of the coin, while the other side is dealing treatment of sequalae of initial or recurrent treatment.

AUTHOR CONTRIBUTIONS

CR, FC-J, and LK: manuscript writing. All authors contributed to the article and approved the submitted version.

REFERENCES

- 1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. (2020) 70:7–30. doi: 10.3322/caac.21590
- Gray PJ, Lin CC, Cooperberg MR, Jemal A, Efstathiou JA. Temporal trends and the impact of race, insurance, and socioeconomic status in the management of localized prostate cancer. *Eur Urol.* (2017) 71:729–37. doi: 10.1016/j.eururo.2016. 08.047
- Nam RK, Cheung P, Herschorn S, Saskin R, Su J, Klotz LH, et al. Incidence of complications other than urinary incontinence or erectile dysfunction after radical prostatectomy or radiotherapy for prostate cancer: a population-based cohort study. *Lancet Oncol.* (2014) 15:223–31. doi: 10.1016/S1470-2045(13) 70606-5
- Hamdy FC, Donovan JL, Lane JA, Mason M, Metcalfe C, Holding P, et al. 10-Year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. N Engl J Med. (2016) 375:1415–24. doi: 10.1056/NEJMoa16 06220

- Donovan JL, Hamdy FC, Lane JA, Mason M, Metcalfe C, Walsh E, et al. Patient-reported outcomes after monitoring, surgery, or radiotherapy for prostate cancer. *N Engl J Med.* (2016) 375:1425–37. doi: 10.1056/NEJMoa16 06221
- Heesakkers J, Farag F, Bauer RM, Sandhu J, De Ridder D, Stenzl A. Pathophysiology and contributing factors in postprostatectomy incontinence: a review. *Eur Urol.* (2017) 71:936–44. doi: 10.1016/j.eururo.2016. 09.031
- Tilki D, Chen MH, Wu J, Huland H, Graefen M, Wiegel T, et al. Adjuvant versus early salvage radiation therapy for men at high risk for recurrence following radical prostatectomy for prostate cancer and the risk of death. *J Clin Oncol.* (2021) 39:2284–93. doi: 10.1200/JCO.20. 03714
- Parker CC, Clarke NW, Cook AD, Kynaston HG, Petersen PM, Catton C, et al. Timing of radiotherapy after radical prostatectomy (RADICALS-RT): a randomised, controlled phase 3 trial. *Lancet.* (2020) 396:1413–21. doi: 10.1016/S0140-6736(20)31 553-1

- Vale CL, Fisher D, Kneebone A, Parker C, Pearse M, Richaud P, et al. Adjuvant or early salvage radiotherapy for the treatment of localised and locally advanced prostate cancer: a prospectively planned systematic review and meta-analysis of aggregate data. *Lancet.* (2020) 396:1422– 31. doi: 10.1016/S0140-6736(20)31952-8
- Roehl KA, Han M, Ramos CG, Antenor JA, Catalona WJ. Cancer progression and survival rates following anatomical radical retropubic prostatectomy in 3,478 consecutive patients: long-term results. J Urol. (2004) 172:910– 4. doi: 10.1097/01.ju.0000134888.22332.bb

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2022 Rosenbaum, Campos-Juanatey and Kluth. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.