Clinical and Translational Radiation Oncology 5 (2017) 20–27

Contents lists available at ScienceDirect

Clinical and Translational Radiation Oncology

journal homepage: www.elsevier.com/locate/ctro

Original Research Article

Survival and failure types after radiation therapy of vulvar cancer

Christina Steen Vorbeck *, Ivan Richter Vogelius, Marie Louise Vorndran Cøln Banner-Voigt, Hanne From Mathiesen, Mansoor Raza Mirza

Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Denmark

ARTICLE INFO

Article history:
Received 2 February 2017
Revised 2 June 2017
Accepted 5 June 2017

Keywords:
Vulvar cancer
Chemoradiation
Radiation
Failure types
Elderly

ABSTRACT

Background and purpose: Describe the survival rates and distribution of events on competing failure types in vulvar carcinoma after treatment with chemoradiation (CRT) or radiation (RT) alone.
Material and methods: We included patients with vulvar carcinoma treated with CRT or RT between 2009 and 2014. Survival was estimated using the Kaplan-Meier method. We performed a competing risk analysis and included five competing events: loco-regional failure (LRF), distant metastasis, LRF plus distant metastasis, and death without evidence of disease, with the remaining patients denoted alive without evidence of disease.
Results: 87 patients were treated. Progression free survival (PFS) and overall survival (OS) at 3 years were 40% and 57%, respectively. 41.3% of patients relapsed, most often loco-regionally. We saw significantly worse PFS and OS for patients older than 68 ($p = 0.011$/$p = 0.010$) and for patients treated with definitive RT ($p = 0.004$/$p = 0.005$). Competing risk analysis showed increased risk of LRF, and that death was most often related to vulvar cancer. Death without disease recurrence was less frequent, even in the elderly.
Conclusions: LRF was the most common event. PFS and OS were inferior for elderly patients and patients treated definitively. A better understanding of these differences may be used to define risk adapted treatment strategies.
© 2017 The Authors. Published by Elsevier Ireland Ltd on behalf of European Society for Radiotherapy and Oncology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Vulvar cancer is a rare gynecological malignancy, annually affecting 2–3 per 100,000 women worldwide [1]. In Denmark, the incidence is 80–100 per year, accounting for approximately 0.5% of all cancers in women [2]. The majority of vulvar cancers are squamous cell carcinomas (SCC) (76%) [3]. Vulvar cancer mainly affects elderly women with a median age of 65–70 years. During the past decades, the incidence of vulvar cancer has been increasing, with a trend of younger women under the age of 60 being affected.

Due to the lack of randomized trials and to the low incidence of vulvar cancer, many questions regarding treatment remain unanswered. Surgery is still the main treatment modality for vulvar cancer, but radiation (RT) also has an important role in management. RT is typically delivered either as an adjuvant to surgery or as a definite modality typically in conjunction with chemotherapy. The optimal radiation dose prescription strategy is disputed, and many treatment decisions are guided from clinical trials of cervical- and anal cancer in the absence of sufficient vulvar cancer research [4,5].

The risk of recurrence is correlated to tumor size, lymph node involvement, and vascular invasion [3,6], and, unfortunately, recurrence inside the radiation field is not uncommon. Due to the rarity of this disease, knowledge of the pattern of loco-regional failure after RT is limited.

We describe the fate of vulvar carcinoma patients after treatment with chemoradiation (CRT) or RT in a large single institution series. In particular we investigated the competing risks of death from other causes, local and distant failure.

Materials and methods

At the Department of Oncology, Rigshospitalet, Copenhagen University Hospital, Denmark, we searched the patient registry for referrals with ICD-10 diagnostic codes DC51-529. We excluded patients with cancer of the clitoris and patients with vaginal cancer and retrospectively reviewed the medical records of the remaining patients with vulvar cancer. Patient data including medical history, patient characteristics, tumor type, histopathological information,

* Corresponding author at: Department of Oncology, 3994, Rigshospitalet, Copenhagen University Hospital, Blegdamsvej 9, 2100 Copenhagen, Denmark.
E-mail address: christina.steen.vorbeck@regionh.dk (C.S. Vorbeck).

http://dx.doi.org/10.1016/j.ctro.2017.06.002
2405-6308/© 2017 The Authors. Published by Elsevier Ireland Ltd on behalf of European Society for Radiotherapy and Oncology.
This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

patient scans, treatment, follow-up, response, recurrence status, recurrence location, disease and survival status were obtained from hospital records and registered.

For the primary staging procedure, patients were assessed by both gynecologists and clinical oncologists at diagnosis and later assessed by the multidisciplinary team of gynecologists, radiologists, pathologists and clinical oncologists in order to determine the best treatment option for the individual patient. All patients had CT, FDG PET-CT or MRI scans performed for diagnostic purposes. Patients were staged according to the system of the International Federation of Gynecology and Obstetrics (FIGO). The primary treatment was surgery if possible. Patients who underwent surgery with positive margins or positive lymph nodes were referred to adjuvant RT and thus included in this series, as were patients with medically inoperable tumors referred for definitive RT.

