EUR. J. ONCOL.; Vol. 20, n. 3/4, pp. 183-192, 2015

Role of [18F]FDG PET/CT scan in management of gynecologic malignancies: a literature review

Luca Tagliabue[1], *Silvia Seghezzi*[2]

[1] Department of Diagnostic Imaging, Nuclear Medicine Unit, University Hospital "S.Paolo", Milan, Italy; [2] Department of Diagnostic Imaging, Nuclear Medicine Unit, Azienda Ospedaliera Treviglio-Caravaggio, Treviglio, Bergamo, Italy

Summary. *Introduction:* Tumors of the female genital tract are a major cause of mortality among women in Western countries: the most frequent of these cancers is endometrial cancer, while the most lethal is ovarian cancer. *Aim:* The aim of the present work was to review the published literature on the utility of metabolic imaging in the staging, re-staging and post-treatment monitoring of cervical, endometrial and ovarian cancer. We also evaluated the relevance of evidence as to the cost-effectiveness of introducing PET/CT in the work-up of gynecological malignancies. *Methods:* EMBASE and Pub-Med Literature searches were made from 2007 to 2014. *Results:* Despite the availability of multiple imaging techniques, estimating the extent of primary disease and locoregional lymph node involvement is still based on clinical and surgical evaluation, while distant metastases may be assessed accurately and non-invasively using PET/CT. PET/CT may also be a useful tool in planning radiotherapy and in predicting response to treatment. Moreover when recurrence occurs, PET/CT accurately evaluates its extent and orients further therapies. Finally PET/CT seems to be cost-effective for ovarian cancer, whereas there is little evidence for cervical cancer and no data for endometrial cancer. *Conclusion:* A body of evidence is growing about the usefulness of PET/CT in management of gynecological malignancies as a complementary tool in addition to clinical evaluation and biochemical surveillance; moreover few data are available about the cost-effectiveness of introducing this method in clinical practice and further evaluations are needed addressing this topic.

Key words: ginecologic malignancies, [18F]FDG PET/CT, cost-effectiveness

«Ruolo della [18F]FDG PET/CT nella gestione dei tumori maligni ginecologici: una revisione della letteratura»

Riassunto. *Introduzione:* I tumori del tratto genitale femminile sono la più importante causa di morte tra le donne nei paesi occidentali; tra questi il cancro dell'endometrio è il più frequente e quello dell'ovaio il più letale. *Scopo:* Lo scopo del lavoro è quello di rivedere i dati pubblicati in letteratura circa l'utilità delle immagini ottenute mediante PET/CT nella stadiazione, restadiazione e nel monitoraggio post-trattamento del cancro della cervice uterina, dell'endometrio e dell'ovaio. Inoltre abbiamo valutato la rilevanza delle evidenze circa il rapporto costo-beneficio legata all'introduzione di questa tecnologia nella gestione dei tumori maligni ginecologici. *Metodi:* Sono state effettuate ricerche su lavori pubblicati in riviste censite da data-base internazionali come EMBASE e Pub-Med dal 2007 al 2014. *Risultati:* Nonostante la disponibilità di molteplici tecniche di imaging, la valutazione dell'estensione della malattia primitiva ed il coinvolgimento linfonodale sono ancora valutati sulla base della stadiazione clinica e delle evidenze derivate dalla chirurgia, mentre il coinvolgimento metastatico a distanza può essere accuratamente studiato in maniera non invasiva mediante PET/CT; questa tecnologia può essere anche utilizzata efficacemente nel pianificare la radioterapia quando necessaria e nel valutare le risposte alle terapie. Inoltre, quando la malattia recidiva, la PET/CT valuta accuratamente l'estensione e orienta eventuali ulteriori terapie. Infine la PET/CT sembra avere un buon rapporto costo-beneficio

per il cancro dell'ovaio mentre i dati disponibili sono ancora scarsi per il cancro della cervice e non esistono dati per il cancro dell'endometrio. *Conclusioni:* Una sempre maggiore quantità di evidenze è disponibile circa l'utilità della PET/CT nella gestione dei tumori maligni ginecologici come strumento complementare alla valutazione clinica ed alla sorveglianza biochimica. I dati disponibili sul rapporto costo-efficacia nell'introdurre questa metodica pratica, sono pochi; sono pertanto necessarie ulteriori valutazioni in merito.

Parole chiave: tumori maligni ginecologici, [18F] FDG PET/CT, rapporto costo-efficacia

Abbreviations:
PET: positron emission tomography; FDG: fluoro deoxy glucose; CT: computed tomography; ceCT: contrast enhanced computed tomography; MRI: magnetic resonance imaging; DWI: diffusion weighted imaging.

Introduction

Among gynecological malignancies, endometrial cancer has the highest incidence rate while ovarian cancer is the most lethal form, having a greater than 60% mortality rate in diagnosed cases (1).

Screening procedures and immunization against human papillomavirus (HPV) are decreasing the incidence of cervical cancer in Western countries (2, 3).

Adenocarcinoma of the endometrium is the most common cancer of the female genital tract. Risk factors include a fat-rich diet, diabetes, chromosomal aberrations, older age and tamoxifen use (4): its incidence is expected to rise as a result of the increasing prevalence of obesity.

Ovarian cancer is the leading cause of gynecological cancer death; it consists of several histopathological types but most are epithelial (5). The median time at diagnosis is 63 years and more than 70% are diagnosed at an advanced stage of the disease.

