Correlation between Preoperative Diagnosis and Final Pathological Diagnosis of Endometrial Cancer Impact on Management

Thesis

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By

Jilan Tarek Mohammed

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Faculty of Medicine - Ain Shams University

Under supervision of

Prof. Dr. Mohamed Ibrahim Laban

Professor of Obstetrics and Gynecology

Faculty of Medicine - Ain Shams University

Prof. Dr. Alaa Sayed Hassanin

Assistant Professor of Obstetrics and Gynecology

Faculty of Medicine – Ain Shams University

Dr. Salma Ashraf Mohamed Nassar

Lecturer of Obstetrics and gynecology

Faculty of Medicine - Ain Shams University

Faculty of Medicine - Ain Shams University

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Jilan Tarek Mohammed

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Abb.	Full term
AGC	*Atypical glandular cells*
BMI	*Body mass index*
BSO	*Bilateral salpingo-oophorectomy*
D&C	*Dilation and curettage*
EC	*Endometrial carcinoma*
EIN	*Endometrial intraepithelial neoplasia*
FACT-G	*Functional Assessment of Cancer Therapy-General*
FIGO	*International Federation of Gynecology and Obstetrics*
HER2	*Human epidermal growth factor receptor 2*
HNPCC	*Hereditary nonpolyposis colon cancer*
HNPCC	*Hereditary nonpolyposis colorectal cancer*
LACE	*Laparoscopic Approach to Cancer of the Endometrium*
LND	*Lymph node dissection*
MIS	*Minimally invasive surgery*
MSI	*Microsatellite instability*
OS	*Overall survival*
PCOS	*Polycystic ovary syndrome*
PFS	*Progression-free survival*
QOL	*Quality of life*
SLND	*Sentinel lymph node dissection*
TH	*Total hysterectomy*
TLH	*Total laparoscopic hysterectomy*
WHO	*World Health Organization*

INTRODUCTION

Endometrial cancer is the most frequent gynecological malignancy in developed countries and is the second most common in developing countries ***(Ferlay et al., 2013)***. However, the majority of patients suffering of this tumor are diagnosed at an early-stage, which fortunately results in overall high cancer-specific survival rates after a surgical treatment ***(Benedet et al., 2000)***. In these settings, simple total hysterectomy (TH) plus bilateral salpingo-oophorectomy (BSO) remains a cornerstone for the management of endometrial cancer ***(Benedet et al., 2000)*** whereas the value of systematic lymph node dissection is a matter of great debate ***(Creasman et al., 2010).***

The standard diagnostic evaluation for endometrial cancer includes pelvic ultrasonography and endometrial biopsy regardless of the diagnostic method: dilatation and curettage (D&C), Pipelle, or hysteroscopy ***(Oncoguı´a, 2016)***. Although some authors recommend hysteroscopy-guided biopsy in the diagnostic evaluation for endometrial cancer, Pipelle-guided biopsy and D&C have also demonstrated an acceptable diagnostic accuracy ***(Lee et al., 2011)***.

Due to the lack of benefit of systematic lymphadenectomy for women with clinically early-stage endometrial cancer at low risk of lymph node metastasis ***(Benedetti Panici et al., 2008),*** the preoperative identification

of these patients emerged as key for the proper surgical management of this malignancy ***(Kang et al., 2012)***. Accordingly, several models have been proposed to predict nodal metastasis taking into account preoperative parameters**,** whereas the histology and grade of endometrial cancer are well-known predictors of nodal involvement ***(Son et al., 2015).***

Comprehensive surgical staging allows precise diagnosis of the disease and its extent, identification of high-risk patients for recurrence, tailoring of patients for adjuvant therapy to decrease the relapse risk and determination of the prognosis ***(Falcone et al., 2014)***. Despite these advantages, clinical staging still holds significant importance in several instances. It is valuable for patients who are not candidates for a hysterectomy due to morbid obesity or cardiopulmonary dysfunction that render surgery or anesthesia too risky ***(Jones et al., 2014)***.

Thus, the assessment of endometrial sampling as a predictor of final surgical pathology in endometrial cancer is an important point to be scrutinized, since the surgical staging decisions are often based on a preoperative biopsy in most of oncological centers ***(Tuomi et al., 2015)***.

This current study aimed to identify the accuracy of preoperative endometrial sampling obtained by dilatation and curettage, Pipelle and hysteroscopy compared to the final pathology and grading of endometrial cancer patients after surgical staging and to determine whether patients were over-, under- or properly treated.

AIM OF THE WORK

To asses retrospectively the impact of the method used in pre-operative diagnosis of endometrial cancer on final diagnosis and plan of management.

Research question:

Is the preoperative method used in the diagnosis of endometrial cancer correlates well with the final histopathological diagnosis?

Research hypothesis:

Method used for pre-operative diagnosis of endometrial cancer has a great impact on the final diagnosis

Chapter 1
ENDOMETRIAL CARCINOMA

Background

Corpus cancer is the most frequently occurring female genital cancer. In developed countries, adenocarcinoma of the endometrium is the most common gynecological cancer; however, in developing countries, it is much less common than carcinoma of the cervix ***(De Haydu et al., 2015)***.

