



Original Research Article

PET/CT and MRI directed extended salvage radiotherapy in recurrent prostate cancer with lymph node metastases



Hans Christian Rischke^{a,b,*}, Ann-Kristin Eiberger^a, Natalja Volegova-Neher^a, Karl Henne^a, Tobias Krauss^d, Anca-L. Grosu^a, Cordula A. Jilg^c

^aDepartment of Radiation Oncology, Albert-Ludwigs University Hospital of Freiburg, Freiburg, Germany

^bDepartment of Nuclear Medicine, Albert-Ludwigs University Hospital of Freiburg, Freiburg, Germany

^cDepartment of Urology, Albert-Ludwigs University Hospital of Freiburg, Freiburg, Germany

^dDepartment of Radiology, Albert-Ludwigs University Hospital of Freiburg, Freiburg, Germany

ARTICLE INFO

Article history:

Received 14 October 2015

Accepted 22 January 2016

Available online 3 February 2016

Keywords:

Choline PET

PET/CT

MRI

Prostate cancer recurrence

Salvage radiation therapy

ABSTRACT

Purpose: PET/CT directed extended salvage radiotherapy (esRT) of involved lymph-node (LN) regions may be a salvage strategy for patients with nodal recurrent prostate cancer (PCa) after primary therapy or after previous prostate fossa salvage RT. The aim of the study was to determine the time until prostate-specific antigen (PSA) progression, pattern of failure and toxicity after esRT.

Material and methods: 25 patients with nodal or nodal + local recurrent PCa confirmed by Choline-PET/CT and Magnetic Resonance Imaging (MRI) were treated with esRT at the sites of recurrence. Acute and late toxicity was recorded. In case of subsequent PSA progression, imaging was performed to confirm next relapse. Mean follow-up was 2.9 years.

Results: According to Choline-PET/CT and MRI findings, 84% (21/25) of esRT were treatment of pelvic only, 12% (3/25) of retroperitoneal only and 4% (1/25) of both pelvic and retroperitoneal regions. 40% (10/25) received concomitant irradiation of the prostatic fossa (after primary radical prostatectomy). Median time to PSA progression of the whole cohort was 19.6 months. Median time to PSA progression for patients with 1–2 PET-positive LN ($n = 15$) was 34.9 months versus median 12.7 months for patients with PET-positive LN ≥ 3 ($n = 10$), p -value: 0.0476. Acute and late toxicity was mild to moderate, no grade-3 adverse events were observed.

Conclusion: PET/CT and MRI directed esRT of nodal recurrent PCa with or without local recurrence is feasible with low acute and late toxicity. Patients with only one or two PET-positive LN treated by esRT achieved prolonged complete biochemical remission.

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1. Introduction

Disease recurrence after primary treatment of Prostate Cancer (PCa) depends on initial tumour stages and occurs in 10–53% [1]. Different recurrence patterns exist: (i) evidence of only local recurrence in the prostate fossa; (ii) evidence of loco-regional metastases in pelvic LN; (iii) distant metastases (nodal, soft tissue, osseous) and (iv) a combination of local and distant metastases [2]. Salvage Radiotherapy (RT) is the mainstay therapy in the

setting of local recurrence in the prostate fossa and it offers the potential of cure [3–5].

Modern functional-imaging methods like MRI, including Dynamic Contrast Enhanced (DCE) protocols and Positron Emission Tomography/Computed Tomography PET/CT have the potential to accurately identify the site of recurrence [2,6–9].

Nodal recurrent PCa after primary treatment or after salvage RT of the prostate fossa is considered an unfavourable situation and androgen deprivation (AHT) is administered as standard therapy in this situation. However, long-term AHT causes serious side effects and is of limited benefit due to development of castration-resistant PCa and therefore serves merely as palliative therapy [10,11].

There is increasing evidence that local ablative therapy of lymph node (LN) involvement in the primary situation could reduce the risk of progression [12]. It has been discussed that there may be a different outcome for patients with solitary or few pelvic

* Corresponding author at: Department of Radiation Oncology, University of Freiburg, Hugstetterstr. 55, 79106 Freiburg, Germany. Tel.: +49 761 270 94010; fax: +49 761 270 94720.

E-mail address: hans.christian.rischke@uniklinik-freiburg.de (H.C. Rischke).

LN metastases compared to patients with bone metastases [13]. Others demonstrated that a limited number of PCA metastases have a better prognosis compared with extensive metastatic disease [14,15].

Recently it has been discussed that choline-PET/CT guided salvage LN ablation therapy may be an effective strategy with prolonged disease control and possible curative potential [16–19]. However, patients may not be candidates for salvage surgery and as a possible alternative to salvage LN dissection modern RT techniques such as Intensity Modulated Radiotherapy (IMRT) and Image Guided Radiotherapy (IGRT) are available. They enable the treatment of PET-positive LN regions with dose escalation to macroscopic lesions and sparing of adjacent normal tissue [4].

The aims of the present study were to retrospectively evaluate the impact of choline-PET/CT and MRI directed esRT on PSA progression, pattern of recurrence and to obtain data about toxicity.

2. Material and methods

2.1. Patients

25 patients with Prostatic Specific Antigen (PSA) recurrence and imaging positive for LN metastases or additional local recurrence in the prostate fossa after radical prostatectomy (RP) using choline-PET/CT (^{11}C -choline or ^{18}F -fluoroethylcholine-PET/CT), CT and DCE-magnetic resonance imaging (DCE-MRI) were treated with extended salvage RT (esRT) at Freiburg University Hospital from 2004 to 2013.