The aim of the present work was to review the published literature on both the utility and the cost-effectiveness of PET/CT in the staging, re-staging and post-treatment surveillance of cervical, endometrial and ovarian cancer.

EMBASE and Pub-Med searches were made from 2007 to 2013 using as key words: FDG, [18F]-FDG PET or PET/CT, cervical cancer, endometrial cancer, ovarian cancer, diagnosis, prognosis, follow-up, cost-effectiveness and health technology assessment.

Finally tables summarizing the potential use of PET/CT in gynecological cancers have been drawn up, taking into account the National Comprehensive Cancer Network® (NCCN) guidelines and the American College of Radiology® (ACR), Appropriateness Criteria®, as well as the Authors' own clinical expertise.

Staging

Cervical Cancer

PET/CT may help planning treatment in cervical cancer, whereas it is not yet accepted as a routine procedure for staging purposes (6); Federation International of Gynecologists and Obstetricians (FIGO) limits staging procedures to colposcopy, biopsy, conization of the cervix, cystoscopy and rectosigmoidoscopy. Radiological procedures are not routinely recommended for staging, even though contrast-enhanced (ce) CT, PET/CT and MRI are often used in the pre-surgical setting (Table 1).

Table 1. Potential uses of PET/CT in cervical cancer according to stage.

Stage	Staging	Surveillance	Restaging
<IB1 (FIGO) T1b1(TNM)	optional	optional	indicated
>IB1 (FIGO) T1b1 (TNM)	indicated	optional (*)	indicated

(*) PET/CT indicated 3-6 months after the end of treatment in patients at high risk of failure (para-aortic lymph node) to allow early detection of any curable recurrence or persistence.

The presence of positive pelvic lymph nodes at PET/CT could allow clinicians to identify patients who should be referred immediately for chemo-radiotherapy; moreover, because pathologic PET/CT uptakes have been associated with poorer post-surgical event-free survival, PET/CT can identify patients at high risk of recurrence who warrant very close monitoring during follow-up (7, 8).

In earlier disease stages, clinical attention is focused on sparing unnecessary lymph-node surgery; because of the low sensitivity of metabolic assessment on regional node spread in cervical tumors staged Ib1-IIa (T< 4 cm), the method has little or no added value in influencing the surgical approach (9).

PET/CT-based prognostic nomograms for locally advanced cervical cancer have been designed: evaluation of metabolic parameters and lymph node involvement predicts recurrence-free survival (RFS), disease-specific survival (DSS), and overall survival (OS), finding that pretreatment PET/CT metabolic parameters of the primitive tumor, combined with lymph node status, create good models for predicting RFS, DSS and OS (10).

Metabolic findings help in defining irradiation fields (11) and PET/CT should be included in the initial workup of patients with locally advanced cervical carcinoma (12), in order to better delineate any active metastatic site (Figure 1). PET/CT findings can guide additional radiation fields to the para-aortic nodal region, achieving more complete disease control (13).

It has also been demonstrated that PET/CT is effective in brachytherapy planning and its introduction can pave the way to optimized 3D brachytherapy treatment (14).

As in other types of cancer the possibility of false positive results should be remembered: any pathologic uptake that could change the clinical stage and/or clinical management of the patient must always be verified (15).

Endometrial cancer

Although the staging of endometrial carcinoma is primarily a clinical and surgical procedure, many studies have shown clinical staging to be inaccurate (16).

Ultrasound (US), PET/CT and MRI are comparable in predicting myometrial invasion and distant spread, but none of them can currently replace surgical staging; moreover for cervical invasion and lymph node metastases, PET/CT performs very well (17).

Unfortunately the high positive predictive value (PPV) of PET/CT is not matched by any high negative predictive value (NPV): for this reason PET/CT

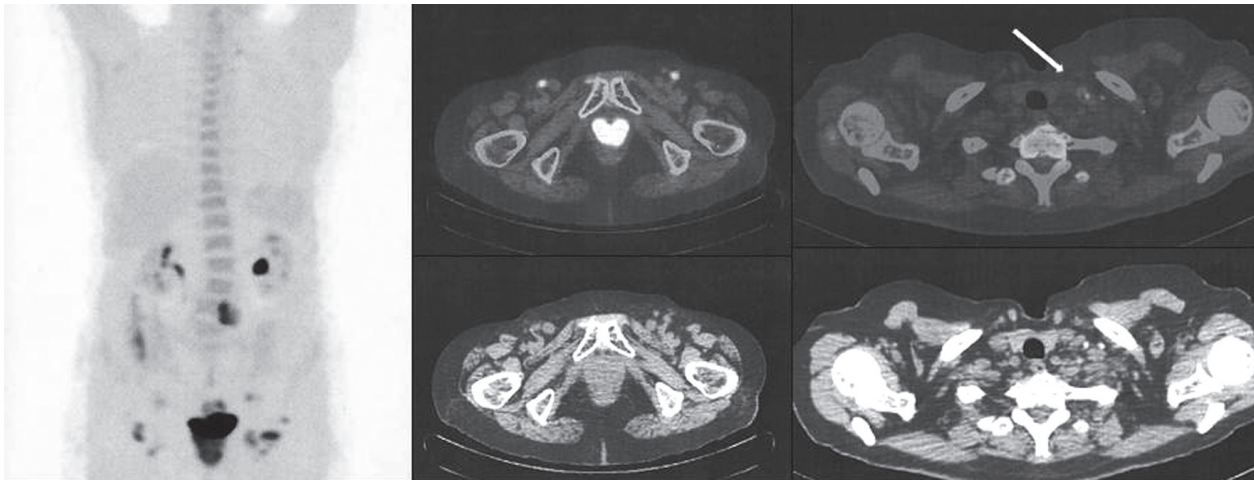

Figure 1. 56-year-old woman with cervical cancer and bilateral, pathological iliac and inguinal lymphadenopathies; FDG PET/CT showed a left supraclavicular positive node (white arrow), subsequently histopathologically confirmed as metastatic lymphadenopathy.

cannot replace surgical staging in the pre-operative setting (18).

