ELSEVIER

Brachytherapy ■ (2017) ■

BRACHYTHERAPY

Long-term evaluation of urinary, sexual, and quality of life outcomes after brachytherapy for penile carcinoma

Dimitri Gambachidze[1,*], Cédric Lebacle[1], Pierre Maroun[1], Alexandre Escande[1], Alberto Bossi[1], Pierre Blanchard[1], Eric Deutsch[1,2,3], Christine Haie-Meder[1], Cyrus Chargari[1,2,3,4,5]

[1]*Radiotherapy Department, Gustave Roussy Cancer Campus, Villejuif, France*
[2]*INSERM, U1030, Villejuif, France*
[3]*Université Paris Sud, Université Paris-Saclay, Le Kremlin-Bicêtre, France*
[4]*Institut de Recherche Biomédicale des Armées, Brétigny sur Orge, France*
[5]*French Military Health Service Academy, Ecole du Val-de-Grace, Paris, France*

ABSTRACT

PURPOSE: Brachytherapy (BT) is an effective organ-preserving treatment for selected localized penile carcinoma, providing high local control rates. Long-term functional results however, are still insufficiently evaluated.

METHODS AND MATERIALS: All consecutive patients treated with low-dose-rate or pulse-dose-rate BT in our institute for a localized penile cancer and who were in first complete remission and followed for at least 3 years were included. A self-reporting questionnaire was sent, to assess: 1/urinary function, 2/sexual function, 3/cosmetic aspect of the penis, and 4/quality of life.

RESULTS: Thirty-nine patients fulfilled inclusion criteria and were sent the questionnaire. Twenty-three patients (59%) answered. Median age was 63.4 years, (interquartile range [IR]: 49.7−67.0). Median followup was 5.9 years (IR: 5.2−6.7). The urinary scores showed moderate lower urinary tract symptoms. During the followup, a urethral dilation or self-catheterization had been necessary in 30% and 13%, respectively. Sixteen (70%) patients continued to maintain a sexual activity and the erectile dysfunction was mild. Finally, quality of life was good with a median score of 80/100 (IR = 65−90) and was only impacted by pain ($p = 0.02$). Overall, 57% and 39% declared having none or moderate pain/discomfort, respectively.

CONCLUSIONS: Although this questionnaire needs to be validated in an independent cohort, our results show the moderate impact of BT on functional outcomes, confirming that it is an adequate first-intent organ-sparing strategy in patients with localized penile carcinoma.

Keywords: Brachytherapy; Functional assessment; Penile carcinoma; Quality of life; Toxicity

Introduction

Penile carcinoma is a very rare disease, with an overall incidence of less than 0.1% males in Western countries (1). Most frequently, histological type is squamous cell carcinoma, accounting for more than 95% of penile carcinoma. Some risks factors are well identified such as human papillomavirus infection, tobacco, low socioeconomic status, multiple sexual partners, phimosis, and chronic penile inflammation (2).

In more than 60% of the cases, the disease is diagnosed at an early stage (T1-T2 lesions and <4 cm) (3) and for these tumors, guidelines recommend an organ-preserving strategy to conserve functional, cosmetic, and quality of life (QoL) outcomes (4). Brachytherapy (BT) can be proposed for lesions confined to the penile glans (without extension to corpus cavernosum). This strategy provides high local control rates with mild to moderate toxicity (5). Long-term functional outcomes after BT for penile cancer, however, are still insufficiently evaluated. A few studies have examined the impact of BT on sexual function or the

Received 24 July 2017; received in revised form 20 September 2017; accepted 21 September 2017.

Conflict of interest: The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

Financial disclosure: The authors declared no financial disclosures.

* Corresponding author. Brachytherapy Unit, Radiotherapy Department, Gustave Roussy Cancer Campus, 114 rue Edouard Vaillant, 94800, Villejuif, France. Tel.: +33-1-42-11-45-66.

E-mail address: dimitri.gambachidze@gmail.com (D. Gambachidze).

1538-4721/$ - see front matter
https://doi.org/10.1016/j.brachy.2017.09.006

incidence of severe local toxicities, such as painful ulcerations or urethral stenoses (6, 7). No study, however, has specifically assessed urinary function, sexual function, and QoL in these patients.

