The emerging role of PET/CT scanning in the treatment planning of ovarian cancer: A mini-review

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ABSTRACT

Given the many obstacles faced during the treatment of ovarian cancer, usually due to diagnosis at advanced stages, it is crucial to use different means to plan the therapeutic procedure in order to achieve optimal results. Positron emission tomography–computed tomography (PET/CT) is a recent hybrid method of medical imaging that can provide various information on the anatomic and biochemical status of a tumor, as well as possible metastases and hence provide better insights to clinicians for the therapeutic procedure. To this end, the present mini-review explores the role of PET/CT scanning in planning surgical procedures, systemic anticancer therapy and radiotherapy and summarizes the current status of studies that examine the use of PET/CT in the personalized therapy of ovarian cancer. Nonetheless, more clinical and observational studies are required to further verify the use of PET/CT in planning therapeutic procedures for patients with ovarian tumors.

KEYWORDS

PET/CT, ovarian cancer, staging, surgical resection, systemic therapy, radiotherapy

Introduction

Ovarian cancer is the third most common gynecologic cancer in the global population with a relatively high incidence rate [1]. Unfortunately, various obstacles are faced during the treatment of ovarian cancer, mainly because it is often diagnosed at a late stage and quickly spreads to regions of the abdomen and pelvis [2, 3]. Hence, for cases of ovarian cancer there is a crucial need for tools that can assist medical professionals to plan their therapeutic procedure in order to achieve optimal results. One of the widely used means in cancer treatment planning is medical imaging, which can provide information for planning surgical operations, systemic therapy and radiotherapy [4–6].

Positron emission tomography–computed tomography (PET/CT) is an emerging hybrid method of nuclear imaging which is widely used in the field of oncology due to its high precision in detecting tumors [7]. PET/CT scanning can detect both biochemical and anatomical alterations across regions of the body, giving it the ability to detect even small numbers of tumor cells due to the differences in tumor cell metabolism compared to healthy cells [7, 8].

Thus, given the wide use of PET/CT scanning in cancer management, the present narrative review provides an overview of the current status and future perspectives of using PET scanning in the treatment planning of ovarian malignancies.

The use of PET/CT in the surgical management of ovarian cancer

Before the surgical removal of an ovarian tumor, it is of paramount significance to precisely detect the position and the stage of the tumor, in order to detect the resection margins during
the operation and assess the outcomes of the operation [9, 10]. Moreover, lymph node dissections and other operations should be performed by the surgeon in case of lymph node metastases or distant metastases respectively [11]. Therefore, it is crucial to assess all such alterations prior to planning surgical operations, preferably using non-invasive techniques such as medical imaging.

**Preoperative determination of the primary surgical site**

Although PET scanning alone may not be accurate in determining the anatomical site of a tumor, PET/CT can provide accurate information on the site of a tumor and therefore assist the determination of the primary surgical resection margins [12, 13]. In fact, although studies have not assessed the diagnostic performance of PET/CT in the determination of the primary surgical site, rationally PET/CT would show superiority over a CT scan due to the detection of metabolic alterations. Nonetheless, it is worth mentioning that most often PET/CT does not use contrast agents and thus the morphological information it provides may be less than a diagnostic CT scan [14].

**Preoperative determination of lymph node metastases**

The assessment of lymph node metastases status prior to ovarian cancer surgery is very important since it can indicate the need of lymph node dissections [15]. One the main predicaments faced in ovarian cancer is the fact that occult lymph node metastases in distant nodes may be present in patients who apparently seem to be staged as N0 through examinations [16, 17]. By PET/CT, it is possible to detect lymph node metastases in any region of the body, including occult metastases [18, 19]. More specifically, a meta-analysis in 2021, retrieved a sensitivity and specificity of 0.81 (95% confidence interval [CI]: 0.61–0.92) and 0.96 (95% CI: 0.91–0.99) for the diagnostic accuracy of PET/CT in detecting lymph node metastases in patient with ovarian cancer and presented superiority over a normal CT scan [20]. It is also worth noting that studies have indicated that PET scans can accurately detect occult lymph node metastases in patients assumed to be at N0 stage [21, 22]. For example, Fig. 1 depicts such a case, in which the node metastases were detected through PET/CT.

**Preoperative determination of distant organ metastases**

Prior to a surgical operation in ovarian cancer patients, it also necessary to determine any distant organ metastases, especially peritoneal metastases which have already occurred in the majority of patients at the time of diagnosis [23–25]. Medical imaging is deemed crucial for determining distant metastases prior to surgical removal of ovarian tumors, in order to avoid multiple operations and plan the surgical dissection of the tumor as well as metastases sites, if possible [26]. Regarding the use of PET/CT, a systematic review and meta-analysis conducted by Han et al., concluded that PET/CT can accurately identify distant metastases in the peritoneum, the pleural cavity, the lungs and the liver, with an overall sensitivity and specificity of 0.72 (95% CI: 0.61–0.81) and 0.93 (95% CI: 0.85–0.97) respectively [27]. The lower sensitivity of detecting for distant metastases, such as peritoneal metastases, is partly the consequence of the limited spatial resolution of the PET scan [28].