The preoperative SUVmax value (a semi-quantitative measure of FDG uptake) is superior to the apparent MRI-derived diffusion coefficient as a predictor of disease recurrence and survival (19).

SUVmax is related to tumor FIGO stage, grading (20) and post-surgical prognosis (21); in addition SUVmax is related to myometrial invasion, cervical invasion, FIGO stage, risk-stratification and lymph node metastases; however, the SUVmax sensitivity and specificity are not such as to replace surgery (22).

It has been found that preoperative metabolic primary tumor volume is an independent prognostic factor for progression-free survival and is significantly associated with recurrence in patients with endometrial cancer (23).

The diagnostic performance of PET/ceCT, contrast-enhanced MRI, and retrospective image fusion from PET and MRI (fused PET/MRI) for assessing the extent of the primary tumor (T stage) and metastasis to regional LNs (N stage) was evaluated; PET/MRI proved to be more accurate in detecting and staging T but not in pelvic nodal staging (24).

PET/CT in the initial staging of high-grade endometrial cancer is useful in detecting distant metastases in the abdomen and in the extra-abdominal regions (25); however, in the preoperative evaluation of distant lymph-node metastasis PET/ceCT and DWI cannot replace lymphadenectomy (26).

Radiation therapy may cause a wide range of loco-regional complications: for this reason it is crucial to limit toxicity as much as possible. Radiation planning based on PET/CT can reduce loco-regional side effects and improve target definition (27) (Table 2).

Table 2. Potential uses of PET/CT in endometrial cancer according to stage.

Stage	Staging (*)(**)	Surveillance (***)	Restaging
I	indicated	under debate	indicated
II	indicated	under debate	indicated
III	indicated	under debate	indicated
IV	indicated	under debate	indicated

(*) indicated in cases of suspected or known extrauterine spread
(**) always indicated in cases of uterine sarcoma
(***) there is no consensus on strategies for following up these patients. The technique might be adequate in selected cases (patients with high-grade tumors or advanced stages at diagnosis or who report symptoms).

Ovarian cancer

The most important factors influencing the prognosis of ovarian cancer are the stage and grade of the tumor. Unfortunately the most frequent presentation feature is an undiagnosed pelvic mass.

The primary workup includes clinical evaluation, ultrasound and PET/CT.

Because ovarian cancer is normally characterized by a strong glycolytic phenotype, regardless of tumor histology and grade (28), PET/CT proves highly accurate in patients presenting with elevated CA 125 serum levels and a suspicious ovarian mass seen on ultrasound (29).

Although PET/CT is not considered a standard procedure in the staging of ovarian cancer, several studies have investigated the incremental value of using this technique preoperatively to evaluate the feasibility of achieving optimal debulking in advanced disease stages (Table 3).

PET/CT has been shown to identify primary ovarian tumors, regional lymph nodes and distant metastases (Figure 2). PET/CT results when compared to histopathological findings show an excellent diagnostic performance (30) (Figure 3).

With the growing use of PET/CT in pre-surgical staging a number of unexpected extra-abdominal localizations have been identified; the findings of one study suggest that metastatic pathways permeate the diaphragm, mainly reaching the cardiophrenic space and the parasternal lymph nodes (31).

Table 3. Potential use of PET/CT in ovarian cancer according to stage.

Stage	Staging (*)	Surveillance (**)	Restaging (**)
I	optional	indicated	indicated
II	optional	indicated	indicated
III	optional	indicated	indicated
IV	optional	indicated	indicated

(*) PET/CT is indicated in some indeterminate lesions when its results may affect the choice of treatment
(**) Imaging guided by serial CA 125 increases

