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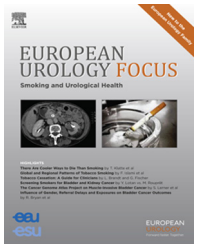

Review – Prostate Cancer

Exploring All Avenues for Radiotherapy in Oligorecurrent Prostate Cancer Disease Limited to Lymph Nodes: A Systematic Review of the Role of Stereotactic Body Radiotherapy

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Abstract

Context: Stereotactic body radiotherapy (SBRT) is emerging as a treatment option in patients affected by oligorecurrent prostate cancer disease limited to lymph nodes, a subgroup of patients who would otherwise be treated only with androgen deprivation therapy (ADT).
Objective: To perform a systematic review of SBRT for oligorecurrent prostate cancer limited to lymph nodes.
Evidence acquisition: We performed a systematic review of PubMed/Medline in October 2016 according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA). We searched for studies reporting on biochemical or clinical progression and/or toxicity or complications of SBRT. Reports were excluded if these end points could not be ascertained or separately analyzed, or if insufficient details were provided.
Evidence of synthesis: A total of 363 patients from nine studies were collected. Of these patients, 211 were treated with SBRT for a total of 270 lymph nodes. With an alpha–beta ratio of 3 Gy, the biologically effective dose in fractionated SBRT was >100 Gy in all studies (range, 88–216 Gy). With a median follow-up of 19.23 mo, local control was achieved in 98.1% of patients. Median progression-free survival (defined as biochemical and/or radiological progression) was 22.5 mo (range, 11–30 mo). Information about ADT during SBRT was available in 281 patients, of whom 114 (40.5%) were on ADT during SBRT, and the duration of hormone therapy ranged from 1 to 17.5 mo. Median ADT-free survival was 32.8 mo (range, 25–44 mo). About toxicity, Common Terminology Criteria for Adverse Events toxicity scale was most used. Acute and/or late grade ≥2 toxicity was reported in only 5.6% of patients, and no patient developed grade 4 toxicity.
Conclusions: SBRT seems to be promising in lymph node oligorecurrent prostate cancer, although there is a weak level of evidence to support such investigational treatment, which is currently based on retrospective studies of single-institution or pooled experiences. ADT-free survival is an interesting end point, which needs to be investigated.
Patient summary: We performed a systematic review to assess outcomes and toxicity of stereotactic body radiotherapy (SBRT) for patients affected by oligorecurrent prostate cancer limited to lymph nodes. We concluded that SBRT is a promising therapy in this setting, but it needs to be validated in randomized controlled trials.

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1. Introduction

Stereotactic body radiotherapy (SBRT) is emerging as an appropriate treatment option in patients affected by limited metastatic disease, defined as "oligometastatic state," which is considered as an intermediate state between localized and widespread cancer, and seems to be characterized by a unique biological profile [1]. In such patients with a limited number of metastases (<3 or <5) from a variety of primary sites, it seems that local therapy (surgery or ablative radiotherapy) might improve overall survival and disease progression-free survival (PFS), and delay the need for systemic therapy [2–6]. In this therapeutic scenario, SBRT seems to be a safe treatment option with a very low toxicity profile, and without the morbidity and risk associated with surgical procedures [7].

In oligorecurrent prostate cancer patients, who eventually develop a low burden of disease after curative treatment, SBRT could mean an appropriate therapeutic strategy with curative intent. SBRT could also defer palliative androgen deprivation therapy (ADT), which is currently the standard of care for such patients, despite the fact that it can have a detrimental effect on their quality of life. The subset of prostate cancer patients with oligorecurrence confined to lymph nodes represents a very early metastatic setting in which local treatment such as SBRT might have a great impact on disease control [8–10].

The aim of our study was to review the available literature on SBRT for lymph node recurrent prostate cancer patients, in order to evaluate efficacy and toxicity of this high-precision noninvasive ablative treatment in such an early metastatic setting. In the Discussion section, we also provide an analysis of the major studies investigating the role of prophylactic irradiation of regional lymph nodes in the same setting of patients.