Inclusion criteria were verification of biochemical recurrence, presence of new positive LN metastases (regardless of number) according to imaging criteria mentioned below and availability of follow-up data.

Because of the individual approach of the esRT as an alternative to solely AHT, patients had to sign informed consent. Furthermore, the University of Freiburg Institutional Review Board reviewed and approved the retrospective data analysis and the present study (No. 308/14).

2.2. Choline PET/CT and image interpretation

Depending on radionuclide availability, ^{11}C -choline or ^{18}F -fluoroethylcholine PET/CT was performed. Imaging was done using routine in-house acquisition protocols extending from the skull base to the proximal femora. Intravenous and oral contrast medium was used for enhanced CT. Experienced board-certified nuclear medicine specialists and radiologists evaluated PET/CT studies with the ability to display co-registered PET/CT images. Using choline-PET/CT for staging, a lesion was defined as focal tracer accumulation greater than background activity with a corresponding LN in pelvic or retroperitoneal regions in the co-registered CT [20] or a focus in the prostate fossa. Radiological criteria for regarding a LN as metastatic were pelvic or retroperitoneal lymph node with a short-axis diameter >10 mm [21].

2.3. MRI technique and image interpretation

MRI scans were acquired on a 1.5-T system (Siemens Medical Solutions, Erlangen, Germany), equipped with surface-phased array. Imaging of the pelvis and post-prostatectomy fossa was performed by acquiring T1- and T2-weighted (turbo spin echo, TSE) sequences in axial plane, followed by a 3D, fast low-angle shot (FLASH), T1-weighted spoiled gradient-echo sequence in axial slices to perform 4–10 measurements in rapid succession, immediately following completion of an intravenous bolus injection of 0.15 ml/kg gadopentetate dimeglumine (Multihance,

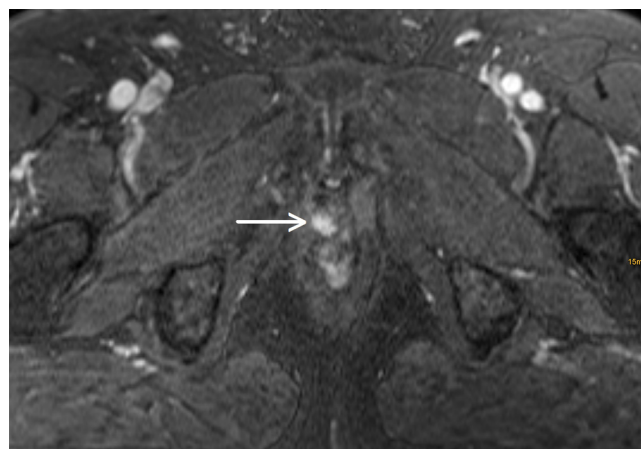


Fig. 1. DCE-MRI of a patient with a contrast enhancing nodule (arrow) in the right prostatic fossa representing local recurrence.

Bracco) using a power injector (Medtron) at 2 ml/s followed by a 30 ml saline flush. Therefore, time resolution varied between 20 and 40 s. A suspicious early contrast-enhancing lesion (visually determined peak enhancement within 90 s post injection) in the post-prostatectomy fossa was considered as local recurrent cancer as described in [6]. Due to the high accuracy of DCE-MRI in detecting local recurrence, representing the gold standard for this finding [2,6,9], MRI findings overruled inconclusive choline-PET/CT findings in the prostate fossa [22]. Every suspicious contrast enhancing nodule in the fossa prostatica or in the area of the vesicourethral anastomosis was taken as a local recurrence in accordance to [6,9] (Figs. 1 and 2). MRI findings triggered irradiation of the prostate fossa.

2.4. Treatment planning of esRT

Imaging findings directed irradiation of LN regions and fossa prostatica after RP. Three gross LN regions were defined: pelvic LNs left/right and retroperitoneal LNs according to [20]. Pelvic and retroperitoneal great vessels served as guidance to define Clinical Target Volume (CTV) of a LN region. The cranial border of the retroperitoneal LN region were the renal vessels, the inferior border the aortic bifurcation. The cranial border of a pelvic LN region (left/right) was the aortic bifurcation, the lower border was the top of the femoral heads. An approximately 8 mm margin around the vessels was drawn to define the CTV. Planning Target Volume (PTV) was approximately 6–8 mm around the CTV. Due to dose constraints in adjacent normal tissues (small bowel, colon)

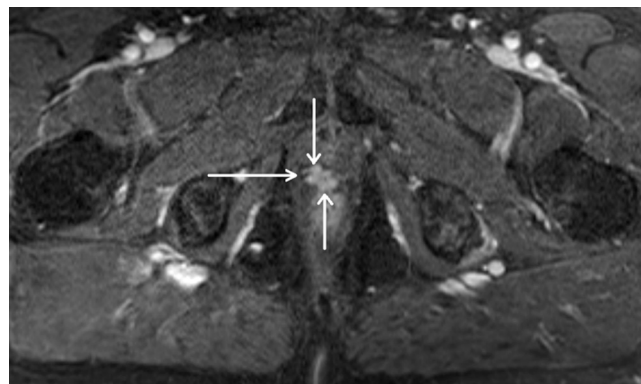


Fig. 2. DCE-MRI of a patient with irregular contrast enhancing tissue (arrows) in the area of the vesicourethral anastomosis representing local recurrence.

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