A Retrospective Study of the Treatment Results & Patterns of Failure of Type II Endometrial Cancer Patients treated at Radiotherapy Department, NCI, Cairo University during the period from January 2000 till December 2012

Thesis
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ABSTRACT

Aim of the study: To identify all clinico-pathological data, different treatment modalities and the different prognostic factors which affected the locoregional control (LC), disease-free survival (DFS), and overall survival (OS) of Type II endometrial cancer patients

Patients and methods: Data of Type II endometrial carcinoma patients who presented to the Radiation Oncology department, National Cancer Institute, Cairo University during the period from (2000-2012) were retrospectively reviewed .

Results and conclusions: Multivariate analysis identified stage as an independent prognostic factor for OS & DFS, and age was an independent prognostic factor for DFS and LC. Low pretreatment hemoglobin levels significantly affected OS.

Large and multicentric clinical trials are required to further study this group of patients and define optimum treatment modalities.

Keywords: Endometrial carcinoma, Radiotherapy, Chemotherapy

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List of abbreviations

BSO	Bilateral Salpingo-Oophorectomy
BT	Brachytherapy
CA	Cancer Antigen
CI	Confidence Interval
CR	Complete Remission
CRC	Colorectal Cancer
CT	Computed Tomography
CTV	Clinical Target Volume
D&C	Dilatation and Curettage
DFS	Disease-Free Survival
DM	Diabetes Milletus
DSS	Disease-Specific Survival
EBRT	External Beam Radiotherapy
ECOG	Eastern Cooperative Oncology Group
EIC	Endometrial Intraepithelial Carcinoma
EIN	Endometrial Intraepithelial Neoplasia
EORTC	European Organization for the Research and Treatment of Cancer
ESGO	European Society of Gynecologic Oncology
ESMO	European Society of Medical Oncology
ESTRO	European Society of Radiothearpy and Oncology
FDG	Fluorodeoxyglucose
FIGO	International Federation of Gynecology and Obstetrics
GOG	Gynecologic Oncology Group
GIT	Gastrointestinal Tract

Gy	Gray
HB	Hemoglobin
HDR	High Dose Rate
HIR	High Intermediate Risk
HNPCC	Hereditary Non-Polyposis Colorectal Cancer
HR	Hazard Ratio
HRT	Hormone Replacement Therapy
HTN	Hypertension
ICRU	International Commission on Radiation Units and Measurements
IGF	Insulin-like Growth Factor
IHD	Ischemic Heart Disease
IR	Insulin Resistance
LC	Local Control
LDR	Low Dose Rate
LH	Luteinizing Hormone
LND	Lymph Node Dissection
LOE	Level Of Evidence
LUS	Lower Uterine Segment
LVSI	Lymphovascular Space Invasion
MMMT	Malignant Mixed Mesodermal Tumor
MRI	Magnetic Resonance Imaging
NCI	National Cancer Institute
NCRP	National Cancer Registry Program
NGR	No Gross Residual
NSOG	Nordic Society of Gynecologic Oncology
OAP	Overall Treatment Period

OCP	Oral Contraceptive Pills
OS	Overall Survival
PCOS	Polycystic Ovarian Syndrome
PET	Positron Emission Tomography
PFS	Progression-Free Survival
PORTEC	Post Operative Radiotherapy in Endometrial Cancer
PTV	Planning Target Volume
RCT	Randomized Controlled Trial
RH	Radical Hysterectomy
RR	Response Rate
RT	Radiotherapy
RTOG	Radiation Therapy Oncology Group
SCC	Squamous Cell Carcinoma
SGO	Society of Gynecologic Oncology
SEER	Surveillance, Epidemiology & End Results
SHBG	Sex Hormone-Binding Globulin
SLN	Sentinel Lymph Node
SPSS	Statistical Package for Social Sciences
TAH	Total Abdominal Hysterectomy
TCC	Transitional Cell Carcinoma
TVUS	Transvaginal Ultrasonography
UTI	Urinary Tract Infection
WAPI	Whole Abdominal and Pelvic Irradiation

Introduction:

Endometrial cancer is the sixth most common cancer in women worldwide & one of the most frequently occuring female genital cancers, with 320,000 new cases diagnosed in 2012. **(Global cancer Atlas - Globocan- 2012)**

The main risk factor to developing endometrial cancer is prolonged periods of unopposed estrogen. This may be due to nulliparity, late menopause, obesity, polycystic ovarian syndrome (PCOS), hormonal replacement therapy (HRT) or the prolonged use of Tamoxifen. **(Braun et al. 2016)**

The most common presenting symptom is postmenopausal vaginal bleeding (90%). **(Salman et al. 2013)**

Endometrial carcinomas are classified into two major histological subtypes: **(Bokhman et al. 1981).**

Type I are tumors of endometrioid histology, these comprise approximately 80 percent of endometrial carcinomas. These tumors typically have a favorable prognosis, are estrogen responsive, and may be preceded by an intraepithelial neoplasm (atypical and/or complex endometrial hyperplasia). **(Albertini et al. 2012)**

Type II tumors on the other hand account for 10 to 20 percent of endometrial carcinomas. These include tumors of non-endometrioid histology: serous, clear cell, squamous, transitional cell, and undifferentiated. Uterine carcinosarcomas are also included in this subtype. **(Albertini et al. 2012)**

The primary treatment of endometrial carcinoma is surgery. Total Hysterectomy, Bilateral salpingo-oophorectomy (BSO) with or without sampling or removal of pelvic lymph nodes is generally performed. **(Bourgin et al. 2016)**

Patients are then risk stratified according to many factors such as age, stage, grade, histological subtype, and lymphovascular invasion. Providing further adjuvant treatment with radiotherapy / chemotherapy will depend on this risk stratification. (**Colombo et al. 2015)**

The Proposed Aim of this work is to:

- Study the clinical and pathological characteristics of Type II endometrial carcinoma patients.
- Study the patient management and their outcomes.
- Identify the common treatment-related side effects & toxicities.
- Analyze the potential prognostic factors affecting Locoregional Control, Disease-Free Survival and Overall Survival.

1.1. Epidemiology:

Endometrial cancer is the sixth most common cancer in women worldwide (fourteenth most common cancer overall), with almost 320,000 new cases diagnosed in 2012 worldwide. **(Global cancer Atlas -Globocan- 2012)**

The global incidence of this cancer was 8.3 women per 100,000 female population in 2012, which represents 4.8% of total cancer incidence. About 1,200,000 women were estimated to be alive with the disease within the last 5 years, ie; the 5 year prevalence of this cancer worldwide was 46.8 women per 100,000 female population in 2012. **(Global cancer Atlas -Globocan- 2012)**

It is estimated that endometrial cancer was the cause of death of 76,000 women worldwide in 2012, a mortality rate of 1.8 women per 100,000 female population. **(Global cancer Atlas -Globocan- 2012)**

According to the National Cancer Registry Program (NCRP) in Egypt, the crude rate of endometrial carcinoma between years 2008-2011 was 0.7 cases per 100,000 females, representing 0.62% of total cancers. The incidence was highest among women above 75 years of age (12.1 cases per 100,000 women). **(Ibrahim et al. 2014)**

According to the cancer pathology registry data at National Cancer Institute (NCI), Cairo University for years 2003-2004, endometrial tumors represented 14.72% of all female cancers and 0.69% of total cancers presented to NCI during the study period. **(Mokhtar et al. 2007)**

Uterine cancer is typically a cancer of postmenopausal women. According to the Surveillance, Epidemiology & End Results (SEER) registry, most cases are