2. Evidence acquisition

We searched for articles reporting on oncological outcome (biochemical response and/or PFS) and toxicity of prostate cancer patients, affected by oligorecurrent disease limited to lymph nodes and treated with SBRT. SBRT was defined as a radiotherapy dose of at least 5 Gy per fraction to a biologically effective dose of 80 Gy with an alpha–beta ratio of 3 Gy. A PubMed literature search was conducted using the Preferred Reporting Items and Meta-Analyses (PRISMA) [11]. We identified articles published within the last 10 yr up to September 30, 2016, using Medline search with the following selection criteria: English language, full papers, oligorecurrent prostate cancer limited to lymph nodes treated with SBRT, and oncological and toxicity data available. The following Medline terms were used: prostate cancer, lymph node metastasis, lymph node recurrence, oligometastatic prostate cancer, oligorecurrent prostate cancer, stereotactic radiotherapy, stereotactic body radiotherapy, radiosurgery, and stereotactic ablative radiotherapy. If multiple publications from the same center were available, the most recent one was selected. We reviewed the full version of each article. The following information was abstracted from all primary reports: primary author, reference, year of publication, number of patients, patient population, age, number of patients treated with SBRT for node metastasis, number of irradiated metastases, study design, treatment of the primary prostate cancer, dose and fractionation of SBRT, oncological outcome (PFS and overall survival), local control, prognostic factors (univariate and multivariate), and toxicity.

3. Evidence synthesis

The flowchart of the systematic review is reported in Fig. 1. In total, 363 patients from nine studies [12–20] were collected (Table 1). Of these patients, 211 were treated with SBRT for a total of 270 lymph nodes (Table 2). In Table 3, we reported the site (pelvic or extrapelvic) of nodes irradiated with SBRT: 162 (76.7%) patients were affected by pelvic oligorecurrence. Information about the primary treatment was available in 334 (92%) patients: 250 (75%) underwent radical prostatectomy ± radiotherapy ± ADT, 78 (23.3%) underwent radiotherapy ± ADT, and six (1.7%) received chemotherapy as primary treatment.

Median time from primary treatment to oligorecurrent disease was available only in seven studies (Table 1), with an overall median value of 37.45 mo (range, 11.5–75.6 mo). Choline-positron emission tomography (PET)/computed tomography (CT) was used in almost all studies to detect disease in patients with biochemical recurrence after primary treatment. The median prostate-specific antigen (PSA) value at oligorecurrent disease, available in six studies, was 4.2 ng/ml (range, 1.77–16 ng/ml). Median follow up was 21.9 mo (range, 4.4–36 mo).

SBRT was delivered with a linear accelerator in almost all studies (Table 2). Several radiotherapy schedules were used, varying from 5 to 11 Gy per fraction, to a total dose of 25–50 Gy, whereas four metastatic nodes were irradiated using a single fraction (range, 12–24 Gy). With an alpha–beta ratio of 3 Gy, the biologically effective dose in fractionated SBRT was >100 Gy in all studies (range, 88–216 Gy). The median gross tumor volume–planning target volume margin was 5 mm. In all studies, image guidance was used prior to radiotherapy delivery.

Between studies, biochemical recurrence after SBRT was defined in different ways: some authors considered it as a

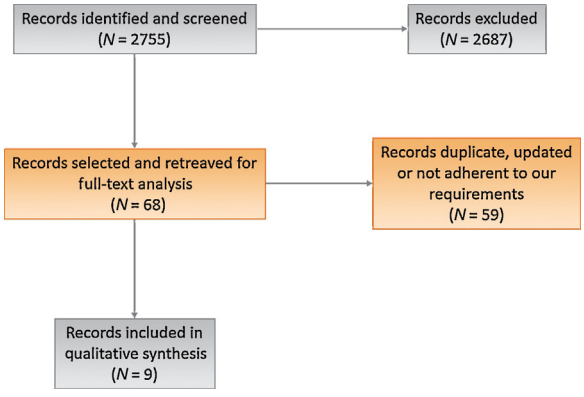

Fig. 1 – Flowchart of the systematic review.

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