

# Accuracy of two dimensional ultrasonography in detecting lymph node metastasis in cases of uterine and cervical malignancies seen in a tertiary hospital: A five year retrospective study\*

BY KATHLYNN ANN R. DELA LLANA, MD AND KAREEN N. REFORMA, MD, FPOGS

Department of Obstetrics and Gynecology, Philippine General Hospital, University of the Philippines-Manila

## ABSTRACT

**Objective:** This study aims to determine the accuracy of two dimensional ultrasound in detecting lymph node metastasis in uterine and cervical (stage IA2-IIA) malignancies.

**Materials and Methods:** This is a five-year retrospective, cross sectional study conducted for 6 months among uterine and cervical malignancy patients who underwent bilateral pelvic lymph node dissection and para-aortic lymph node sampling with ultrasound performed within two months prior to surgery in a tertiary hospital. Ultrasound findings were compared with histopathologic results as gold standard.

**Results:** The study included 319 patients, 267 uterine and 52 cervical malignancies. Uterine cancer (pelvic-7.1% and para-aortic-2.6%) and cervical cancer (pelvic-1.95%) nodal involvement showed majority having round shape. Mean pelvic nodal size was 1.75 x 0.93cm-uterine, 1.83 x 0.93cm-cervical and para-aortic 3.3x2.0cm-uterine. The study revealed accuracy, sensitivity, specificity, PPV and NPV of 91.5%, 29.4%, 96.4%, 25.0% and 96.0% respectively for pelvic node metastasis and 95.6%, 11.1%, 98.1%, 14.3% and 97.4% respectively for para-aortic involvement. Ultrasound accuracy in detecting pelvic node extension was 98.1%-cervical and 90.3%-uterine (sensitivity-50% vs 26.7%; specificity-100% vs 94.1%; PPV-100% vs 21.1% and NPV-100% vs 95.6%). Para-aortic nodal metastasis detection among cervical and uterine cancer patients showed the following: accuracy (98.1% vs 95.1%), specificity (100% vs 97.7%), and NPV (98.1% vs 97.3%).

**Conclusion:** Two-dimensional ultrasound is reliable in ruling in the presence of pelvic and para-aortic lymph node metastasis among patients with uterine and cervical malignancies. However, its low sensitivity of detection makes it less dependable in ruling out nodal involvement. Larger size and round shape of lymph nodes represent nodal metastasis.

*Keywords: uterine malignancy, cervical malignancy, pelvic lymph nodes, para-aortic lymph nodes, nodal metastasis, two-dimensional ultrasound*

## INTRODUCTION

Worldwide, uterine malignancy is the sixth most common malignancy affecting women. It is the fourteenth most common cancer in the general population.<sup>1</sup> In the United States, it is the fourth most common cancer and the most commonly diagnosed gynecologic malignancy in the female population.<sup>2</sup> The International Federation of Gynecology and Obstetrics (FIGO) staging system for endometrial cancer use surgical and pathological staging for carcinoma of the uterus. Pathologic assessment includes lymph node status.<sup>3</sup>

Uterine sarcomas on the other hand, compose 3 to 8% of uterine malignancies. It includes leiomyosarcoma, endodermal stromal tumors, adenosarcoma and carcinosarcoma.<sup>4</sup>

Cervical cancer is the fourth most common cancer in women, with an estimated 520,000 new cases every year and 266,000 deaths reported worldwide in 2012.<sup>5</sup> More than 85% of the global burden of cervical cancer occurs in developing countries (such as the Philippines). The FIGO cervical cancer staging is based on clinical examination findings, to include tumor size, vaginal and/or parametrial involvement, bladder/rectum extension and distant metastases. It requires radiological imaging such as chest X-ray and intravenous pyelogram. Computed tomography (CT) can detect pathologic lymph nodes, while magnetic resonance imaging can determine tumor size, degree of stromal invasion, vaginal extension and corpus extension

\*Third Place, Philippine Society of Ultrasound in Obstetrics and Gynecology (PSUOG) Research Paper Contest, October 21, 2016, 5/F Function Room 1 & 2 PCAS Tower Wilson Street, Greenhills, San Juan City

with high accuracy. Presence of tumor infiltration lymph node status and the number of lymph nodes infiltrated are the most important prognostic factors.<sup>6</sup>

Most, if not all staging and classification systems for a variety of malignancies include lymph node status and require modalities to assess lymph node invasion. In gynecologic oncology, the most widely used staging system is that derived by the International Federation of Gynecology and Obstetrics (FIGO).<sup>7</sup> A number of diagnostic modalities are available for the assessment of lymph nodes in the background of a gynecologic malignancy. Computed tomography or CT scan and positron emission tomography or PET scan and magnetic resonance imaging or MRI are examples.<sup>3,6</sup> However, these modalities are not readily available in most tertiary centers in the Philippines and, being a developing country with most patients belonging to the low- to medium-level income brackets, cost for these modalities are actually prohibitive. Funds and resources would rather be diverted into the actual treatment of these patients rather than not cost effective pre-operative diagnostics. In the low-resource setting such as the Philippines, therefore the more affordable ultrasound has become an acceptable and affordable pre-operative diagnostic modality, even for assessment of pelvic and para-aortic lymph nodes.

