

Original article

# False-positive fluorodeoxyglucose positron emission tomography results after chemotherapy in patients with metastatic seminoma

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## Abstract

**Introduction:** The treatment of residual masses after chemotherapy in seminomas remains a controversial topic. Postchemotherapy retroperitoneal lymph node dissection (PC-RPLND) in all patients would lead to severe overtreatment with a high rate of complications and additional procedures. For this reason, fluorodeoxyglucose positron emission tomography (FDG-PET) was introduced. FDG-PET has an accuracy of 88%. In 15% of cases, FDG-PET findings are false positive (FP) with unclear consequences. Therefore, we retrospectively investigated the rate of unnecessary procedures due to FP results on FDG-PET.

**Materials and methods:** Between July 2003 and September 2013 we performed 305 PC-RPLNDs in 277 patients, 22 because of metastatic seminoma. Of them, 11 patients had a preoperative FDG-PET at least 6 weeks after chemotherapy. Indication for surgery was a marker-negative progression of the lesion in 7 patients who did not undergo FDG-PET, a marker-negative progression with a negative result on FDG-PET in 2 patients, and a positive result on FDG-PET with normal markers in 9 patients. Furthermore, PC-RPLND was indicated in 3 patients because of ureteral compression/infiltration with ureteral stents or nephrostomies. In 1 patient, there was uncertainty whether the initial retroperitoneal tumor contained choriocarcinoma elements. Standardized uptake values (SUVs) were recorded for all patients undergoing FDG-PET.

**Results:** The FDG-PET findings were FP in 7 of 11 (64%) patients. The median age of the patients was 45.4 years (39–49). The median SUV in the patients was 6.6 (3.1–11.6), and the median diameter of the residual mass was 6.8 cm (2.9–11). In 4 of 7 patients, intraoperative or postoperative complications occurred (polar artery ligation with functional loss, bilateral non-nerve-sparing technique with retrograde ejaculation, ureteral replacement with an ileal segment, and pulmonary embolism).

**Conclusion:** In patients with metastatic seminoma who received chemotherapy, FDG-PET is a valuable tool to evaluate whether the residual mass contains viable tumor tissue or only necrosis. Nevertheless, because of FP results, a subgroup is overtreated with consecutive mortality or morbidity. We suggest an alternative therapy algorithm. In case of a positive result on FDG-PET studies, at least 8 weeks after the end of the chemotherapy, only a minority require surgery (e.g., patients with ureteral compression, patients with high risk of recurrence, or patients with unclear initial histology). In all other cases, we suggest a repeat FDG-PET study at least 6 weeks after the initial PET scan. Only in cases of increased SUVs or progressive disease histology should be obtained, all others can be on active surveillance. © 2014 Elsevier Inc. All rights reserved.

**Keywords:** Seminoma; Positron-emission tomography; Postchemotherapy retroperitoneal lymph node dissection (PC-RPLND); Testicular cancer

## 1. Introduction

In the young male, testicular cancer is the most important malignancy, with >10 new cases per 100,000 males per

year in Europe and a mortality of 0.3 cases per 100,000 males per year. Seminomas comprise up to 60% of all germ cell tumors, with its incidence still increasing over time [1,2]. Approximately 85% of patients with seminoma present with a tumor confined to the testis. Most patients can be cured with orchiectomy, in some cases, adjuvant radiotherapy or carboplatin-based chemotherapy is discussed. Of them, 15% have metastases at diagnosis and eventually up to 25% will require chemotherapy [3].

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Without further treatment after chemotherapy, approximately 10% to 20% of patients have a relapse [4–6].

The treatment of residual masses after chemotherapy in seminomas remains a controversial topic. Viable tumor tissue is present in less than 10% of the lesions <3 cm and in 12% to 30% of larger residual tumors. Therefore, postchemotherapy retroperitoneal lymph node dissection (PC-RPLND) in all patients would lead to severe overtreatment with a high rate of complications and additional procedures (e.g., nephrectomy, ureteral reconstruction, and vascular procedures) [7].

For this reason, fluorodeoxyglucose positron emission tomography (FDG-PET) was introduced. In patients with residual masses >3 cm, a positive result on FDG-PET has a high prognostic value. A histologic analysis should be obtained in marker-negative cases, preferably by RPLND. In masses <3 cm, the use of FDG-PET is optional. In case of a negative result on FDG-PET, no further treatment is indicated [8].

