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The role of preoperative routine computed tomography scanning in the estimation of high-risk factors in endometrial cancers

G. Coban[1], G. Erbay[2], F. Kose[3], S. Alemdaroglu[1], C. Onal[4], H. Celik[1]

[1] Başkent University, Medical School, Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, (Adana Campus), Adana; [2] Başkent University, Medical School, Department of Radiology, (Adana Campus), Adana
[3] Başkent University, Medical School, Department of Medical Oncology, (Adana Campus), Adana
[4] Başkent University, Medical School, Department of Radiation Oncology, (Adana Campus), Adana (Turkey)

Summary

Objective: To examine the role of preoperative computed tomography (CT) in estimation of the high-risk factors in endometrial cancer cases. *Materials and Methods:* The data from 161 cases who were diagnosed with endometrioid adenocarcinoma with endometrial biopsy, and staged surgically were retrospectively analyzed. The diagnostic performance of a whole abdominal CT scan in terms of tumor diameter, myometrial invasion, cervical, adnexal, omental involvement, as well as pelvic para-aortic nodal involvement was examined. In addition, extra-uterine and extra-nodal incidental signs were identified. *Results:* The accuracy rate of preoperative CT scanning was found to be 42%, 78%, 80%, 95%, 97%, 88%, 89%, and 88% for tumor diameter, myometrial invasion, cervical, adnexal, and omental involvement, as well as pelvic para-aortic nodal involvement, respectively. Extra-uterine and extra-nodal incidental signs were identified in 18% of the cases. Incidental findings entailed a modification of management only in one case (0.62%). *Conclusion:* Preoperative CT scan findings do not present an alternative to intraoperative frozen section analysis or surgical staging. However, based on the findings from the preoperative CT scan, accuracy of predictions about which patients require more complex procedures (lymphadenectomy) can be improved, and therefore preoperative CT scanning may prove useful in more effective use of operating rooms.

Key words: Computed Tomography; Endometrioid endometrial cancer; Imaging.

Introduction

The surgical approach to endometrioid type endometrial cancer has undergone a radical change in recent years. In the past, pelvic (PLN) and para-aortic lymphadenectomy (PALN) was performed along with hysterectomy and bilateral salpingo-oophorectomy (BSO) in all patients, while recently it has become common practice not to perform lymphadenectomy (LND) routinely in endometrial cancer patients categorized as low-risk (limited to corpus; tumor diameter (TD) over 2 cm; myometrial invasion (MI) over 50%; grade-1, 2 endometrioid type), as the risk of nodal involvement in endometrial cancer patients is very low [1, 2]. Currently, endometrium cancer patients with low-, intermediate-, and high-risk factors are identified through the intraoperative frozen section analysis of hysterectomy material. Studies report a high degree of consistency between the intraoperative frozen section analysis findings and final histopathology results [3, 4]. However, in cases who are found to be not low-risk and require LND, the current management based on frozen analysis does not appear optimal, given the factors such as LND being a more specific operation, requiring a different preoperative preparation, necessitating additional expertise and time, as well as entailing more effective use of the time in the operating room.

Numerous studies have been conducted with imaging methods including magnetic resonance imaging (MRI), ultrasonography (US) and computed tomography (CT), and positron emission tomography CT (PET-CT) in order to determine the metastasis of the disease and/or uterine risk factors in the preoperative period [5]. Still, a consensus could not be reached on an optimal imaging method that is able to meet the expectations in the preoperative period in consideration of the accuracy, cost-effectivity, and availability of the method, its acceptability by the patient, and the rates of modifying the treatment plan, and there is an obvious need for further research in this area [6].

Interestingly, there are relatively fewer studies conducted with CT as a preoperative imaging method [5]. However, CT scanning enjoys significant advantages, like being more available and inexpensive, as well as faster in providing images, and having a high spatial resolution. Furthermore, accuracy of CT scans has improved in recent years through the spiral/helical and multidetector technologies. In a limited number of studies, CT scanning was reported to have high rates of accuracy in myometrial invasion and cervical involvement and high specificity and negative predictive values in nodal involvement [7, 8].