For years, sonologists from the Philippine General Hospital were trained to scan the pelvic and para-aortic regions for the presence of enlarged lymph nodes in cases of gynecologic malignancies, particularly malignancies arising from the cervix and corpus uteri. These sonographic reports guide the surgeons and clinicians in the following: staging, treatment, performing surgery (particularly lymph node dissection), prognosticating and planning post-treatment follow up. This study was conducted to determine the diagnostic accuracy of ultrasound in detecting lymph node metastasis in cases of uterine and cervical cancer. Sonographic characteristics, specifically the size and the shape of the lymph nodes associated with nodal metastasis. Correlation was done with histopathologic results as gold standard for diagnosis.

## **SIGNIFICANCE OF THE STUDY**

---

This study determined the accuracy of pre-operative two dimensional ultrasonography in detecting lymph node metastasis in cases of cervical and uterine malignancies. The pre-operative ultrasound was limited to two months or less prior to surgery. The study correlated the sonographic characteristics of lymph nodes, particularly the size and shape to the final histopathologic reports. It is hoped that the results will help both the Sections of Ultrasound and Gynecologic Oncology in diagnosis and management of

pelvic malignancies in the surgical and post-treatment care of their patients.

## **SCOPE AND LIMITATIONS OF THE STUDY**

---

The study was limited to cases of uterine (carcinoma and sarcoma) and cervical malignancies who underwent bilateral pelvic lymph node dissection and para-aortic lymph node sampling and an ultrasound performed within two months prior to the surgery. Both the ultrasound scan and surgery were performed at the Philippine General Hospital. The aim of the study was to determine the accuracy of ultrasound in detecting lymph node metastasis confirmed by histopathology. The study population in cases of cervical malignancies was limited to stages IA2 to IIA2 where surgery was a treatment option. Correlation of the skill of the sonologists was not done in this study.

## **GENERAL OBJECTIVE**

---

To determine the accuracy of two dimensional ultrasound in detecting lymph node metastasis in cases of uterine and cervical (stage IA2 to IIA) malignancies.

### **Specific Objectives**

1. To describe the demographic profile of patients with uterine and cervical malignancies.
2. To describe the histologic type of uterine and cervical malignancies seen over the past five years.
3. To describe the sonographic features in terms of size and shape of lymph nodes in cases of uterine and cervical malignancies.
4. To determine the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ultrasound in detecting lymph node metastasis.
5. To stratify the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ultrasound in detecting pelvic and para-aortic lymph node metastasis according to the type of malignancy.

### **Definition of Terms**

For the purpose of this study, the following terms are defined as:

**UTERINE CANCER/MALIGNANCY** – a malignancy (carcinoma or sarcoma) arising primarily from the uterine corpus either the endometrium or myometrium regardless of histologic type or stage, and no sonographic nor histopathologic evidence of a secondary malignancy arising from any pelvic and/or extra-pelvic organ.

**CERVICAL CANCER/MALIGNANCY** – a malignancy arising primarily from the cervix uteri regardless of histologic type, with stages IA2 to IIA2 and no sonographic nor

histopathology evidence of secondary malignancy arising from any pelvic and/or extra-pelvic organ.

**LYMPH NODES** – a component of the lymphatic system that are round or oval linked by lymphatic vessels that filters infectious particles and/or malignant cells. Sonographically, they are well-defined, hypoechoic structures located adjacent or along a blood vessel (i.e. iliac vessels or aorta).

**ULTRASOUND REPORT** – a print out or electronic file of a complete sonographic report derived after conduct of either transabdominal or transvaginal ultrasound or both performed solely by a consultant or fellow of the Section of Ultrasound under the Department of Obstetrics and Gynecology of the tertiary hospital within two months from the patient's surgery. The report must have complete identifying data, sonographic description and impression of the disease. In this study, the shape of the lymph node will be derived using the formula as described by Duda, et al. 2012. It will be considered ovoid in shape if the longitudinal axis (L) divided by the transverse or short axis (S) is  $\geq 2$ . It will be considered round if the value of L/S is  $< 2$ .

**HISTOPATHOLOGIC REPORT** – a print out or an electronic file of a complete histopathologic report and gross and microscopic examination of a specimen from a case diagnosed as either uterine or cervical malignancy performed solely by a consultant or resident of the Department of Pathology of a tertiary institution. The reports must have a complete identifying data, histopathologic description and impression of the disease.

## **METHODOLOGY**

---

### Study Design

This is a five-year diagnostic validation study employing a retrospective, cross sectional study design.

### Setting

Section of Ultrasound, Department of Obstetrics and Gynecology, in a tertiary hospital.

### Duration

This study was conducted for 6 months.

### Sampling Design

This study utilized purposive sampling, provided that all of the subjects/cases within the study period were included based on the inclusion and exclusion criteria.

### Sample Size

Based on the previously stated sensitivity (67%) and specificity (88%), with a precision of twenty percent (20%), a ninety five percent (95%) confidence level and, seven

percent (7%) of the patients had positive lymph nodes on histopathology, a minimum sample size of 315 cases were needed for this study. This sample size was computed using template of Naing (2004).