In the meta-analysis by Mueller et al. [9] comprising data from 4 studies and 130 patients, 10 of 33 FDG-PET scans with positive results turned out to be false positive (FP), thus leading to overtreatment and possible intraoperative and postoperative complications.

We investigated the rate of unnecessary procedures owing to FP FDG-PET in our institution.

## 2. Materials and methods

We retrospectively collected data from patients with metastatic germ cell tumors undergoing PC-RPLND in the period from July 2003 until September 2013. A total of 305 operations were performed on 277 patients. Of them, 22 patients with a pure seminoma underwent PC-RPLND. Histology was obtained from orchiectomy specimens or, in the case of primary extragonadal tumors, from diagnostic biopsies or laparotomies. Patients with elevated alpha-fetoprotein levels were excluded. In 1 patient, a pure seminoma was found after orchiectomy, but because of tumor marker constellation (alpha-fetoprotein 1,590 ng/ml), it was managed as a nonseminomatous germ cell tumor and thus excluded.

Standardized uptake values (SUVs) were recorded for all patients undergoing FDG-PET, which was performed at least 6 weeks after chemotherapy.

All PET scans were correlated with the histology of the resected specimens (necrosis vs. viable tumor tissue). A positive result on PET of a lesion containing viable tumor tissue was rated as a true positive. Positive results on PET scans of necrotic lesions were rated as FP. In case of a negative result on PET scan and an absence of remarkable findings on histology, the scan was considered as true negative, and in case of viable tissue as false negative.

Indication for surgery was a marker-negative progression of the lesion in 7 patients who did not undergo FDG-PET, a

marker-negative progression with a negative result on FDG-PET in 2 patients, and a positive result on FDG-PET with normal markers in 9 patients. Furthermore, PC-RPLND was indicated in 3 patients because of ureteral compression/infiltration with ureteral stents or nephrostomies. In 1 patient, there was uncertainty whether the initial retroperitoneal tumor contained choriocarcinoma elements.

## 3. Results

The patient characteristics are shown in Table 1. The mean age in the seminoma group was 43.9 years vs. 33.3 years in the nonseminoma group.

Of 22 patients, 11 had an FDG-PET before surgery, 7 of them (64%) had FP results. The patient with the false-negative result on PET had growing retroperitoneal masses, and so an indication for the RPLND was given, the histology showed viable seminoma. The operation was performed in case of the true-negative result on PET because of the inhomogeneous nature of the mass in computed tomography (CT) and the high anxiety level of the patient. In 11 patients, no PET scan was performed before the operation or no data could be recollected (Fig. 1).

The characteristics of the 7 patients with FP results on FDG-PET are shown in Table 2. The mean age in this group was 45.4 years (range: 39–49), mean preoperative tumor diameter was 6.8 cm (range: 2.9–11), and mean SUV was 6.6 (range: 3.1–11.6); blood loss was approximately 400 ml (range: 50–800), with a mean operative time of approximately 200 minutes (range: 120–270). Patients stayed for approximately 10 days in our department (range: 7–14). Patient 7 received 1 cycle of carboplatin after orchiectomy, had a relapse 2 years later, and was then treated with bleomycin, etoposide, and cisplatin (BEP)-chemotherapy. All others had primary metastatic gonadal or extragonadal seminomas. Patient 2 had a relapse 3 months after primary BEP-chemotherapy and thus received high-dose

Table 1  
Characteristics of the 22 patients undergoing PC-RPLND for metastatic seminoma

Patient characteristics	
Number of patients	22
Median age at PC-RPLND (range)	43.9 (28–53)
Median follow-up in months (range)	2 (0–134)
Primary tumor site testis	17 (77%)
Median initial HCG (range), IU/l	1.3 (0.1–6293)
Median initial LDH (range), IU/l	423 (185–4691)
Median diameter of lesions after chemotherapy (range), cm	5 (2.9–15)
Histology	
Viable tumor tissue	8 (36%)
Necrosis	14 (64%)

HCG = human chorionic gonadotropin; LDH = lactate dehydrogenase.

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