In this retrospective single center study, we evaluated the results of BT with a long-term followup in terms of urinary, sexual, and QoL outcomes through a self-reported questionnaire of 23 questions.

Patients and methods

Patients

A self-reported questionnaire was sent to eligible patients with Institutional Review Board approval. They were identified from a retrospective database of patients treated between 1991 and 2015 with low-dose-rate (LDR) or pulse-dose-rate (PDR) BT in our institute for a localized penile cancer confined to penile glans. These patients had been treated for an invasive tumor of the penile glans (± presence of *in situ* disease), stage T1-T2 according to the American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) seventh edition TNM classification, without extension to the corpus cavernosum. The eligibility criteria were: consecutive patients in complete remission after treatment, at least 3-year follow-up, and native French speaker to be able to answer the self-assessment questionnaire. Exclusion criteria were age >80, metastases at diagnosis, and penile surgery other than circumcision.

Treatment and BT technique

Treatment characteristics have been previously described in detail: (7, 8). Circumcision was systematically performed 3−4 weeks before BT to limit side effects of irradiation and to facilitate implantation.

Briefly, the BT implantation was performed under general anesthesia. A Foley catheter was inserted to well determine the position of urethra and therefore to avoid it at the time of implantation. The target volume encompassed the gross tumor volume plus a safety margin of 5−10 mm. Interstitial needles were implanted through the glans, perpendicular to the axis of the penis, following Paris System rules. The implant was maintained with an applicator, made of two square plates of Plexiglas, with perforated equidistant holes allowing a perfect parallelism between needles or plastic tubes. Finally, the system was secured in prepubic position, with a sponge that maintained it away from testes.

After digitization of the implant in the treatment planning system, the dose was prescribed to the reference isodose (85% of the basal isodose according to Paris system rules). BT was delivered using iridium-192 wires (for continuous LDR irradiation) or using a PDR remote afterloader (delivering continuous hourly pulses of 0.42 Gy *per* pulse), keeping the dose below 10 Gy *per* day for both dose rates. No dose constraint was used for the urethra.

Description of assessment method and questionnaire

After a close discussion with urologic surgeons, we convened to assess three fields that could be directly impacted by BT toxicity: urinary function, sexual function, and quality of life. A self-reported questionnaire of 23 questions was sent to patients by mail (Appendix A).

The urinary function was evaluated through eight summative questions derived from the International Continence Society male Short Form questionnaire (9) and generating a LUTS (lower urinary tract symptoms) score between 0 (asymptomatic) and 32 (most symptomatic). Questions (Q) one to five evaluated the voiding function, Q 6−7 evaluated the incontinence score, and Q8 evaluated the impact of LUTS on QoL. In addition, a Peeling's voiding picture Q9 (10) was inserted and past and/or present self-catheterization and/or urethral dilatation were searched.

Two aspects of sexual function were assessed: First, the erectile dysfunction (ED) was evaluated with the International Index of Erectile Function questionnaire (IIEF-5) (11) generating a score between 6 and 30 and five levels of ED (6−10: severe; 11−16: moderate; 17−21: mild to moderate; 22−25: mild; 26−30: normal). Second, the male genitalia image was evaluated with five summative questions derived from the Index of Male Genitalia Image (IMGI) (12) assessing penile size and appearance factors, with a score ranging from 5 (extremely dissatisfied) to 35 (extremely satisfied).

Finally, overall QoL was evaluated through two questions derived from EuroQol 5-dimension three-level questionnaire, one exploring the pain/discomfort dimension and the other one using a visual analogue scale between 0 (worst imaginable health state) to 100 (best imaginable health state) (13).

Statistical analysis

Data are presented as mean ± standard deviation or frequency and percentage for continuous and categorical variables. Statistical analyses were performed using IBM SPPS Statistics v.20.0.0 (IBM Corp. Armonk, NY). Categorical variables were compared using χ^2 and Wilcoxon-Mann-Whitney test. For continuous variables, Kruskall-Wallis and Student test were used. Physical doses were converted into biological effective doses normalized to a radiobiologically weighted dose equivalent of 2 Gy/fraction (EQD2, $\alpha/\beta = 10$ Gy for tumor and 3 Gy for late reactions, half-time of repair of 1.5 h for both). Given the small volumes of urethra making any dose calculation uncertain, no dose volume parameter for urethra was examined.