### Study Maneuvers

This is a validation study based on a five-year retrospective review of cases of uterine and/or cervical malignancies. The protocol was technically reviewed and improved by the Section of Ultrasound and Research Committee of the Department of Obstetrics and Gynecology. Thereafter it was sent to the Research Ethics Board for approval. Once approved, the subjects were identified from the 2010, 2011, 2012, 2013 and 2014 logbooks of surgical procedures of the Section of Gynecologic Oncology and the operating room logbooks. Permission to access the logbooks were obtained from the corresponding sections. A manual search was done for all cases of uterine and cervical malignancies wherein surgery with bilateral pelvic lymph node dissection and/or para-aortic lymph node sampling were performed. Their corresponding histopathological reports were obtained from their respective charts and were cross-referenced with the Department of Pathology logbooks. The names of patients appearing on these histopathological reports were then be cross-referenced with the electronic database of the Section of Ultrasound of the Department of Obstetrics and Gynecology. These results were checked for completeness and were validated according to the following inclusion criteria:

### Inclusion Criteria

1. All patients with either uterine or cervical (Stage IA2-IIA2) malignancy who underwent bilateral pelvic lymph node dissection and para-aortic lymph node sampling within the years January 2010 to December 2014, as indicated in the operative technique.
2. A pre-operative ultrasound scan was performed by a consultant or fellow of the Section of Ultrasound in PGH within two months prior to surgery following the usual practice of the Gynecologic Oncology section for their patients undergoing surgery.

### Exclusion Criteria

The following were excluded from the study:

1. Cases whose surgery was performed more than two months from the ultrasound evaluation.
2. Cases that underwent surgery in a different institution.
3. Cases of uterine and/or cervical malignancy associated with a different type of malignancy in another pelvic and/or extra-pelvic organ ("double primary").
4. Cases of cervical malignancies wherein neoadjuvant chemotherapy followed by surgery was performed.

In the event that a patient had multiple ultrasound scans within two months prior to surgery, the ultrasound result nearest or closest to the date of surgery was used for the purpose of this study.

Outcome Measure

The outcome measures included lymph nodes visible on two dimensional ultrasound, lymph node size, shape and location.

Data Analysis and Statistical Evaluation

Data were encoded in Microsoft Excel and processed using Stata 12. Continuous data were presented as means and standard deviations while categorical variables were presented as frequencies. Sensitivity, specificity, positive and negative predictive values and accuracy were computed. At Alpha level set at 0.05, T-test and Fisher’s exact test with Risk Ratio were also used to compare uterine and cervical cancer patients in terms of demographic variables and incidence of lymph nodes.

Ethical Considerations

The protocol of this study was first submitted to the consultant co-investigator and presented to the consultants of the Section of Ultrasound for additional inputs, suggestions and approval. Once approved by the Section, it was then submitted to the Committee of Research and the Chairperson for Research of the Department of Obstetrics and Gynecology for technical review and approval. After doing so, it was then submitted to the Research Ethics Board for review and approval. Conduct of the study was started once final approval by the Board was made. The principal investigator was fully responsible for the conduct of the study, from seeking approval from the necessary bodies, data collection and processing and final report and submission. The consultant co-investigator oversaw the conduct of the study and made sure that the objectives of the study were met within the prescribed study period. Personal data collected from each subject was kept confidential.

Conflict of Interest

There was no conflict of interest in the conduct of this study.

Benefits of the Study

The massive public health and economic impact of gynecologic malignancies and its resulting morbidity and mortality cannot be stressed enough. In developing countries such as the Philippines, the burden of cervical and endometrial cancer often besets women in the low-to medium-level income brackets. Finding more effective means of preventing, diagnosing and treating gynecologic

cancers will greatly lessen the public health burden to the economy of the country. Studies on the pre-operative diagnostic procedures will greatly impact the outcome. Finding a more cost-effective means of documenting and prognosticating gynecologic malignancies translates into shorter hospital stay and maximization of the resources of the patient’s family, the institution and the community. There is, however, no direct benefit to the study subjects.

Risks

There was no foreseeable risk involved.

Duties and Responsibilities

The principal investigator was responsible for the conduct of the study and that the inclusion and exclusion criteria were strictly followed. The principal investigator was fully responsible for the study, from seeking approval from the necessary bodies, data collection and processing and final report and submission. The principal investigator was in-charge of data safekeeping, data analysis and completion of the final study report.

The consultant co-investigator oversaw the conduct of the study, made sure that the objectives of the study were met within the prescribed study period. The co-investigator was informed and updated by the principal investigator as to the progress of the study, number of cases included, development of any problems and changes that were necessary to complete the study.

Time Table

PROTOCOL FORMULATION, REVIEW AND FINALIZATION	MARCH – APRIL 2015
UP MANILA RESEARCH BOARD ETHICS REVIEW	MAY-JUNE 2015
DATA COLLECTION	JUNE-AUGUST 2015
DATA ANALYSIS	AUGUST 2015
FINAL REPORT	SEPTEMBER 2015

Budget

PRINTING AND REPRODUCTION	Php 3, 000.00
OFFICE SUPPLIES	Php 3, 000.00
STATISTICIAN	Php 7, 000.00
<b>GRAND TOTAL/ PROJECTED TOTAL EXPENSE</b>	Php 13, 000.00

The principal investigator shouldered all expenses in the study.

## RESULTS

There were three hundred nineteen (319) patients with uterine and cervical (Stage I-A2 – Stage II-A2) malignancies that underwent bilateral pelvic lymph node dissection and para-aortic lymph node sampling, included in the study.

