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Review

Risk stratification and prognosis determination using ^{18}F-FDG PET imaging in endometrial cancer patients: A systematic review and meta-analysis

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RESEARCH HIGHLIGHTS

- Prognostic importance of 18-F-FDG PET in endometrial cancer is reviewed.
- Pooled average SUVmax was higher in high risk patients vs. low risk ones.
- Pooled HR of pre-operative SUVmax for disease free survival was 7.415.

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ABSTRACT

Objectives. In the current study, we systematically searched and analyzed the available literature on the prognostic value of semi-quantitative ^{18}F-FDG PET imaging (SUVmax/mean) in patients with endometrial cancer and presenting the results in a meta-analytic format.

Methods. Pubmed, SCOPUS, and ISI Web of Knowledge were searched using "endometr* AND PET" as the search algorithm. All studies evaluating the ^{18}F-FDG PET performance in pre-operative risk stratification or its prognostic value in patients with endometrial cancer were included. Statistical pooling of diagnostic accuracy indices was performed using random effects model. Cochrane Q test and I^2 index were used for heterogeneity evaluation.

Results. Ten studies (771 patients) were included in the systematic review. Pooled average SUVmax values in patients with risk factors [grade III, lymphovascular invasion (LVI), cervical invasion (CI), myometrial invasion (MI) $\geq$ 50%] were statistically higher than those in patients without risk factors. Pooled HR of pre-operative SUVmax for disease free survival was 7.415 [2.892–19.432] ($p = 0.000046$).

Conclusion. Despite higher average SUVmax in the high-risk group compared to the low-risk group of patients with endometrial cancer, the usefulness of ^{18}F-FDG PET SUVmax in classifying patients into pre-defined risk groups seems to be limited. However, pre-operative SUVmax of endometrial tumors seems to be an independent prognostic marker of recurrence and death. Further large multicenter studies with adequate follow-up are needed to confirm our findings.

Contents

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Introduction

Endometrial cancer is the most common gynecological malignancy in the western countries characterized by favorable prognosis due to its early diagnosis [1]. Surgery is the mainstay of treatment which consists of hysterectomy and bilateral salpingo-oophorectomy. A challenging issue in the surgical management of endometrial cancer is the selection of patients with high-risk cancer who would benefit from a more radical surgery and lymphadenectomy [2]. Many researchers have identified several risk factors which are associated with poor prognosis and extra-uterine involvement in patients with endometrial cancer such as myometrial invasion (MI), pathological grade (G), cervical invasion (CI), lymphovascular invasion (LVI), and histological features. For example high grade tumors and those with more than 50% of MI are associated with higher risk of pelvic lymph node involvement and recurrence [3–5]. However, these risk factors can only be identified by surgical staging. Alternative methods such as sentinel node mapping [6] and pre-operative radiological risk stratification have been used in order to identify patients who would benefit from a more radical surgery [7].

Fluorine-18-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) is a functional imaging method used in staging or restaging of numerous malignancies including endometrial cancer and uterine tumors [8–11]. Several studies evaluated the prognostic implication of ^{18}F-FDG PET imaging and its potential value for risk stratification in patients with endometrial cancer by using semi-quantitative indices [maximal and/or mean standardized uptake values (SUVmax and/or SUVmean)]. In the current study, we systematically searched and analyzed the available literature on the prognostic value of ^{18}F-FDG PET imaging in patients with endometrial cancer presenting the results in a meta-analytic format.

Material and methods

The PRISMA guidelines were followed for performing the current systematic review and meta-analysis (http://www.prisma-statement.org). We searched Pubmed and SCOPUS database using the following search algorithm: "endometr* AND PET". The literature search was performed by two authors independently (GH and SR) and it was updated until October 2013 without language or time limit. The reference lists of relevant studies were reviewed for possible missing articles. Articles cited were also searched to find out any other relevant citation (using SCOPUS and Google scholar citation tracking).

Inclusion criteria

Studies which fulfilled one of the following criteria were included in the systematic review: 1 — Evaluation of ^{18}F-FDG PET performance in pre-operative risk stratification of patients with endometrial cancer comparing the SUVmax/mean in the high-risk vs. low-risk patients; and 2 — evaluation of the prognostic value of ^{18}F-FDG PET imaging in patients with endometrial cancer comparing the overall and/or disease free survival in patients with high vs. low SUVmax/mean.

Case reports, letters to editor and review articles were excluded. Studies performed on uterine sarcomas were not included, since uterine sarcoma is different from cancer of the endometrium in terms of cell origin, epidemiology and prognosis [12].

Two authors reviewed independently the retrieved articles. All discrepancies were resolved by the third author opinion (SG). Possible duplicate publications were discussed and only the most recent reports were included. Corresponding authors were contacted when further information was necessary.

Data abstraction

Two authors independently performed the data abstraction, and data on authors, publication year, imaging method, patient characteristics, quality of the included study, semi-quantitative values (SUVmax or SUVmean) were recorded. The SUV is the ratio of the tissue radioactivity concentration and the injected activity divided by the body weight. Outcomes of interest were difference in average SUVmax between high-risk and low-risk patients with endometrial cancer (the risk stratification according to grade, MI, CI, and LVI), sensitivity and specificity of ^{18}F-FDG PET imaging in differentiation between high-risk and low-risk patients, and hazard ratio (HR) of disease free survival and/or overall survival. For estimation of HR from survival curves, Parmar et al. method was used [13]. Oxford center for evidence based medicine guideline was used to assess the quality of prognostic studies [14]. For cross-sectional studies (those evaluating the potential risk stratification of ^{18}F-FDG PET imaging) modified STROBE statement was used [15].

Statistical analysis

Statistical pooling was performed using Dersimonian and Laird method (random effects model) [16]. Cochrane Q test was used for heterogeneity evaluation ($p < 0.05$ was considered statistically significant). The I^2 index was applied to quantify the heterogeneity.

For publication bias evaluation, funnel plots and Egger's regression intercept [17] were used.

All statistical analyses were performed by using Comprehensive Meta-analysis (version 2, Biostat Inc., US) and Meta-Disc (version 1.4, Madrid, Spain) software [18].

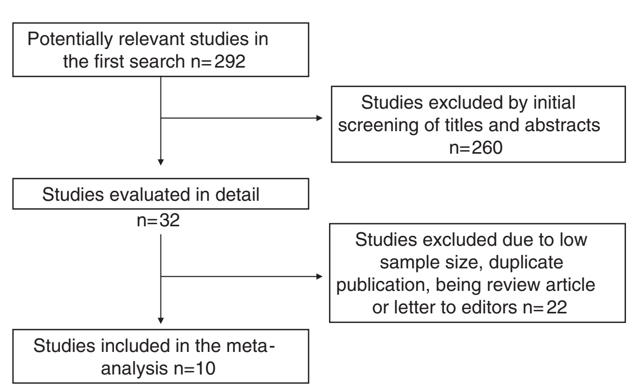

Fig. 1. PRISMA flowchart of the study.