The present study aims to examine the role of the use of routine preoperative CT to identify uterine high-risk fac-

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tors and extra-uterine disease in cases with endometrioid type endometrial cancer.

Materials and Methods

The study was conducted on the retrospective records of consecutive patients who were diagnosed with endometrial cancer with endometrial biopsy and surgically treated from February 2012 to September 2016.

In the study, data from 280 cases who were operated on by the same surgical team were collected. The study included 161 patients who were diagnosed with endometrioid type endometrial cancer and on whom preoperative whole abdominal CT scanning and standard staging surgery (hysterectomy + BSO + PLN + PALN + omental biopsy + collection of wash fluid) were performed. Cases who did not undergo PLN and PALN because of having non-endometrioid or mix histopathology or being low-risk, and those whose preoperative CA was 125>35 IU were not included in the study. Additional morbidities, symptoms, and sociodemographic characteristics of all patients were determined as preoperative clinical information.

Among the preoperative CT findings, MI, TD, cervical, adnexal and omental involvement, and pelvic, and para-aortic nodal involvement were evaluated in all cases diagnosed with endometrial cancer by biopsy. The final histopathological evaluation included, in addition to the histopathological confirmation of all cases, histopathological type, TD, MI, Grade, lympho-vascular space invasion (LVSI), cervical, parametrial, adnexal, omental, pelvic-para-aortic lymph node involvement, and wash fluid. The final histopathological signs were compared with the results of routinely performed preoperative CT to examine the diagnostic performance of preoperative CT scanning in detecting uterine high-risk factors and extra-uterine disease in relation to endometrial cancers. Additionally, the effects of the signs incidentally found in CT evaluation were considered.

The authors' routine approach in cases with endometrial cancers can be briefly described as follows: Preoperative whole abdominal CT is followed by hysterectomy, BSO and frozen-section analysis, and in cases where the analysis reveals results such as grade 2-3, tumor diameter over 2 cm, myometrial invasion over 50%, cervical involvement, adnexal involvement, PLN, and PALN + omental biopsy are added to the operation. When CA-125 was found 125 > 35 IU, staging surgery was performed irrespective of intraoperative frozen-section analysis results. Before hysterectomy, pelvic-abdominal wash fluid was collected from all patients. The operation was performed by laparoscopy or laparotomy.

The radiologist who evaluated the CT results was not blinded to the preoperative endometrial cancer diagnosis. When CT results were analyzed, an intrauterine hypodense mass or endometrial thickening was evaluated as presence of a tumor. MI was categorized as higher or lower than 50%. TD was classified as under or over 2 cm. Cervical involvement was considered the expansion of the internal cervical ostium or cervical canal and classified as present or absent. The evaluation of lymph nodes was expressed as absent or present (larger than 5 mm). Additionally, abnormal adnexal appearance, abnormal omental appearance, peritoneal thickening and irregularities, if any, and abnormal appearance in the parenchymatous organs like liver, kidneys, and surrenal glands was reported.

The routine CT technique can be briefly described as follows: a 16-row CT scanner with 27.5-mm scanning span per rotation was used in CT examinations. As preparation, the patients were administered 1,000 ml of water orally before the examination. To carry out the CT protocol, 120 ml of non-ionic iodinated contrast material (320 mg I/ml, flow rate 3 ml/s) was intravenously administered and the abdomen was scanned with the following parameters: detector collimation 16×1.25 mm, pitch 1.375, rotation time 0.7 s, and kV 120. Before starting scanning, 70 s (portal phase) was left to pass after the administration of contrast material. Dose modulation (DOM) and automatic current settings (DoseRight) were both used and for each scan, the mean mAs per rotation was calculated at 110. A workstation was employed for the interpretation of images. The images obtained from the workstation software were sagittal reformatted images, parasagittal reformatted images (parallel to the longitudinal axis of the uterus body), and oblique transverse images (both perpendicular to the main axis of the uterus body and of the cervical canal), which were 1.25 mm in thickness, at 1.25 mm intervals. Both standardized window settings (W: 350 HU, L: 50 HU) and narrow window settings (W: 250 HU, L: 100 HU) were utilized when interpreting the CT data, narrow window settings serving the purpose of enhancing the contrast between the tumor and the normally enhancing myometrium.