Out of the three hundred nineteen (319) patients, there were two hundred sixty seven (267) or 84% of the patients had uterine malignancy. The remaining fifty two (52) or 16% patients have cervical malignancy.

The average age of patients with uterine malignancy was 53.0 years ( $\pm 9.7$  SD). The youngest was 21 years-old while the oldest was 76 years-old. Most patients fell under the age bracket of 49-59 years of age (49.4%). The study also showed that most of the patients with uterine cancer had gravidity of zero (0) to one (1) or (36.3%) and parity of zero (0) to one (1) or 40.2 %. (Table 1)

On the other hand, cervical cancer patients had a mean age of 46.7 years ( $\pm 11.3$  SD) with age ranging from 22 to 65 years. Most patients were under the age bracket of 39 to 48 years (30.8%). They had a higher gravidity and

**Table 1.** Demographic Profile of Subjects

Variable	Uterine	Cervical	Both Uterine and Cervical
<b>Number of Patients</b>	267	52	319
<b>Age (yo)</b>			
Mean	53.0	46.7*	52.0
SD	9.7	11.3	10.2
Range	21-76	22-65	21-76
18-28	5 (1.9%)	1 (1.9%)	6 (1.9%)
29-38	17 (6.4%)	14 (26.9%)	31 (9.7%)
39-48	49 (18.4%)	16 (30.8%)	65 (20.4%)
49-59	132 (49.4%)	10 (19.2%)	142 (44.5%)
$\geq 60$	64 (24.0%)	11 (21.2%)	75 (23.5%)
<b>Gravidity</b>			
Mean	2.8	4.4*	3.1
SD	2.5	1.9	2.5
Range	0-13	0-9	0-13
G0-G1	97 (36.3%)	2 (3.9%)	99 (31.0%)
G2-G3	67 (25.1%)	13 (25.0%)	80 (25.1%)
G4-G5	71 (26.6%)	26 (50.0%)	97 (30.4%)
>G5	32 (12.0%)	11 (21.1%)	43 (13.5%)
<b>Parity</b>			
Mean	2.4	4.0*	2.7
SD	2.2	1.7	2.21
Range	0-11	0-8	0-11
P0-P1	107 (40.2%)	2 (3.9%)	109 (34.3%)
P2-P3	83 (31.2%)	17 (32.7%)	100 (31.5%)
P4-P5	55 (20.7%)	25 (48.1%)	80 (25.2%)
>P5	21 (7.9%)	8 (15.4%)	29 (9.1%)

% refers to column percentage. The data may not sum to 100% due to rounding off.

\*there is significant difference between uterine and cervical malignancies at 0.05 level of significance

parity of 4 to 5 (gravidity 4-5, 50% and parity 4-5, 48.1%) compared to uterine cancer patients. (Table 1)

Stratified according to the type of malignancy, age, gravidity, and parity of patients with cervical malignancies were significantly higher than those of uterine malignancies ( $p < 0.05$ ). (Table 1)

Table 2 showed the different histologic types classifies under uterine and cervical malignancies. The most common histologic type among patients with uterine cancer was adenocarcinoma endometrioid type (82.2%). Among all cervical malignancies, squamous cell carcinoma, large cell, non-keratinizing (SCCA, LCNK) was the most common type comprising 51.9% of cases.

Sonographic findings in Table 3 revealed that the pelvic lymph nodes were present in 7.1% of the uterine malignant patients and had an average longitudinal axis diameter of 1.75 cm ( $\pm 0.89$  SD, range from 0.6 - 4.2cm) and transverse or short axis diameter of 0.93 cm ( $\pm 0.49$  SD, range from 0.4 - 2.6cm). The majority of the shape was round, at 66.7%.

Amongst all the cervical cancer patients, presence of pelvic lymph node was detected by ultrasound in one (1) of the fifty two (52) cases. This node was characterized as round in shape with a longitudinal axis diameter of 1.83 cm and transverse or short axis diameter of 0.93cm.

**Table 2.** Histologic Type of Uterine or Cervical Malignancy

Histologic Type*	Uterine	Cervical
Adenocarcinoma Clear Cell	11 (4.1%)	1 (1.9%)
Adenocarcinoma Endometrioid Type	221 (82.8%)	4 (7.7%)
Adenocarcinoma Endometrioid w/ Squamous Differentiation	7 (2.6%)	0 (0.0%)
Adenocarcinoma Endometrioid w/ Mucinous Features	1 (0.4%)	0 (0.0%)
Adenocarcinoma Endometrioid w/ Focal Papillary Features	1 (0.4%)	0 (0.0%)
Mixed Epithelial Type	1 (0.4%)	0 (0.0%)
Malignant Mixed Mullerian Tumor (MMMT) or Carcinosarcoma, Homologous Type	7 (2.6%)	0 (0.0%)
Malignant Mixed Mullerian Tumor (MMMT) or Carcinosarcoma, Heterologous Type	10 (3.7%)	0 (0.0%)
Serous Papillary Adenocarcinoma	2 (0.8%)	0 (0.0%)
Adenosarcoma	2 (0.8%)	0 (0.0%)
Squamous Cell Carcinoma, Well Differentiated	1 (0.4%)	0 (0.0%)
Mullerian Adenosarcoma	1 (0.4%)	0 (0.0%)
High-Grade Serous Carcinoma with Endometrioid Features	1 (0.4%)	0 (0.0%)
Serous Carcinoma	1 (0.4%)	0 (0.0%)
Squamous Cell Carcinoma, Large Cell Non-Keratinizing (SCCA LCNK)	0 (0.0%)	27 (51.9%)
Squamous Cell Carcinoma, Large Cell Keratinizing (SCCA LCK)	0 (0.0%)	6 (11.5%)
Adenocarcinoma, Endo-Cervical Type	0 (0.0%)	6 (11.5%)
Adenocarcinoma, Endo-Cervical Type & Neuroendocrine	0 (0.0%)	1 (1.9%)
Adenocarcinoma W/ Focal Squamous Differentiation	0 (0.0%)	1 (1.9%)
Adenosquamous Carcinoma	0 (0.0%)	1 (1.9%)
Mucinous Adenocarcinoma	0 (0.0%)	4 (7.7%)
Small Cell Carcinoma w/ Neuroendocrine Features	0 (0.0%)	1 (1.9%)