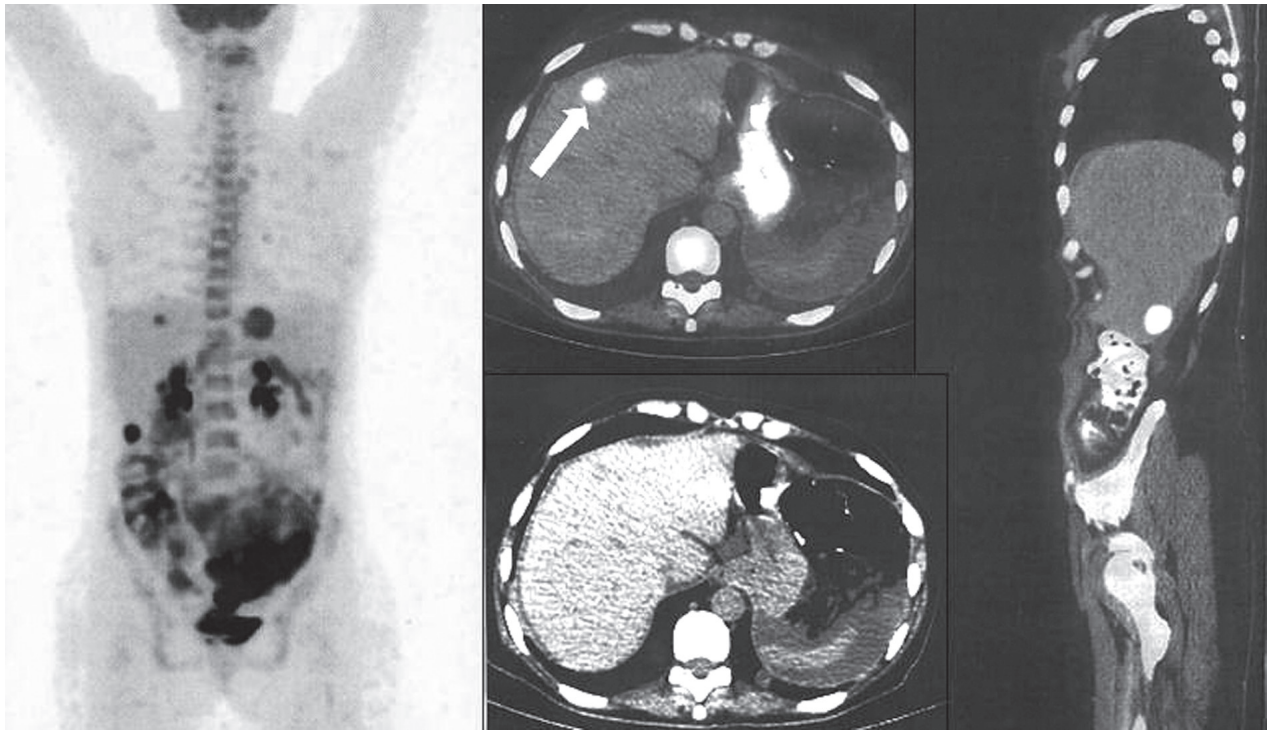

Figure 2. 48-year-old woman with epithelial left ovarian cancer, ascitic fluid and inconclusive liver CT imaging; FDG PET/CT showed a left ovarian mass, diffuse carcinomatosis and a right hepatic lobe metastasis (white arrow).

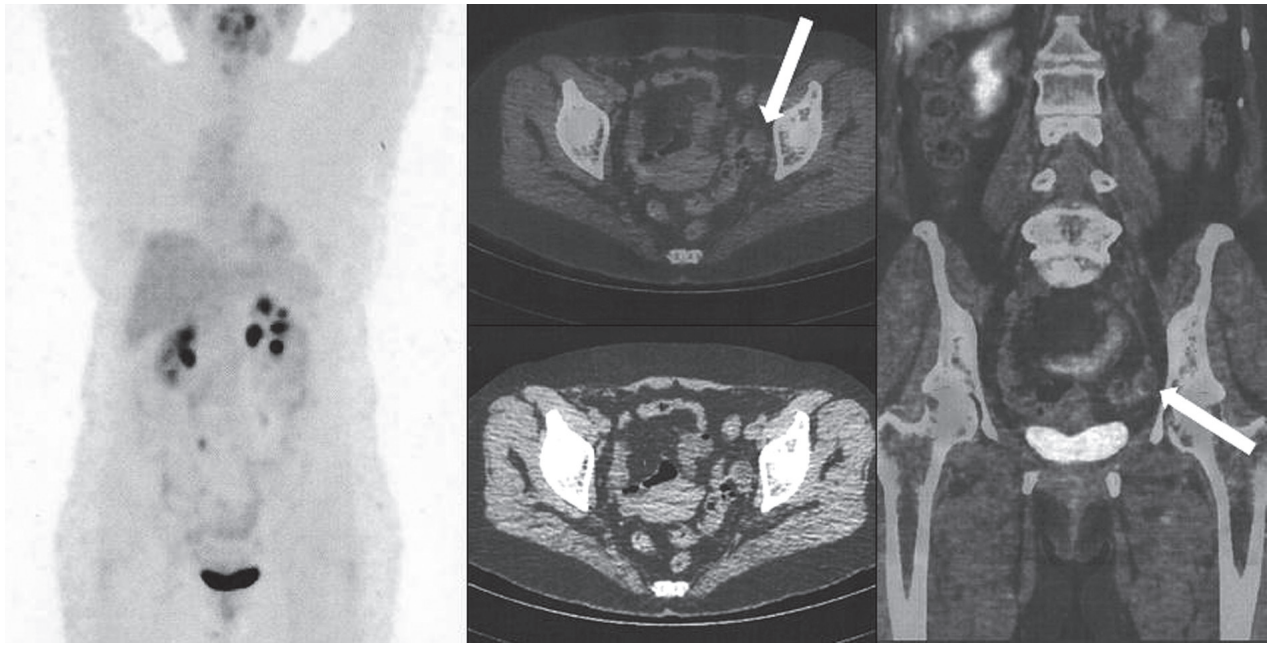

Figure 3. 43-year-old woman with left adnexal mass at CT scan; FDG PET/CT did not show significant uptake (white arrow); histopathology demonstrated to be a benign lesion.

In more advanced disease, a cytoreduction may be appropriate prior to surgery: the probability of achieving a complete cytoreduction is lower in patients presenting with mediastinal lymph node FDG uptake (32).