The data were presented as percentage (%) or mean ± standard deviation in the statistical evaluation. Student *t*-test was used in comparisons. Values for which $p < 0.05$ were accepted as significant. Final histopathological findings were taken as the gold standard and the sensitivity, specificity, positive predictive value, and negative predictive value, as well as the accuracy of preoperative CT scanning, were calculated.

Results

Table 1 shows the sociodemographic and clinical features of the cases. It was found that 29% of the operations were performed by laparoscopy and 71% by laparotomy.

There was no difference between the preoperative clinical and sociodemographic features of the patients who had laparotomy and laparoscopy ($p > 0.05$). The final histopathological evaluation did not show any difference between the rates of patients who had uterine high-risk factors and those with extra-uterine disease ($p > 0.05$). The mean number of removed lymph nodes was 71.9 ± 24.7 in the laparotomy group and 47.8 ± 16.7 in the laparoscopy group ($p < 0.05$).

The reported final histopathological results of the patients are presented in Table 2. Of the cases that were found to have adnexal tumor, two had synchronous sex cord-stromal tumor, two had synchronous epithelial ovarian tumor, and one had endometrial cancer metastasis. Histopathological evaluation of lymph nodes revealed that one case had only pelvic lymph node positive, one case had only para-aortic lymph node positive, while all the other cases had both pelvic and para-aortic nodal metastasis.

Retrospective CT analyses of para-aortic nodal metastases showed that only one case (11%) had a tumor larger than 10 mm, while others (89%) had tumors between 5 and 10 mm. Similarly, when CT scans of pelvic nodal metastases were retrospectively analyzed, one patient (11%) was found to have a tumor larger than 10 mm, whereas the tumors in others (89%) were 5 to 10 mm.

In 18% of the cases, CT scanning showed incidental find-

Table 1. — *Sociodemographic and clinical properties of patients (mean ± SD, min-max).*

n: 161	Endometrioid type (mean ± SD)	Min-max
Age (years)	58.8 ± 8.8	35-85
BMI	35.4 ± 8.3	20.4-58.6
HTA (%)	55.6%	
DM (%)	36.6%	
Gravida (mean ± SD)	3.4 ± 2.6	0-16
Parity (n)	3.9 ± 2.1	0-10
Laparotomy	71%	
Laparoscopy	29%	
Presentation symptoms	83% PMB, 6% discharge, 11% AUB	
Other morbidities (thyroid, VHD; CPD)	%33.8	

n: number, mean ± SD: mean ± standard deviation, Min-Max: minimum-maximum, BMI: body mass index, HTA: hypertension, DM: diabetes mellitus, PMB: postmenopausal bleeding, AUB: abnormal uterine bleeding, Thyroid: thyroid diseases, VHD: valvular heart diseases, CPD: chronic pulmonary disease.