% refers to column percentage. The data may not sum to 100% due to rounding off. \*comparison of histologic type percentage distribution between uterine and cervical is significant ( $p < 0.05$ )

The occurrence of pelvic lymph nodes was almost four times higher in patients with uterine malignancy compared to patients with cervical malignancy (7.1% vs 1.9%, RR=3.7, p=0.1576). The Table also revealed that para-aortic lymph nodes were not identified among cervical cancer patients included in the study. Moreover, the incidence of para-aortic lymph node metastasis was relatively lower among patients with uterine malignancies occurring at 2.6%.

According to the histologic findings depicted in Table 4, nodal metastasis among uterine cancer patients occur in 5.6% in the pelvic lymph nodes and 3.0% in the para-aortic lymph nodes. On the other hand, patients with cervical malignancy showed pelvic lymph node tumor extension in 3.9% of cases and only 1.9 % in the para-aortic nodes.

Patients with uterine cancer had relatively higher chance of having pelvic and para-aortic lymph node metastasis than patients with cervical malignancy. The

**Table 3.** Sonographic Lymph Node Findings of Subjects

Findings	Uterine	Cervical
Pelvic Lymph Nodes		
Absent	248 (92.9%)	51 (98.1%)
Present	19 (7.1%)	1 (1.9%)
Longitudinal axis (cm)		
Mean	1.75	1.83
SD	0.89	-
Range	0.6-4.2	1.83-1.83
Transverse or short axis (cm)		
Mean	0.93	0.93
SD	0.49	-
Range	0.4-2.6	0.93-0.93
Shape		
Round	12 (63.2%)	1 (100%)
Ovoid	7 (36.8%)	0 (0%)
Para-aortic Lymph Nodes		
Absent	260 (97.4%)	52 (100%)
Present	7 (2.6%)	0 (0%)
Longitudinal axis (cm)		
Mean	3.32	-
SD	2.82	-
Range	0.8-9.1	-
Transverse or short axis (cm)		
Mean	2.03	-
SD	0.97	-
Range	0.9-3.9	-
Shape		
Round	6 (85.7%)	-
Ovoid	1 (14.3%)	-

incidence of pelvic and para-aortic lymph involvement is 1.46 (RR 1.46, p=0.6028) and 1.56 (RR 1.56, p=0.6690) times higher among uterine than cervical cancer patients.

Ultrasound specificity and negative predictive value (NPV) were higher in detecting pelvic lymph nodes (speci= 96.4%, NPV=96.0%) and para-aortic lymph nodes (speci=98.1%, NPV=97.4%). However, due to the limited number of patients who became positive for lymph node metastasis both on ultrasound and histologic examination, the sensitivity and positive predictive value were noted to be low. Ultrasound correctly diagnosed the presence of pelvic lymph node metastasis in 5 out of 17 cases (29.4%) and para-aortic lymph node metastasis in 1 out of 9 cases (11.1%). The overall accuracy of ultrasound in detecting pelvic and para-aortic lymph node metastasis was 91.5 % and 95.6 % respectively.

Ultrasound correctly detected the presence of nodal metastasis in 4 out of 15 cases of pelvic lymph nodes and 1 out of 8 cases of para-aortic lymph nodes among uterine cancer cases. There were 11 and 7 false positive cases of pelvic and para-aortic node involvement detected by ultrasound, respectively. On the other hand, ultrasound correctly diagnosed the absence of nodal involvement in 237 out of 252 cases of pelvic lymph nodes and 253 out of 259 cases of para-aortic lymph nodes. Furthermore, the accuracy of ultrasound in detecting pelvic and para-

aortic lymph node metastasis among patients with uterine malignancy was 90.3 % and 95% respectively. (Table 6)

Half of the cases of pelvic lymph node metastasis were correctly detected sonographically among cervical cancer subjects. All cases diagnosed by ultrasound as having no lymph node involvement were indeed negative histopathologically. The accuracy of ultrasound in detecting nodal metastasis was 98.1% for both pelvic and para-aortic lymph nodes.