Etiology

Multiple epidemiological risk factors have been identified in patients who have adenocarcinoma of the endometrium.

Endogenous factors

Obesity

Nulliparity

An individual who has had a late menopause (aged >52 y)

Unopposed estrogen

Unopposed estrogen, either as replacement therapy or endogenously produced (eg, granulosa cell tumor, polycystic ovarian disease), increases the risk of endometrial cancer ***(Njorge et al., 2010)***.

Obesity is known to increase endogenous estrogen because the presence of fat appears to be responsible for the conversion of androstenedione to estrogen compounds at a much higher rate than if fat is not present. Anovulation, which may be secondary to unopposed estrogen, also appears to contribute to this situation ***(Zeimet et al., 2013)***.

Tamoxifen

The most widely used anticancer drug is tamoxifen, and this drug has been suggested by some studies to cause an increased incidence of adenocarcinoma of the endometrium. These data were derived from retrospective analyses in which adenocarcinoma of the endometrium was not an end point in multiple prospective randomized studies evaluating the role of tamoxifen in patients with breast cancer ***(Bernstein et al., 1999)***.

Combination oral contraceptives

In contrast to tamoxifen, increasing data indicate that the use of combination oral contraceptives (OCs) decreases the risk of developing endometrial cancer ***(Chan et al., 2006)***.

Cigarette smoking

Smoking apparently decreases the risk of developing endometrial cancer. The effects of smoking are related to body weight. Heavier women who smoke have the greatest reduction

in risk. Women who smoke are known to undergo menopause 1-2 years earlier than women who do not smoke ***(Seagle et al., 2017)***.

Associated medical conditions

Some associated medical conditions have been found to increase the incidence of endometrial cancer. Breast, colon, and ovarian cancers are frequently observed in women with endometrial cancer. Data suggest that women who have had breast cancer have a 2- to 3-fold increased risk of subsequently developing endometrial cancer ***(Colombo et al., 2013)***.

Women who have hereditary nonpolyposis colon cancer (HNPCC) appear to have a markedly increased risk for developing endometrial cancer. Women with HNPCC account for only 2-10% of all female cases of colon cancer, but approximately 5% of all endometrial cancers occur in women with this risk factor. These women have a 27-60% lifetime risk of developing endometrial cancer, and the disease tends to occur at a younger age (46-54yo). The greatest risk of developing endometrial cancer in women with HNPCC occurs from age 40-60 years, at which time the absolute risk is greater than 1% per y ***(Corpus et al., 2010)***.

Family history

Individuals with a family history of endometrial cancer appear to be at increased risk ***(Klopp et al., 2014)***.

Phenotype characteristics

At one time, a classic phenotypic characteristic was thought to exist for a woman who would develop endometrial cancer. This phenotype included patients who were obese, nulliparous, and anovulatory in many instances ***(Salani et al., 2011)***.

Prognosis

Multiple prognostic factors exist for endometrial cancer. These prognostic factors generally are related to surgical pathologic findings. As in all cancers, the stage of the disease is the most important prognostic factor. Obviously, the surgical procedure helps determine the stage. Listed below are prognostic factors that may relate specifically to the stage of the disease and, thereby, may affect overall survival ***(National Cancer Institute, 2018)***.

Prognostic factors - histopathologic subtypes

Most endometrial carcinomas are endometrioid adenocarcinomas. Adenoacanthomas (benign squamous components) and adenosquamous carcinoma (malignant squamous components) make up the next largest category.

Clear cell and papillary serous adenocarcinomas represent approximately 10% of all endometrial cancers and are considered to be poor histopathologic subtypes. These latter subtypes tend to have deeply invasive myometrial involvement, and they have a propensity for extrauterine spread, even though the myometrium may be superficially involved ***(Trovik et al., 2013)***.

Histologic differentiation

The degree of histologic differentiation of endometrial cancer has long been accepted as a sensitive indicator of prognosis. Patients with well-differentiated adenocarcinomas tend to have involvement of the endometrium or superficial myometrium, and extrauterine disease is unusual ***(Hubbs et al., 2013)***.

However, if a poorly differentiated lesion is present, these cancers tend to be much more aggressive, involving significant myometrial invasion, and often have extrauterine metastasis, either with positive peritoneal cytology, retroperitoneal spread, or involvement of the pelvic and/or para-aortic lymph nodes. Because papillary and clear cell carcinomas are associated with a relatively poor prognosis, these subtypes are not usually graded but are considered in the same category as a poorly differentiated cancer ***(National Cancer Institute, 2018)***.

Myometrial invasion

The degree of myometrial invasion continues to be a consistent indication of tumor virulence. As the depth of myometrial invasion increases, the chance of having extrauterine disease is greater ***(Colombo et al., 2013)***.

As noted above, grade and depth of invasion, as a generalization, are interrelated. As the grade of the tumor increases, an increase usually occurs in the depth of myometrial invasion; however, exceptions exist in that a grade 1 lesion can have deep myometrial invasion and a grade 3 lesion can be limited to the endometrium. When grade and depth of invasion are evaluated separately, the depth of invasion appears to be a more important prognostic factor than the grade of the tumor ***(Klopp et al., 2014)***.