Table 2. — *Final histopathological evaluation.*

TD	Over 2 cm (79.5%), below 2 cm (20.5%)
MI	Over 50% (20.5%), below 50 % (65.8%), none (13.7%)
Cxinv	4.3% (+) (6% glandular, 13% stromal + glandular, 17% stromal involvement)
OPM	1.2%
Adnex	3.1% (+)
Grade	Grade 1 (42.1%), Grade 2 (49.7%), Grade 3 (8.2%)
LVSI	30.6%
Wash fluid	1.2% (+)
Para-aortic LNM	5.6% (+)
Pelvic LNM	5.6% (+)

TD: tumor diameter, cm: centimeter, MI: myometrial invasion, Cxinv: cervical involvement, PLNM: pelvic lymph node metastasis; PALNM: para-aortic lymph node metastasis; Total LNM: total lymph node metastasis; OPM: omental peritoneal metastasis, Adnex: adnexal involvement, LVSI: lynpho-vascular space invasion, LNM: lymph node metastasis, (+): positive

Table 3. — *Incidental findings in the preoperative CT.*

Incidental findings 5	n
Simple cyst in the liver	2
Cholelytiasis	2
Cortical cyst in the kidney	13
Surrenal adenoma	6
Nephrolytiasis	1
Pancreatic cyst	1
Colon diverticula	2
Retroaortic left renal vein	1
Right colon tumor	1

Table 4. — *Predictive values for uterine and extra-uterine high risk factors with CT*

	TD	MI	Cx inv.	Adnex	PLNM	PALNM	OPM	Total LNM
Se. (%)	34	18	43	33	75	100	50	87.5
Sp. (%)	76	93	93	99.3	88.5	89.1	97	88.2
PPV (%)	84	42	10	25	14	19	50	28
NPV (%)	23	81	85	96.1	99.2	100	97	99.2
Acc. (%)	42	78	80	95	88	89	97	88

Se: sensitivity, E/E+NE: endometrioid/ endometrioid + non-endometrioid; Sp: specificity, PPV: positive predictive value, NPV: negative predictive value, Acc: accuracy, TD: tumor diameter, MI: myometrial invasion, Cxinv: cervical involvement, Adnex: adnexal involvement, PLNM: pelvic lymph node metastasis, PALNM: para-aortic lymph node metastasis, Total LNM: total lymph node metastasis, OPM: omental peritoneal metastasis.

ings (Table 3). Of these patients, only one was found to have right colon cancer in the preoperative CT scan. After the diagnosis was confirmed by colonoscopy, right hemicolectomy was performed with surgery in the same session. Management was modified in this single case only (0.62%). There was no need for an additional procedure or modification of management in the other cases.

The predictive value of the preoperative CT scan in examining high risk factors in terms of endometrial cancer (TD: over 2 cm, MI: over 2 50%, cervical adnexal, omental/peritoneal, extra-peritoneal nodal involvement) is presented in Table 4.

Discussion

When cases diagnosed with endometrial biopsy are considered, preoperative imaging is not a standard, with the exception of thoracic imaging by chest radiography performed to examine uterine and extra-uterine disease [9]. However, many clinicians generally use one or more preoperative imaging technologies to perform surgical predictions and to form an optimal treatment and follow-up plan.

In the present study, use of the preoperative CT scan to evaluate uterine and extra-uterine risk factors in endometrioid endometrial cancer cases produced high accuracy rates, except tumor diameter. As far as we know, there is no study examining tumor diameter with CT in endometrial cancer. The main explanation for the low accuracy rates found in the present study may be that endometrial biopsy was already performed in all the cases. For the endometrial biopsy procedure, at least one of the hysteroscopic biopsy, pipelle biopsy, and dilatation/curettage methods were used either at the present center or the referring center. CT results may have also been affected by the endometrial changes following the intra-uterine procedure, and conditions like bleeding and collection.