Among patients with cervical malignancy, ultrasound had a higher sensitivity (cervical- 50%, uterine- 26.7%), specificity (cervical- 100%, uterine- 94.1%), positive predictive value (cervical- 100%, uterine- 21.1%) negative predictive value (cervical- 98.0%, uterine- 95.6%) and accuracy (cervical- 98.1%, uterine- 90.3%) in detecting pelvic lymph node metastasis compared to those with uterine malignancy. On the other hand, the specificity (cervical- 100%, uterine- 97.7%), negative predictive value (cervical- 98.1%, uterine- 97.3%) and accuracy (cervical- 98.1%, uterine- 95.1%) were comparable.

## DISCUSSION

The use of ultrasound in detecting gynecological malignancies, specifically cervical and uterine, have helped and guided clinicians in the management of their patients. Moreover, assessment of lymph node status will guide clinicians pre-operatively in planning the type of surgery, post-operative follow-up and in prognosticating the disease entity.

Demographic profiling is important in this specific study because the first and easiest step in predicting the approach of clinicians is from the gathered general information data. The data gathered, applicable to this study are age, gravidity and parity of the patient.

In this particular study, the age bracket of the patients having uterine cancer ranged from 49 to 59 years with gravidity and parity of 0-1. In the Society of Gynecologic Oncologists of the Philippines, Inc. (SGOP), Practice Guidelines Second Edition (2010), it transcribed that most women diagnosed with uterine cancer fall

**Table 4.** Histologic Lymph Node Findings of Subjects

Findings	Uterine	Cervical
Pelvic Lymph Nodes		
Absent	252 (94.4%)	50 (96.1%)
Present	15 (5.6%)	2 (3.9%)
Para-aortic Nodes		
Absent	259 (97.0%)	51 (98.0%)
Present	8 (3.0%)	1 (1.9%)

**Table 5.** Validity of Ultrasound in Detecting Lymph Node Metastasis

Lymph nodes	Sensitivity	Specificity	PPV	NPV	Accuracy
Pelvic	29.4% (5 of 17)	96.4% (287 of 302)	25.0% (5 of 20)	96.0% (287 of 299)	91.5% (292 of 319)
Para-aortic	11.1% (1 of 9)	98.1% (304 of 310)	14.3% (1 of 7)	97.4% (304 of 312)	95.6% (305 of 319)

**Table 6.** Validity of Ultrasound in Detecting Pelvic Lymph Node and Para-aortic Lymph Node Metastasis by Type of Malignancy

Lymph nodes	Uterine Malignancy					Cervical Malignancy				
	Sensi	Speci	PPV	NPV	Acc	Sensi	Speci	PPV	NPV	Acc
Pelvic	26.7% (4 of 15)	94.1% (237 of 252)	21.1% (4 of 19)	95.6% (237 of 252)	90.3% (241 of 267)	50% (1 of 2)	100.0% (50 of 50)	100.0% (1 of 1)	98.0% (50 of 51)	98.1% (51 of 52)
Para-aortic	12.5% (1 of 8)	97.7% (253 of 259)	14.3% (1 of 7)	97.3% (253 of 260)	95.1% (254 of 267)	-	100% (51 of 51)	- (304 of 312)	98.1% (51 of 52)	(51 of 52)

between ages of 50-60 years old.<sup>7</sup> Consequently, the age bracket of this study is fairly parallel with the result of the previously mentioned literature. Nonetheless, patients aged 60 years and above had the second most number in terms of population in their age group.

The gravidity and parity in this study was reported low, only between 0 – 1. As a result of lower gravidity and parity, a significant risk factor in acquiring uterine malignancy is apparent. According to the SGOP Practice Guidelines, nulliparity confers a two-fold risk in developing a uterine malignancy compared with parity of one and more.<sup>7</sup> Therefore, the said study is consistent with that of the literature.

In this study most cervical cancer patients were between 39-48 years old. They were relatively younger compared to the patients with endometrial malignancy. Most of the cases included in this study were of higher gravidity and parity. Parity of 7 or more, increases the risk of cervical cancer.<sup>7</sup>

The most common histologic type among the uterine cancer cases in this study was Adenocarcinoma - Endometrioid type. According to Di Saia et. al. (2012), the authors stated that the most common among all histologic type was also Adenocarcinoma - Endometrioid Type.<sup>4</sup>

Reports by Colombo et. al. (2013) stated that squamous cell carcinoma accounts for 70% - 80% of cervical cancer.<sup>6</sup> In this particular study, amongst cervical cancer patients, squamous cell carcinoma, large cell, non-keratinizing likewise was the most predominant histologic type.

Reportedly, in this study, the average longitudinal axis diameter was 1.75 cm (17.5 mm) among uterine cancer patients and 1.83 cm (18.3 mm) among cervical cancer patients, and a transverse or short axis (axial) diameter of 0.93 cm (9.3 mm) for both groups. In this particular report, the smallest longitudinal axis diameter detected was 0.6

cm (6 mm) and the transverse axis diameter was 0.4 cm (4 mm). In a study by Ryo et. al. (2013), lymph nodes with a transverse diameter of 5 mm were considered enlarged.<sup>12</sup> Likewise in this study, the mean transverse diameter of lymph nodes detected was 9.3 mm, signifying that they were indeed already considered as enlarged. According to the local study by Famador et. al. (2010), the average size of lymph nodes readily seen sonographically was 1 cm (10 mm). Very small masses less than 0.5 cm (5 mm) was hardly evident but larger masses 1.5 cm (15 mm) or more are discriminatory.<sup>10</sup>