Peritoneal carcinomatosis is a common type of metastatic spread in ovarian cancer: it has been shown that PET/CT imaging was efficient in the diagnosis of peritoneal carcinomatosis and superior to ceCT (33); as documented in other cancer types, PET/CT leads to stage migration, although the strongest determinant of patient outcome remains the residual abdominal tumor after primary surgery (34). Furthermore, volumetric parameters such as metabolic tumor volume (MTV) and total lesion glycolysis (TLG) show significant association with recurrence in patients with epithelial ovarian cancer (35).

Post-treatment surveillance and restaging

Surveillance strategies are a subject of continuous debate and there is no evidence of the clinical usefulness of detecting recurrences in asymptomatic women. As therapeutic strategies improve, there might emerge some advantages of an early diagnosis of recurrence in terms of Disease Free Survival (DFS), Progression Free Survival (PFS), Overall Survival (OS) and Quality Of Life (QOL).

Cervical Cancer

Post-treatment surveillance protocols include physical examination, Pap smear and chest radiograph. However, asymptomatic cases are unlikely to be detected using such protocols. Pelvic examination and vaginal or cervical cytology have low diagnostic accuracy because of post-radiation changes. (36).

The role of PET/CT in cervical cancer surveillance is nowadays ongoing and post-treatment PET/CT is able to stratify the risk of recurrence (37), mainly in identifying local recurrence and distant metastasis (38).

PET/CT can be useful in early diagnosis of recurrence mainly among asymptomatic women. Patients with early detection of loco-regional or central recurrence can be offered a variety of therapeutic solutions ranging from combined chemo-radiotherapy to pelvic exenteration with significant prognostic advantages (39).

In restaging conventional imaging can show a suboptimal sensitivity mainly in evaluating peritoneal involvement; PET/CT performs better than conventional imaging in peritoneal recurrences among various cancers including ovarian, endometrial and cervical; adding contrast enhancement to PET/CT seems to offer no advantages in uterine cancer recurrence (40).

Changes in cervical cancer metabolic activity during concurrent chemo-radiation through "interim" PET/CT scans performed at the 2nd and 4th weeks of treatment have been analyzed. SUVmax is found to decline during treatment and to decrease more quickly than MTV: the 4th week of treatment emerges as the best time point for response prediction (41).

PET/CT performs better than MRI alone in predicting one-month detection of response in patients undergoing adjuvant chemo-radiotherapy, but there are no differences when the same patients are evaluated at the end of therapy (42).

Moreover a significant correlation between survival outcome and the interim metabolic response of pelvic lymph nodes has been shown. Patients presenting complete metabolic response had an excellent OS and DSF (43, 44).

Endometrial Cancer

There are no available prospective randomized studies on the routine use of [18F]FDG PET/CT imaging in post-treatment surveillance of endometrial cancer. Periodic physical examination for two years, as well as vaginal cytology and chest x-ray annually, constitute the cornerstones for endometrial cancer surveillance (45).

PET/CT may be useful in treatment planning for women with recurrent disease; nevertheless PET/CT seems to be an accurate method of detecting recurrence in the post-therapy follow-up of endometrial carcinoma (46).

PET/CT was found to be a more useful modality than either conventional imaging or CA 125 in the evaluation of suspected recurrence in post-treatment endometrial cancer patients (47); moreover PET/CT

is highly sensitive and specific in detecting disease in patients with suspected recurrence (48).

On the other hand, the PPV may be sub-optimal due to relatively low specificity whereas NPN approaches 100% due to excellent sensitivity (49, 50).

PET/low-dose non-enhanced CT (PET/ldCT), PET/full-dose contrast-enhanced CT(PET/ceCT), contrast-enhanced MRI, and retrospective fused PET/MRI studies have been evaluated in different clinical settings: it may be concluded that fused PET/MRI combines the MRI and PET advantages and is a valuable technique for assessment of intra-pelvic recurrence of gynecological cancers (51).

Ovarian Cancer

Clinical surveillance and repeated testing of CA 125 serum levels are the cornerstones of follow-up in ovarian cancer patients. The add-on value of early detection of disease recurrence is controversial as benefits in terms of survival time and quality of life are not yet clearly evident.

PET/CT is most helpful in the evaluation of patients with suspected recurrent ovarian carcinoma, especially when CA-125 levels are rising and CT findings are normal or equivocal. Addition of PET/CT to the evaluation of these patients changes management in approximately a third and reduces overall treatment costs by accurately identifying patients who will benefit from surgery (52).

When disease recurs, the clinician needs to know its extension. This information is crucial to the decision whether to attempt a second debulking or not; furthermore, if the disease is disseminated, the clinician needs a reliable method for monitoring treatment results. On the basis of the wide review by Limei *et al.* it can be concluded that PET/CT is an useful tool for diagnosing, restaging and predicting suspected recurrent ovarian carcinoma (53).

Cost-effectiveness of PET/CT in gynecologic malignancies

Cost-effectiveness analysis evaluates if the added costs are balanced by the clinical impact on survival. Few reports on this topic are available at the moment.

Analyzing the cost-effectiveness of primary surgery versus chemoradiation in the treatment of FIGO IB2 cervical cancer patients introduces the idea that PET/CT can not only be useful but also cost-effective in managing a particular type of patients diagnosed with cervical cancer (FIGO IB2) (54) .

