Review Article

The use of F-FDG PET/CT in testicular cancer

Robert Dotzauer, Christian Thomas, Wolfgang Jäger

Department of Urology, University Hospital Mainz, Mainz, Germany

Contributions: (I) Conception and design: W Jäger, R Dotzauer; (II) Administrative support: C Thomas; (III) Provision of study materials or patients: C Thomas, R Dotzauer; (IV) Collection and assembly of data: R Dotzauer; (V) Data analysis and interpretation: R Dotzauer; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Dr. Robert Dotzauer; Dr. Wolfgang Jäger. Department of Urology, University Hospital Mainz, Langenbeckstraße 1, 55131 Mainz, Germany. Email: robert.dotzauer@unimedizin-mainz.de; wolfgang.jaeger@unimedizin-mainz.de.

Abstract: Testicular germ cell tumors are one of the most common neoplasms in young men. After inguinal orchiectomy is performed, treatment options range from active surveillance to chemotherapy, radiation therapy or retroperitoneal lymphadenectomy. For the accurate use of the different treatment options, precise imaging techniques are necessary to reduce side effects of the aggressive therapies but also to avoid undertreatment exposing the patient to the risk of recurrence. F-FDG PET/CT is already recommended in the European guidelines for the follow up of seminomas under certain conditions but conventional primary staging or restaging is still performed with CT or MRI. Recently, the importance of F-FDG PET/CT in this context has become an interesting topic of academic discussion and subject of various clinical trials which are reviewed in the following.

Keywords: F-FDG PET/CT; testicular cancer; testicular germ cell tumor; unclear scrotal mass

Submitted Sep 05, 2018. Accepted for publication Sep 14, 2018.
doi: 10.21037/tau.2018.09.08
View this article at: http://dx.doi.org/10.21037/tau.2018.09.08

Introduction

Testicular cancer is a disease which mainly affects men between 15 and 35 years (1). It has a share of 1% of all solid tumors in the western world with an increasing incidence of 3–10/100,000 (2). There are various risk factors for testicular cancer, like cryptorchidism which increases the relative risk for developing cancer about 3.6. A positive family history and testicular cancer of the contralateral testis are also significant risk factors (3). Furthermore, the cancer risk is associated with the ethnical background. A large survey including data from more than 80% of the US population showed a greater risk for Hispanic or Caucasian Americans as compared to African Americans (4,5).

Testicular cancer can be classified into two entities, germ cell tumors and stromal tumors. Germ cell tumors have a share of 90–95% of testicular cancer and can be further classified into seminoma, non-seminoma and mixed germ cell tumors. Non-seminomas can be divided into teratoma, embryonal cell carcinoma, yolk sac tumor and choriocarcinoma. Mixed germ cell tumors have amounts of seminoma and non-seminoma tumor types. Testicular stromal tumors are a rare but important differential diagnosis and can be classified into Leydig cell tumors and Sertoli cell tumors.

Usually, testicular cancer is accidentally noticed by palpation by the patient himself. Sometimes an injury or an epididymitis can let to medical examination and primary diagnosis. Ultrasound of the testis is the main imaging procedure in the primary diagnosis with a sensitivity of nearly 100%. MRI has an even higher sensitivity and a specificity from 95% to 100% but it plays a secondary role in clinical use due to its higher costs (6). Up to this date the role of F-FDG PET/CT for evaluation of scrotal masses is a controversial issue. Positron emission tomography is a scintrigraphic imaging procedure, where a beta radiator, in many cases fluorine-18 fluorodeoxyglucose (^{18}F-FDG), is used. In a process called annihilation, gamma radiation emerges because of interaction of positrons and electrons. This gamma radiation is detected and mostly merged with

MRI or CT scan. Because of their high sugar metabolism tumor cells can be visualized in that way.

After inguinal orchiectomy is performed, adjuvant treatment strategies depend on clinical staging by CT scan and MRI. Treatment options range from active surveillance to retroperitoneal lymphadenectomy, chemotherapy or radiation therapy. Because these therapies are very effective and show excellent cure rates a focused use is important to avoid overtreatment, for example to reduce the toxic side effects of the cytostatic chemotherapy. Therefore, a consistent active surveillance or aftercare including the correct use of imaging technologies is essential. The importance and clinical use of F-FDG PET/CT is a topic of current debate and has been subject of various clinical trials.