The sonographic feature of majority of lymph nodes included in this study was round. This particular characteristic was described by Dudea et. al. (2012) as one of the criterion differentiating malignant from a benign lymph node. Furthermore, the previously mentioned study stated that malignant lymph nodes were usually seen as large and round in shape, while benign lymph nodes were categorized as small and ovoid.<sup>15</sup>

The rate of nodal metastasis among patients with uterine carcinoma is 9%.<sup>4</sup> On the other hand, the incidence of lymph node metastasis among cervical cancer patients is 15-20% for stage I disease and 25-40% for stage II disease. Para-aortic involvement occurs in 6.3% of stage I cases and 16.5% of stage II cases.<sup>5</sup> Histopathologic results in this study revealed that metastasis to the pelvic lymph nodes occur in 5.6% and para-aortic nodes in 3.0% of cases of uterine cancer patients. The values obtained were lower compared to that of the literature. Likewise, among cervical cancer subjects, involvement of the pelvic lymph nodes occurs in 3.9% of cases and para-aortic nodes in only 1.9% of cases. The lower pick up rate of nodal involvement in this study may be affected by the skills and years of practice of the surgeon as well as the habitus of the patients that made the dissection challenging.

Patients with uterine cancer had relatively higher

chance of having pelvic and para-aortic lymph node metastasis than patients with cervical malignancy as indicated in this study. The incidence of pelvic and para-aortic lymph nodes is 1.46 (RR 1.46,  $p=0.6028$ ) and 1.56 (RR 1.56,  $p=0.6690$ ) times higher among uterine than cervical cancer patients. The lower incidence of lymph node metastasis among cervical cancer patients could be largely affected by the smaller population of subjects included in the study. Furthermore, only low stage (Ia2-IIA2) cervical cancer patients were included wherein surgical management was warranted as compared to uterine cancer patients where surgery was the primary treatment of choice regardless of the stage.

In this study, ultrasound was 96.4% specific and 29.4% sensitive with a positive predictive value (PPV) of 25.0% and negative predictive value of 96.0% in identifying pelvic lymph node metastasis with an overall accuracy of 91.5%. Ultrasound detection of para-aortic nodal metastasis revealed a specificity of 98.1 %, sensitivity of 11.1 %, positive predictive value (PPV) of 14.3%, negative predictive value of 97.4% and accuracy of 95.6%. This was somewhat similar to the study done by Sawicki et. al. (2003). He inscribed a specificity number of 100% and sensitivity of 33.3%. The positive predictive value (PPV) was posted at 100% and negative predictive value (NPV) at 88.2%.<sup>14</sup> In comparison, the values from this research compared to the values from Sawicki's data were fairly consistent, except for sensitivity and positive predictive values. Famador et. al. on the other hand, publicized a rating of 88% for specificity, 67% for sensitivity, 29% for positive predictive value, 97% for negative predictive value and 87% for accuracy. Majority of the results of this study were comparable with the previously mentioned research.

Computed Tomography (CT) scan has a sensitivity of 45 % and specificity of 88 % in identifying nodal involvement while MRI is 92% sensitive and 97% specific.<sup>9</sup> In this study, two dimensional ultrasound was 29.4% sensitive and 96.4% specific in detecting pelvic nodal metastasis and 11.1% sensitive and 98.1% specific in identifying para-aortic nodal extension. Comparing CT scan and ultrasound, CT scan is superior in terms of the sensitivity of detection pelvic nodal metastasis but the values were not distant. In fact, ultrasound is more specific than CT scan in identifying both pelvic and para-aortic nodal involvement. MRI on the other hand is superior to both previously mentioned modalities. Considering the high cost of CT scan and MRI for that matter, ultrasound, which is readily available, is a cost-effective modality of choice.

There are several factors that may affect the accuracy of ultrasound in detecting lymph node metastasis. Ultrasound is operator-dependent. The skills and years of experience of the sonologist will greatly influence the

ultrasound findings. At the same time, the resolution of the machine will affect identification of nodes. Higher resolution probes will easily distinguish enlarged lymph nodes suggestive of tumor involvement. The habitus of the patient also impacts on the findings. A thicker abdominal wall will preclude detection of nodal involvement while a thinner one will identify with ease enlarged nodes. The surgical skills of the surgeon should also be taken into consideration. The enlarged nodes identified sonographically may not have been meticulously harvested by the surgeon during the operation which may significantly affect the histopathologic results as well.

Positive or enlarged nodes identified on ultrasound but negative on histopathology may signify the presence of only an inflammatory process but not necessarily metastasis. Other features, as described by Dudea, such as the presence of hilum, echogenicity, margins, structural changes (focal cortical nodules, intranodal necrosis, reticulation, calcification, matting) and Doppler criteria (flow, vessel location, vascular pedicles, vascular pattern, impedance values) will help in differentiating benign from malignant lymph nodes which is beyond the scope of this study.<sup>15</sup>

In comparing the validity of ultrasound in detecting lymph node metastasis between patients with uterine and cervical malignancies, ultrasound had a higher sensitivity, specificity, positive predictive value, negative predictive value and accuracy of detection of pelvic lymph nodes among cervical cancer subjects. The higher values obtained among cervical cancer patients may be significantly due to the limited number of cases included. There were only two patients who were positive for pelvic node involvement and ultrasound was able to detect only one. Compared to the patients with uterine malignancy, 15 cases were positive for pelvic node metastasis and ultrasound was able to detect 4. On the other hand, detection of tumor extension to the para-aortic nodes between the two groups was comparable in terms of the specificity, negative predictive value and accuracy.