** Determination of postoperative recurrence**

Despite a successful surgical operation and a maintenance systemic therapy regimen, ovarian cancer relapses in approximately 80% of patients due to a delay in the initial diagnosis [29]. In such cases, studies have indicated that a secondary surgical operation may benefit patients and medical oncologists usually suggest a secondary operation to remove new tumors or prior residuals alongside with chemotherapy [30, 31]. The use of PET/CT for detecting ovarian cancer recurrence and new tumor sites is recommended, since the specificity and sensitivity of $^{18}$F-FDG...
PET/CT for detecting the recurrence of ovarian carcinoma have been found to be 0.88 (95% CI: 0.79–0.93) and (95% CI: 0.72–0.96) respectively in a recent meta-analysis [32]. This can help a successful planning process for secondary surgical operations. Figure 2 shows imaging results of a patient with recurrent ovarian cancer.

**The use of PET/CT in the systemic therapy planning of ovarian cancer**

Recently, various clinical studies are being undertaken to assess whether the use of PET/CT can predict patient prognosis after chemotherapy and thus conclude whether the conduction of chemotherapy or targeted therapy cycles would benefit the patient, especially regarding neoadjuvant chemotherapy prior to surgery [34]. Indeed, a study by Martoni et al. suggests that ovarian cancer patients who present a plunge in the Maximum Standard Unit Value (SUVmax) after three courses of chemotherapy, are more likely to respond to the regimen and would benefit from undergoing another three sessions [35]. Moreover, it has been suggested that there is a positive correlation between the fluorine 18-fluorodeoxyglucose (FDG) uptake of ovarian cancer cells in PET/CT and the prognosis of patients following cycles of neoadjuvant or maintenance chemotherapy in patients with primary tumors, as well as patients with recurrent disease [36]. It is also worth mentioning that recent studies have revealed that using the novel fluorine-fluorothanatrace (18F-FTT) radiotracer, it is possible to evaluate poly-ADP-ribose polymerase 1 (PARP-1) expression with PET scanning in ovarian tumors, and therefore evaluate to what extent targeted therapy using PARP-1 inhibitors would benefit the patient [37–39].

**The use of PET/CT in the radiotherapy planning of ovarian cancer**

Prior to the initiation of radiotherapy in ovarian cancer patients, information regarding the exact position of the tumor as well as possible metastases must be provided to the radiation oncologist [40]. As known, PET/CT can help provide this information in both patients with primary and recurrent ovarian cancer with high accuracy [12, 20, 27, 32]. Moreover, when it comes to radiotherapy one of the main principles is to adjust the radiation dose with accordance to the number of cancer cells present in a specific region and this can be done through the use of PET/CT which can determine metabolic alterations across the regions of a tumor [41].

It is worth noting that there is a new emerging method of radiotherapy known as intensity-modulated radiation therapy (IMRT), which uses linear accelerators controlled by computers to deliver radiation beams with different intensities across a tumor with accordance to the characteristics of a tumor and its metastases in order to increase the precision and the effectiveness of the therapeutic procedure [42, 43]. More specifically, clinical trials are being undertaken in the recent years in order to evaluate the use of IMRT in the treatment of advanced and recurrent ovarian cancer [44, 45]. Since IMRT requires accurate data, the use of medical imaging techniques such as PET/CT prior to treatment planning is necessary [46]. Indeed, studies have confirmed that the use of PET/CT scanning in patients with advanced or recurrent ovarian cancer can assist the treatment planning of IMRT and result in more effectiveness of the therapeutic procedure [47, 48]. Figure 3 depicts the case of an ovarian cancer patient with colon metastases, prior to and after a complete cycle of radiotherapy.

**Discussion and conclusions**

Overall, one can conclude that results from PET/CT scanning in ovarian cancer patients can be effectively used to assist different medical professionals (e.g., surgeons, medical oncologists and radiation oncologists) to plan different therapeutic procedures more effectively. Although other imaging methods, such as ultrasound and MRI imaging are also clinically used for imaging ovarian cancer.
imaging, they are unable to provide any information regarding any biochemical changes and thus may fail to detect recurrence at earlier stages [49]. More specifically, PET/CT can contribute to the progress of personalized treatment planning for in different fields of oncology, including ovarian cancer therapy [50–52]. Nevertheless, the use of PET/CT in some fields, such as systemic therapy planning has not been yet included in some guidelines. Hence, there is a significant need of conducting further clinical and observational studies and subsequently, meta-analyses, in order to further verify the use of PET/CT in treatment planning procedures. Most likely, the use of PET/CT in treatment planning will expand in the near future.

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REFERENCES


The emerging role of PET/CT