RT was planned and delivered as follows: FDG PET-CT was used for treatment planning unless contraindicated. The FDG PET-CT was merged into the treatment planning system. Target volumes were delineated following department guidelines: Nuclear Medicine Physicians delineated FDG-PET avid volumes (GTV-PET), radiologists with oncologists delineated gross tumor volumes (GTV) and oncologists delineated the clinical target volumes (CTV). Planning target volumes (PTV) were produced by adding a margin of 7 mm to CTV. In patients with no macroscopic disease, only CTV was delineated. The whole vulva was always included in the CTV, if vulva had to be irradiated. If there was metastatic disease in the nodes, the next nodal region was included in the CTV e.g. if patients had metastatic disease in the superficial inguinal lymph nodes, the deep inguinofemoral lymph nodes and lower half of the external iliac lymph nodes were included in the CTV. Furthermore, the nodal CTV included gross tumor of nodes with a 1 cm margin. See Table 1 for average volumes and dose coverage of the delineated regions. Adjuvant or definitive RT was delivered as external-beam RT to the vulva and/or inguinal nodal regions. Patients were treated with either IMRT or Volumetric Modulated Arc Therapy (VMAT). Prescribed dose was 60–64 Gy (2 Gy per fraction) to the GTV for patients with macroscopic disease at the time of treatment, with 50 Gy to regions without macroscopic involvement, delivered as simultaneous integrated boost. For patients without macroscopic disease, the prescribed dose was 46–50.5 Gy (usually 1.8–2 Gy per fraction according to guidelines, but two patients received 1.6 Gy/fraction). For patients deemed fit for chemotherapy, concomitant cisplatin was administered weekly 40 mg/mm^2 with an upper limit to the total cisplatin dose of 70 mg. Neoadjuvant or adjuvant chemotherapy is not a standard of care according to department guidelines.

First follow-up visit after end of RT was at 12 weeks. Subsequent follow-up visits were with 3–4 months interval for 5 years. If a patient at the time of RT planning had macroscopic disease in the nodal area, first follow-up at 12 weeks included an FDG PET-CT scan. If patients relapsed after RT, the multidisciplinary team assessed them once again, in order to determine management of the disease including possible post-radiation surgical resection and/or chemotherapy. Patients with post-radiation treatment failure were offered surgical resection if possible. If the recurrence was unresectable or the patients had disseminated disease, they were offered palliative chemotherapy and/or RT. Patients not eligible for resection and CRT were referred to palliative care units.

The endpoints in our study were progression free survival (PFS), overall survival (OS), time to local recurrence, distant recurrence or simultaneous local and distant recurrence.

PFS was defined as the interval from the date of RT start to the date of recurrence of the disease, death from any cause or last follow-up (LFU) whichever came first. OS was defined as the interval from the date of RT start to the date of death due to any cause. We used a cut off in January 2015 for the OS analysis of the whole series. Survival after a recurrence following RT or CRT was analyzed separately with a cut off in May 2015. Relapse date was defined as the date of documentation of conclusive relapse i.e. relapse determined unequivocally by either pathologist, clinical oncologist or radiologist. For patients with recurrences, OS was defined as the interval from the date of relapse to the date of death due to any cause.

The data were analyzed using IBM SPSS statistics version 22. Survival rates were calculated using the Kaplan-Meier method. Comparisons were made using the log-rank test and a 2-sided p-value of 0.05 was considered significant. Additionally we performed Cox proportional hazards modeling of the impact of age on a continuous scale. Cox regression was used to perform the univariate and multivariate analysis, stratifying for adjuvant versus definitive therapy. Age, tumor stage, use of cisplatin and primary vs. recurrent disease were entered as prioritized covariables. We performed competing risk analysis using the statistical software R version 3.1.2 and the CMPRSK package [7]. We included the following five competing events in our analysis: loco-regional recurrence, distant metastasis, loco-regional recurrence plus distant metastasis, and death without evidence of disease, with the remaining patients denoted alive with no evidence of disease.

The study was approved by The Danish Data Protection Agency (approval No. 30-1322) and The Danish Health and Medicines Authority (approval No. 3-3013-893/1).

Results

Our search produced 160 patients with the previously mentioned ICD-10 codes treated at the Department of Oncology, Rigshospitalet between January 2009 and October 2014. 124 patients had confirmed vulvar cancer. In total, 37 patients were excluded – see

Table 1
Planning target volumes definitions, median target volumes and dose.

Volumes	Definition	Dose	Adjuvant RT (median target volume, cm^3 (range))[1]	Definitive RT (median target volume, cm^3 (range))[1]
GTV-PET	FDG-PET avid volumes	64 Gy	3 (1–30)	17.5 (3–232)
GTV_{64}[2]	All GTV volumes prescribed 64 Gy	64 Gy	2 (1–342)[3]	105.5 (5–320)
PTV_{64}	All PTV volumes prescribed 64 Gy	64 Gy	62 (10–663)	488.5 (54–1036)
CTV_{50}	All CTV volumes prescribed 50 Gy	50 Gy	821 (71–3704)	1157 (242–2685)
Volumes	Definition	Dose	Adjuvant RT (median dose, Gy (range))[1]	Definitive RT (median dose, Gy (range))[1]
$D_{98\%}$ GTV_{64}[4]	Given dose to 98% of GTV_{64}	64 Gy	64.1 Gy (61.3–66.8)	62.9 Gy (62.3–65.4)
$D_{98\%}$ CTV_{50}	Given dose to 98% of CTV_{50}	50 Gy	48.8 Gy (43.1–53.4)	49.2 Gy (48.1–50.9)

One patient was excluded from the entire analysis. The patient was treated with electron fields that could not be reconstructed.
[1] Patients without the target volume/dose in question were excluded in the analyses for median target volumes/dose.
[2] One patient was excluded from the GTV_{64} volume analysis since the boost dose was only 60 Gy.
[3] GTV in the adjuvant setting may include the entire remaining vulva in case of positive surgical margins.
[4] For patients without GTVs, only CTVs are reported.

Download English Version:

https://daneshyari.com/en/article/8922485

Download Persian Version:

https://daneshyari.com/article/8922485

Daneshyari.com