## CONCLUSION

---

Two-dimensional ultrasound is reliable in ruling in the presence of pelvic and para-aortic lymph node metastasis among patients with uterine and cervical malignancies. However, its low sensitivity of detection makes it less dependable in ruling out nodal involvement.

Sonographic feature suggestive of nodal involvement revealed a round characteristic. The average longitudinal diameter of pelvic lymph node detected on ultrasound among uterine cancer patients is 1.75 cm with a transverse or short axis diameter of 0.93 cm. For para-aortic nodes, the average longitudinal diameter was 3.32 cm with a transverse or short axis diameter of 2.03 cm. On the other

hand, patients with cervical malignancy have a mean longitudinal diameter of 1.83 cm and transverse or short axis diameter of 0.93 cm for pelvic lymph nodes.

MRI is highly specific and sensitive than CT scan or ultrasound in detecting lymph node metastasis. CT scan, on the other hand, is more sensitive than ultrasound in identifying lymph node involvement. However, the specificity of ultrasound is even higher than CT scan and comparable with that of MRI. Ultrasound, which is easily available and affordable, is still a cost-effective modality that will greatly help clinicians in the management of uterine and cervical malignancies.

## RECOMMENDATIONS

---

The authors of the study recommend further research on the sonographic ultrasound features differentiating benign from malignant lymph nodes in terms of echogenicity, presence and absence of hilum, edema and Doppler studies criteria.

The authors also recommend that interobserver assessment of the clinicians in detecting lymph node metastasis be evaluated as well.

And lastly, a prospective study of this particular topic is highly suggested. ■

## REFERENCES

---

1. <http://www.wcrf.org/int/cancer-facts-figures/data-specific-cancers/endometrial-cancer-cancer-lining-womb-statistic>.
2. U.S. Cancer Statistics Working Group. United States Cancer Statistics: 1999-2011 Incidence and Mortality Web-based Report. Atlanta (GA): Department of Health and Human Services, Centers for Disease Control and Prevention, and National Cancer Institute; 2014.
3. Plataniotis G, Castiglione M, Endometrial cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Annals of Oncology* 21 (Supplement 5): v41-v45, 2010; Aberdeen Royal Infirmary, Aberdeen, UK and University of Geneva, Geneva, Switzerland.
4. Di Saia P, Creasman W. *Clinical Gynecologic Oncology*. 8th edition. 2012.
5. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F (2013). GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer.
6. Colombo N, Carinelli S, Colombo A, Marini C, Rollo D, Sessa C. Cervical cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Annals of Oncology* 23 (Supplement 7): vii27-vii32, 2012. European Institute of Oncology and Univesita Milano Bicocca, Milan, Italy.
7. Society of Gynecologic Oncologists of the Philippines (Foundation) Inc, *Clinical Practice Guidelines for the Obstetrician-Gynecologist*, Second Edition, November 2010. Manila, Philippines.
8. Callen PW, et al. *Ultrasonography in Obstetrics and Gynecology*, Fifth Edition, 2008.
9. Society of Gynecologic Oncologists of the Philippines (Foundation) Inc, *Clinical Practice Guidelines for the Obstetrician-Gynecologist*, Sixth Edition, November 2012. Manila, Philippines.
10. Famador J, Benavides D, Luna J. The Accuracy of ultrasonography in predicting surgico-pathologic prognostic factors in endometrial cancer, 2010.
11. Yang L, Jia X, Li N, Liu Y, Wang H. Comprehensive clinic-pathological characteristics of cervical cancer in southwestern china and the clinical significance of histological type and lymph node metastases in young patients.
12. Ryo E, Kita T, Yasugi T, Mizutani K, Seto M, Takeshita S, Ayabe T. Effectiveness of intraoperative ultrasonography for para-aortic lymph nodes in preventing unnecessary lymphadenectomy in ovarian carcinoma. *Open Journal of Obstetrics and Gynecology*, 2013, 3, 5-10. Teikyo University and Komagome Hospital, Tokyo, Japan.
13. Kidd E, Siegel B, Dehdashti F, Rader J, Mutch D, Powell M, Grigsby P. Lymph node staging by positron emission tomography in cervical cancer: relationship to prognosis. *Journal of Clinical Oncology*. Volume 28, Number 12, April 2010. Alvin J. Siteman Cancer Center and Washington University School of Medicine, St. Louis, Montana.
14. Sawicki W, Spiewankiewicz B, Stelmachow J, et al. The value of ultrasonography in preoperativce assessment of selected prognostic factors in endometrial cancer. *Eur J Gynaecol Oncol*. 2003.
15. Dudea S, Lenghel M, Botar-Jid C, Vasilescu D, Duma M. Ultrasonography of superficial lymph nodes: benign versus malignant. *Med Ultrason*, 2012, vol 14, no. 4, 294-308. University of Medicine and Pharmacy, Cluj-Napoca, Romania.