Literature studies comparing CT with USG or MRI reported that CT had a more limited value in detecting myometrial invasion and had a sensitivity of 40% to 83%, specificity of 42% to 75%, and accuracy of 51% to 58% [10, 11]. However, a recent study using multidetector CT found it diagnostic in myometrial invasion and cervical involvement with accuracy rates of 95% and 81%, respectively [7]. The fact that the present accuracy values were higher than those in the literature may be associated with the authors' use of multidetector CT. The present results were close to the results obtained in the study where multidetector CT was used [7]. However, in another study using CT with a multidetector system, sensitivity, specificity, and positive and negative predictive values found in the detection of pelvic and para-aortic lymph node involvement were reported to be 52%, 92%, 50%, and 94%, respectively [8]. The high specificity and negative predictive values found in the literature are consistent with the present findings. However, sensitivity value was also found higher in the present study. This can be explained first by the present setting the lower limit for a positive CT result at 5 mm and secondly by the difference in the lymphadenectomy technique used. In fact, in one of the two similar studies, preoperative CT scanning was performed in only 56 cases and lymphadenectomy was used for sampling, and in the other one, the lower limit for nodal involvement in the preoperative CT was taken to be 10 mm (positive: over 10 mm) and routine, systemic lymph node dissection was not performed [8, 12]. In the present study, however, pelvic and para-aortic lymphadenectomy was used routinely and systematically.

Although there is not an intense debate over how to perform lymphadenectomy, the technique is important at least for the interpretation of the results of this study. That is because there is a correlation between the number of removed lymph nodes and the number of lymph nodes found positive in the final histopathological evaluation. It was reported in a large-scale retrospective study involving the data of 11,443 endometrial cancer patients that as the number of extracted lymph nodes increased, the possibility of detecting positive lymph nodes also rose. The number of removed lymph nodes in the study was classified up to 5, up to 10, up to 20, up to 25, and more than 25. The rate of detecting positive lymph nodes was found to be 27%, 46%, 74%, 85%, and 100%, respectively. It was noted that the appropriate number of lymph nodes that could provide incremental gain in identifying the number of positive lymph nodes ranged between 21 and 25 [13]. Likewise, in a randomized study conducted in 2008, it was established that when lymphadenectomy was performed systematically in intermediate- and high-risk endometrial cancer, the rate of nodal positivity was 13.3%, while the rate dropped to 3.2% when only palpable lymph nodes were removed. In the protocol of the concerned study, the number of lymph nodes to be removed in the lymphadenectomy strand was found to be 20 [14]. In the present study, the number of removed lymph nodes both in the patients who had laparotomy and those who underwent laparoscopy was above 20. Consequently, it can be stated that the present results created a more suitable medium for the confirmation of CT findings with histopathological evaluation, which is the gold standard.

In the few literature studies, it was reported that CT findings obtained by preoperative CT scanning changed the management method in 3% to 8% of the patients. This difference can be explained by the fact that the present patients had pure endometrioid type tumor [8, 12]. In this study, preoperative CT changed the treatment plan in only one patient (0.62%). In this patient, the tumor identified in the right colon with preoperative CT was confirmed by colonoscopy, and right hemicolectomy was performed in the same operation. With the exception of this particular patient, preoperative CT evaluation did not affect the treatment plan.

The main treatment plan in endometrial cancer is shaped by intraoperative frozen section analysis. Pelvic-para-aortic LND and omental biopsy are performed in cases that are found to have at least one of the high-risk factors (TD: over 2 cm, MI: over 50%, Grade 3, cervical, and adnexal involvement) in the frozen analysis. The present results suggest that if planning had been based on the findings of the preoperative CT scanning, the cases could have been estimated in the preoperative period with very high predictive values, so that the operating room program could be made more cost effective. However, these values are not even close to offering an alternative to surgical staging. Even the possibility of using methods like MRI or PET/CT, which have higher predictive values, as an alternative to surgical staging is debatable, and more extensive research is needed in this area [15].

In conclusion, high predictive values found in the present study seem to lend considerable support to the use of preoperative planning for the purposes of determining which procedure will be used in which patient. Thus, it may be possible to make a better preoperative preparation for the patient, operating room time can be spent more cost-effectively, and surgeons' time can be used more productively.

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Corresponding Author:
G. COBAN, M.D.
Başkent University, Medical School
Department of Obstetrics and Gynecology
Division of Gynecologic Oncology (Adana Campus)
Adana (Turkey)
e-mail: drgoncacoban@ yahoo.com