Unclear scrotal masses

To evaluate the use of F-FDG PET/CT for differentiation between benign and malign scrotal masses Shao *et al.* investigated retrospectively 53 patients with different histological confirmed testicular masses who had undergone F-FDG PET/CT. There were 32 patients with malignant neoplasms. Thirteen of them had germ cell tumors. One Patient hat a leydig cell tumor and the others showed testicular involvement of lymphomas or leukemia. Twenty one patients had benign lesion. F-FDG PET/CT showed statistically significant measurements for differentiation between malignant and benign lesions with a sensitivity of 90.6% and a specificity of 80.9% (7).

For characterization of unclear scrotal masses MRI is also a helpful tool. It can be used to differentiate between various testicular tumors like solid, cystic, benign, malignant or inflammatory masses (6). Unfortunately, there is still a lack of studies comparing the diagnostic value of F-FDG PET/CT and MRI. A comparison of these two modalities for evaluation of scrotal masses would be an interesting topic for future investigations.

Primary staging

The use of F-FDG PET/CT in predicting relapse in high-risk situations when CT scan shows unclear results was evaluated by Cook *et al.* in a retrospective analysis with 16 patients with testicular germ cell tumors (seminomas and non-seminomas). Eleven patients had unspecific lymphadenopathy CT scans in primary staging and underwent additional F-FDG-PET/CT. In eight of these eleven cases, F-FDG PET/CT showed negative tracer uptake in the unspecific (retroperitoneal) lymph nodes (8).

In a retrospective survey of 51 patients with seminomas and 70 cases with non-seminomas the benefit of F-FDG PET/CT for staging and restaging in comparison to standard follow up with clinical and imaging examinations was evaluated. For seminomas a good sensitivity of 92% and specificity of 84% could be demonstrated. For non-seminomas a lower sensitivity of 77% and specificity of 95% could be found. For evaluation, F-FDG PET/CT results were compared to clinical and imaging follow-up data. The use of F-FDG PET/CT influenced the clinical management in eleven cases of the 51 seminomas (due to these results in six cases chemotherapy was started or continued, in three cases radiation therapy was started or continued and in two cases further surgery was performed). In 18 cases of the 70 non-seminomas the concept of therapy was changed after performing additional imaging with F-FDG PET/CT (9).

Residual masses after chemotherapy

Seminoma

The current EAU Guidelines recommend the use of F-FDG PET/CT in case of seminoma for the follow up of residual masses >3 cm after chemotherapy (10). In a meta-analysis of four studies which included 130 patients F-FDG PET/CT proved to be superior to standard imaging procedures in predicting viable residual tumors. In comparison F-FDG PET/CT had a sensitivity of 72% *vs.* 62%, a specificity of 92% *vs.* 59%, a positive predictive value of 70% *vs.* 28% and a negative predictive value of 93% *vs.* 86%. The use of F-FDG PET/CT led to a significant reduction of overtreatment from 72% to 30% and undertreatment was decreased from 14% to 7% (11). The diagnostic value of F-FDG PET/CT for seminomas in the follow up after chemotherapy was inspected in another meta-analysis of nine selected studies with an overall of 375 patients. The results showed a sensitivity of 78%, a specificity of 86%, a positive predictive value of 58% and a negative predictive value of 94%. A better diagnostic accuracy for lesions >3 cm than <3 cm was also demonstrated. The authors concluded that negative findings in F-FDG PET/CT could avoid unnecessary adjuvant therapy after chemotherapy because of its excellent negative predictive value (12).

Non-seminoma

There is no recommendation for primary staging or

restaging with F-FDG PET/CT in non-seminomas in the current EAU Guidelines because of its similar sensitivity and specificity to conventional restaging in the follow up (13,14). Its ability to predict viable residual masses was evaluated in a prospective clinical trial with 45 patients with poor prognosis non-seminomas. F-FDG PET/CT was compared to conventional radiologic monitoring with CT scans and changes in serum tumor markers. F-FDG PET/CT showed a sensitivity of 59% and a specificity of 92%. CT scan had a sensitivity of 55% and a specificity of 86% and change in serum tumor markers a sensitivity of 42% and a specificity of 100% (15).

Limitations

There are several limitations of the F-FDG PET/CT in case of imaging of seminomas. False negative results can be caused by transitory suppression of tumor cell activity. To reduce this effect, imaging is recommended at the soonest 6 weeks after chemotherapy (16). Moreover, lesions <10 mm are difficult to detect because of the low spatial resolution of F-FDG PET/CT. A major limitation of the F-FDG PET/CT in non-seminomas is the characterization of residual masses. Because there is a variability of absorption of ^{18}F-FDG in teratoma, F-FDG PET/CT cannot distinguish precisely between necrosis and fibrosis areas. Furthermore, false positive results can be found caused by inflammatory or granulomatous tissue (17).