Moreover, although imaging does not appear to improve survival, PET/CT maximizes patient triage to correct treatment, and combined MRI and PET/CT spares most patients unnecessary therapies (55).

On the other hand it has been shown that adding PET/CT to the current treatment strategy of clinical examination, MRI and/or CT scan is significantly more costly with only a minimal increase in effectiveness (56).

When the role of PET/CT "standing alone" and PET/CT after a negative ceCT is evaluated, the former strategy is found to be more expensive but also more effective and seems to be cost-effective, presenting an Incremental Cost-Effectiveness Ratio of €226.77 per surgery avoided (57).

Finally costs have been calculated with and without the use of PET/CT scanning: the results show that the cost saving per patient ranges from $1,941 to $11,766 due to the need for fewer surgical procedures when using PET in the diagnostic evaluation (58).

Conclusion

PET/CT is playing a growing role in the clinical management of gynecological malignancies; in staging procedures it can increase clinical confidence in evaluating distant metastasis but it cannot replace surgery because of the possible presence of false negative results, with a partial exception for cervical cancer staged IB1 or higher in which PET/CT can detect lymph node spread and help in treatment planning.

Pre-radiotherpy PET/CT evaluation allows better definition of irradiation volumes, avoiding unnecessary toxicity and side effects; moreover, pre-treatment, interim or post-treatment SUVmax is related to tumor grading, response to therapy, prognosis and survival.

When recurrence occurs, PET/CT seems to be an excellent diagnostic tool, mainly in assessment of disease spread, tailoring therapies on a per-patient basis.

About cost-effectiveness, PET/CT seems to be cost-effective mainly in ovarian cancer whereas in cervical cancer reports are still discordant. In cervical cancer, PET/CT seems to be too expensive when compared to standard approaches; further studies, focuse on reduction of costs for implementing this technology, may lead to different conclusions.

In ovarian cancer the data available seem to indicate the cost-effectiveness of adding PET/CT during follow-up in terms of eliminating expensive unnecessary procedures.

It can be concluded that metabolic imaging is able to provide accurate information about the nature, degree and spread of these diseases, to offer prognostic information and to predict, diagnose and evaluate disease recurrence.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics. Cancer J Clin 2012; 62(1): 10-29.
2. Sasieni P, Castanon A, Cuzick J, Screening and adenocarcinoma of the cervix. Int J Cancer 2009; 125(3): 525-9.
3. Ault KA. Future II Study Group. Effect of prophylactic human papillomavirus L1 virus-like-particle vaccine on risk of cervical intraepithelial neoplasia grade 2, grade 3, and adenocarcinoma in situ: a combined analysis of four randomised clinical trials. Lancet 2007; 369(9576): 1861-8.
4. Kitchener HC, Trimble EL. Endometrial Cancer Working Group of the Gynecologic Cancer Intergroup. Endometrial cancer state of the science meeting. Int J Gynecol Cancer 2009; 19(1): 134-40.
5. Jelovac D, Armstrong DK. Recent progress in the diagnosis and treatment of ovarian cancer. Cancer J Clin 2011; 61(3): 183-203.
6. NCCN National Comprehensive Cancer Network®, Clinical Practice Guidelines in Oncology, NCCN guideline®, Cervical Cancer, Version 3. www.nccn.org.
7. Zhao Q, Feng Y, Mao X, *et al.* Prognostic Value of Fluorine-18-Fluorodeoxyglucose Positron Emission Tomography or PET-Computed Tomography in Cervical Cancer: A Meta-Analysis. Int J Gynecol Cancer 2013; 23(7): 1184-90.
8. Mirpour S, Mhlanga JC, Logeswaran P, *et al.* The Role of PET/CT in the Management of Cervical Cancer. Am J Roentgenol 2013; 201(2): W192-205.
9. Signorelli M, Guerra L, Montanelli L, *et al.* Preoperative staging of cervical cancer: is 18-FDG-PET/CT really effective in patients with early stage disease? C.Gynecol Oncol 2011; 123(2): 236-40.
10. Kidd EA, El Naqa I, Siegel BA, *et al.* FDG-PET-based prognostic nomograms for locally advanced cervical cancer. Gynecol Oncol 2012; 127(1): 136-40.
11. Herrera FG, Prior JO. The role of PET/CT in cervical cancer. Front Oncol 2013; 3:34.
12. Akkas BE, Demirel BB, Vural GU. Clinical impact of ^{18}F-FDG PET/CT in the pretreatment evaluation of patients with locally advanced cervical carcinoma. Nucl Med Commun 2012; 33(10): 1081-8.
13. Grigsby PW. PET/CT imaging to guide cervical cancer therapy. Future Oncol 2009; 5(7): 953-8.
14. Nam H, Huh SJ, Ju SG, *et al.* 18F-fluorodeoxyglucose positron emisson tomography/computed tomography guided conformal brachytherapy for cervical cancer Int J Radiat Oncol Biol Phys 2012; 84(1): e29-34.
15. Onal C, Oymak E, Findikcioglu A, *et al.* Isolated mediastinal lymph node false positivity of [18F]-fluorodeoxyglucose-positron emission tomography/computed tomography in patients with cervical cancer. Int J Gynecol Cancer 2013; 23(2): 337-42.
16. Cowles TA, Magrina JF, Masterson BJ, *et al.* Comparison of clinical and surgical-staging in patients with endometrial carcinoma. Obstet Gynecol 1985; 66(3): 413-6.
17. Antonsen SL, Jensen LN, Loft A, *et al.* MRI, PET/CT and ultrasound in the preoperative staging of endometrial cancer - a multicenter prospective comparative study. Gynecol Oncol 2013; 128(2): 300-8.
18. Chang MC, Chen JH, Liang JA, *et al.* 18F-FDG PET or PET/CT for detection of metastatic lymph nodes in patients with endometrial cancer: a systematic review and meta-analysis. Eur J Radiol 2012; 81(11): 3511-7.
19. Nakamura K, Joja I, Fukushima C, *et al.* The preoperative SUVmax is superior to ADC min of the primary tumour as a predictor of disease recurrence and survival in patients with endometrial cancer.Eur J Nucl Med Mol Imaging 2013; 40(1): 52-60.
20. Nakamura K, Kodama J, Okumura Y, *et al.* The SUVmax of 18F-FDG PET correlates with histological grade in endometrial cancer. Int J Gynecol Cancer 2010; 20(1): 110-5.
21. Nakamura K, Hongo A, Kodama J, *et al.* The measurement of SUVmax of the primary tumor is predictive of prognosis for patients with endometrial cancer. Gynecol Oncol 2011; 123(1): 82-7.
22. Antonsen SL, Loft A, Fisker R, *et al.* SUVmax of 18FDG PET/CT as a predictor of high-risk endometrial cancer patients. Gynecol Oncol 2013; 129(2): 298-303.
23. Chung HH, Lee I, Kim HS, *et al.* Prognostic value of preoperative metabolic tumor volume measured by (18) F-FDG PET/CT and MRI in patients with endometrial cancer Gynecol Oncol 2013; 130(3): 446-51.
24. Kitajima K, Suenaga Y, Ueno Y, *et al.* Value of fusion of PET and MRI for staging of endometrial cancer: Comparison with 18F-FDG contrast-enhanced PET/CT and dynamic contrast-enhanced pelvic MRI. Eur J Radiol 2013. pii: S0720-048X(13)00240-4.
25. Picchio M, Mangili G, Samanes Gajate AM, *et al.* High-grade endometrial cancer: value of [(18)F]FDG PET/CT in preoperative staging. Nucl Med Commun 2010; 31(6): 506-12.

26. Kitajima K, Yamasaki E, Kaji Y, *et al.* Comparison of DWI and PET/CT in evaluation of lymph node metastasis in uterine cancer. World J Radiol 2012; 4(5): 207-14.
27. Liang Y, Bydder M, Yashar CM, *et al.* Prospective study of functional bone marrow-sparing intensity modulated radiation therapy with concurrent chemotherapy for pelvic malignancies. Int J Radiat Oncol Biol Phys 2013; 85(2): 406-14.
28. Karantanis D, Allen-Auerbach M, Czernin J. Relationship among glycolytic phenotype, grade, and histological subtype in ovarian carcinoma. Clin Nucl Med 2012; 37(1): 49-53.
29. Risum S, Hogdall C, Loft A, *et al.* The diagnostic value of PET/CT for primary ovarian cancer - a prospective study. Gynecol Oncol 2007; 105(1): 145-9.
30. Zytoon AA, Murakami K, Eid H, *et al.* High impact of FDG-PET/CT in diagnostic strategies for ovarian cancer. Acta Radiol 2013; 54(3): 340-8.
31. Hynninen J, Auranen A, Carpén O, *et al.* FDG PET/CT in staging of advanced epithelial ovarian cancer: frequency of supradiaphragmatic lymph node metastasis challenges the traditional pattern of disease spread. Gynecol Oncol 2012; 126(1): 64-8.
32. Bats AS, Hugonnet F, Huchon C, *et al.* Prognostic significance of mediastinal 18F-FDG uptake in PET/CT in advanced ovarian cancer. Eur J Nucl Med Mol Imaging 2012; 39(3): 474-80.
33. Kim HW, Won KS, Zeon SK, *et al.* Peritoneal carcinomatosis in patients with ovarian cancer: enhanced CT versus 18F-FDG PET/CT. Clin Nucl Med 2013; 38(2): 93-7.
34. Risum S, Høgdall C, Loft A, *et al.* Does the use of diagnostic PET/CT cause stage migration in patients with primary advanced ovarian cancer? Gynecol Oncol 2010; 116(3): 395-8.
35. Chung HH, Kwon HW, Kang KW, *et al.* Prognostic value of preoperative metabolic tumor volume and total lesion glycolysis in patients with epithelial ovarian cancer. Ann Surg Oncol 2012; 19(6): 1966-72.
36. Bodurka-Bevers D, Morris M, Eifel PJ, *et al.* Posttherapy surveillance of women with cervical cancer: an outcomes analysis. Gynecol Oncol 2000; 78(2): 187-93.
37. Chung HH, Kim JW, Kang KW, *et al.* Predictive role of post-treatment [18F]FDG PET/CT in patients with uterine cervical cancer. Eur J Radiol 2012; 81(8): e817-22.
38. Chu Y, Zheng A, Wang F, *et al.* Diagnostic value of 18F-FDG-PET or PET-CT in recurrentcervical cancer: a systematic review and meta-analysis. Nucl Med Commun 2014; 35(2): 144-50.
39. Sironi S, Picchio M, Landoni C, *et al.* Post-therapy surveillance of patients with uterine cancers: value of integrated FDG PET/CT in the detection of recurrence Eur J Nucl Med Mol Imaging 2007; 34(4): 472-9.
40. Kitajima K, Suzuki K, Nakamoto Y, *et al.* Low-dose non-enhanced CT versus full-dose contrast-enhanced CT in integrated PET/CT studies for the diagnosis of uterine cancer recurrence. Eur J Nucl Med Mol Imaging 2010; 37(8): 1490-8.
41. Kidd EA, Thomas M, Siegel BA, *et al.* Changes in cervical cancer FDG uptake during chemoradiation and association with response. Int J Radiat Oncol Biol Phys 2013; 85(1): 116-22.
42. Lee JE, Huh SJ, Nam H, *et al.* Early response of patients undergoing concurrent chemoradiotherapy for cervical cancer: a comparison of PET/CT and MRI. Ann Nucl Med 2013; 27(1): 37-45.
43. Yoon MS, Ahn SJ, Nah BS, *et al.* Metabolic response of lymph nodes immediately after RT is related with survival outcome of patients with pelvic node-positive cervical cancer using consecutive [18F]fluorodeoxyglucose-positron emission tomography/computed tomography Int J Radiat Oncol Biol Phys 2012; 84(4): e491-7.
44. Kunos C, Radivoyevitch T, Abdul-Karim FW, *et al.* 18F-fluoro-2-deoxy-D-glucose positron emission tomography standard uptake value ratio as an indicator of cervical cancer chemoradiation therapeutic response. P Int J Gynecol Cancer 2011; 21(6): 1117-23.
45. National Comprehensive Cancer Network®, Clinical Practice Guidelines in Oncology, NCCN guideline®, Uterine Cancer, Version 1.2013. www.nccn.org.
46. Kadkhodayan S, Shahriari S, Treglia G, *et al.* Accuracy of 18-F-FDG PET imaging in the follow up of endometrial cancer patients: systematic review and meta-analysis of the literature. Gynecol Oncol 2013; 128(2): 397-404.
47. Ozcan Kara P, Kara T, Kaya B, *et al.* The value of FDG-PET/CT in the post-treatment evaluation of endometrial carcinoma: a comparison of PET/CT findings with conventional imaging and CA 125 as a tumour marker. Rev Esp Med Nucl Imagen Mol 2012; 31(5): 257-60.
48. Sharma P, Kumar R, Singh H, *et al.* Carcinoma endometrium: role of 18-FDG PET/CT for detection of suspected recurrence Clin Nucl Med 2012; 37(7): 649-55.
49. Belhocine T, De Barsy C, Hustinx R, *et al.* Usefulness of (18)F-FDGPET in the post-therapy surveillance of endometrialcarcinoma. Eur J Nucl Med Mol Imaging 2002; 29(9): 1132-9.
50. Ryu SY, Kim K, Kim Y, *et al.* Detection of recurrence by 18F-FDGPET in patients with endometrialcancershowing no evidence of disease. J Korean Med Sci 2010; 25(7): 1029-33.
51. Kitajima K, Suenaga Y, Ueno Y, *et al.* Value of fusion of PET and MRI in the detection of intra-pelvic recurrence of gynecological tumor: comparison with (18)F-FDG contrast-enhanced PET/CT and pelvic MRI. Ann Nucl Med 2014; 28(1): 25-32.
52. Schwarz JK, Grigsby PW, Dehdashti F, *et al.* The role of 18F-FDG PET in assessing therapy response in cancer of the cervix and ovaries. J Nucl Med 2009; 50(Suppl 1): 64S-73S.
53. Limei Z, Yong C, Yan X, *et al.* Accuracy of positron emission tomography/computed tomography in the diagnosis and restaging for recurrent ovarian cancer: a meta-analysis. Int J Gynecol Cancer 2013; 23(4): 598-607.
54. Jewell EL, Kulasingam S, Myers ER, *et al.* Primary surgery