Conclusions

F-FDG PET/CT can help to differentiate between benign and malignant lesions in primary evaluation of scrotal masses. In case of uncertain CT results in primary staging of testicular germ cell tumors the use of F-FDG PET/CT can provide further information with a good negative predictive value. F-FDG PET/CT is not recommended in the aftercare of non-seminomas where as in the follow up of seminomas it is a precise diagnostic tool.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Boccellino M, Vanacore D, Zappavigna S, et al. Testicular cancer from diagnosis to epigenetic factors. Oncotarget 2017;8:104654-63.
2. Rosen A, Jayram G, Drazer M, et al. Global trends in testicular cancer incidence and mortality. Eur Urol 2011g;60:374-9.
3. Dieckmann KP, Pichlmeier U. Clinical epidemiology of testicular germ cell tumors. World J Urol 2004;22:2-14.
4. Fosså SD, Chen J, Schonfeld SJ, et al. Risk of contralateral testicular cancer: a population-based study of 29,515 U.S. men. J Natl Cancer Inst 2005;97:1056-66.
5. Ghazarian AA, Kelly SP, Altekruse SF, et al. Future of testicular germ cell tumor incidence in the United States: Forecast through 2026. Cancer 2017;123:2320-8.
6. Kim W, Rosen MA, Langer JE, et al. US MR imaging correlation in pathologic conditions of the scrotum. Radiographics 2007;27:1239-53.
7. Shao D, Gao Q, Tian XW, et al. Differentiation and diagnosis of benign and malignant testicular lesions using 18F-FDG PET/CT. Eur J Radiol 2017;93:114-20.
8. Cook GJ, Sohaib A, Huddart RA, et al. The role of 18F-FDG PET/CT in the management of testicular cancers. Nucl Med Commun 2015;36:702-8.
9. Ambrosini V, Zucchini G, Nicolini S, et al. 18F-FDG PET/CT impact on testicular tumours clinical management. Eur J Nucl Med Mol Imaging 2014;41:668-73.
10. EAU Guidelines Office, Arnhem, The Netherlands. EAU Guidelines. Presented at the EAU Annual Congress Copenhagen 2018.
11. Müller J, Schrader AJ, Jentzmik F, et al. Assessment of residual tumours after systemic treatment of metastatic seminoma: (1)(8)F-2-fluoro-2-deoxy-D-glucose positron emission tomography - meta-analysis of diagnostic value. Urologe A 2011;50:322-7.
12. Treglia G, Sadeghi R, Annunziata S, et al. Diagnostic performance of fluorine-18-fluorodeoxyglucose positron emission tomography in the postchemotherapy management of patients with seminoma: systematic review and meta-analysis. Biomed Res Int 2014;2014:852681.
13. Spermon JR, De Geus-Oei LF, Kiemeney LA, et al. The role of (18)fluoro-2-deoxyglucose positron emission tomography in initial staging and re-staging after chemotherapy for testicular germ cell tumours. BJU Int 2002;89:549-56.

14. Karapetis CS, Strickland AH, Yip D, et al. Use of fluorodeoxyglucose positron emission tomography scans in patients with advanced germ cell tumour following chemotherapy: single-centre experience with long-term follow up*. Internal Medicine Journal 2003;33:427-35.
15. Kollmannsberger C, Oechsle K, Dohmen BM, et al. Prospective comparison of [18F]fluorodeoxyglucose positron emission tomography with conventional assessment by computed tomography scans and serum tumor markers for the evaluation of residual masses in patients with nonseminomatous germ cell carcinoma. Cancer 2002;94:2353-62.
16. Bachner M, Loriot Y, Gross-Goupil M, et al. 2-(1)(8) fluoro-deoxy-D-glucose positron emission tomography (FDG-PET) for postchemotherapy seminoma residual lesions: a retrospective validation of the SEMPET trial. Ann Oncol 2012;23:59-64.
17. Oechsle K, Hartmann M, Brenner W, et al. [18F] Fluorodeoxyglucose positron emission tomography in nonseminomatous germ cell tumors after chemotherapy: the German multicenter positron emission tomography study group. J Clin Oncol 2008;26:5930-5.

Cite this article as: Dotzauer R, Thomas C, Jäger W. The use of F-FDG PET/CT in testicular cancer. Transl Androl Urol 2018;7(5):875-878. doi: 10.21037/tau.2018.09.08