versus chemoradiation in the treatment of IB2 cervical carcinoma: a cost-effectiveness analysis. Gynecol Oncol 2007; 107(3): 532-40.
55. Pandharipande PV, Choy G, del Carmen MG, *et al.* MRI and PET/CT for triaging stage IB clinically operable cervical cancer to appropriate therapy: decision analysis to assess patient outcomes. AJR Am J Roentgenol 2009; 192 (5): 1167.
56. Meads C, Auguste P, Davenport C, *et al.* Positron emission tomography/computerised tomography imaging in detecting and managing recurrent cervical cancer: systematic review of evidence, elicitation of subjective probabilities and economic modelling. Health Technol Assess 2013; 17(12): 1-323.
57. Mansueto M, Grimaldi A, Mangili G, *et al.* Positron emission tomography/computed tomography introduction in the clinical management of patients with suspected recurrence of ovarian cancer: a cost-effectiveness analysis Eur J Cancer Care 2009; 18(6): 612-9.
58. Smith GT, Hubner KF, McDonald T, *et al.* Cost Analysis of FDGPET for Managing Patients with Ovarian Cancer. Clin Positron Imaging 1999; 2(2): 63-70.

Received: 2.7.2015
Accepted: 13.10.2015
Address: Dr. Luca Tagliabue
Department of Diagnostic Imaging
Nuclear Medicine Unit, University Hospital “S.Paolo”
Via A. di Rudinì 8
20142 Milan, Italy
Tel. +39281843072
Fax: +39281844062
E-mail to: luca.tagliabue@ao-sanpaolo.it