

# Two years recurrence rate of ovarian and endometrial malignancies following Surgical versus clinical staging

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#### Abstract

**Background and objectives:** Gynecological cancers represent a big burden on national health institutes. Recurrences of these cancers are documented frequently that needed more efforts to prevent or reduce them. The aim of the study was to know the difference between Standard Surgical Staging and Non-Standard Surgical Staging in gynecological cancers in terms of recurrence rate.

**Methods**: This study was a retrospective cross-sectional study conducted at the Maternity Teaching Hospital and Hiwa Hospital in Sulaymaniyah city-Kurdistan region/Iraq over two years from June 2020 to June 2022, on sample of 86 women with gynecological cancer divided into two study groups (42 women underwent standard surgical staging and 44 women underwent non-standard surgical staging). Standard surgical staging for endometrial and ovarian cancers included midline laparotomy, peritoneal washout, samples from the right and left sub-diaphragmatic surfaces, infracoloic Omentectomy, total abdominal hysterectomy & bilateral salpingo-oophorectomy, any peritoneal deposits and pelvic and para-aortic Lymphadenectomy in maternity hospital.

**Results**: The recurrence rate in women with non-standard surgical staging were 25% (p=0.009), while in women with standard surgical staging were 4.8%. 11 women with non-standard surgical staging had advanced cancer stages at recurrence compared to 2 cases with standard surgical staging. Although no significant difference in death outcome between both study groups (p=0.09), no woman who underwent standard surgical staging with recurrence died, while the death rate of women underwent non-standard surgical staging with recurrence was (63.6%).

**Conclusions:** The standard surgical staging in women with gynecological cancer is important in the recurrence rate of these cancers.

**Keywords:** Gynecological cancer, Recurrence, Standard surgical staging.

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### Introduction

Gynecological tumors are common worldwide with about 1.3 million new cases recorded annually<sup>1</sup>.Meanwhile, amongst women, more than one-quarter of new tumor cases are gynecological tumors<sup>2</sup>.The commonest risk factors for gynecological tumors are advanced age, obesity, smoking, Human Papilloma Virus (HPV) infection and contraceptive pills<sup>2</sup>.

The Multidisciplinary Team (MDT) in oncology has revolutionized the field of oncology since its application in the previous century<sup>3</sup>. The decision of MDT in managing gynecological tumors is accompanied by higher survival rates, high recruitment, more educational benefits, and better satisfaction among health workers<sup>4</sup>. Moreover, it improves the quality of Standard Surgical Staging (SSS) for gynecological tumors<sup>4</sup>.

The gynecological tumors staging is used to describe the extension of the tumor throughout the body. It mainly depends on the size of the tumor, involvement of lymph nodes and metastasis to other body organs<sup>5</sup>. After 1988, there was a shift from clinical to surgical staging of gynecological tumors which was based mainly on the site of lymphadenopathy that helps in prognosis and identifying women with a need for adjuvant therapy<sup>6</sup>. The Standard surgical staging (SSS) of endometrial cancer involves removing of uterus, cervix, and adnexa with pelvic and para-aortic lymph node dissection in addition to the sampling of pelvic collections<sup>7</sup>. The International Federation of Gynecology and Obstetrics (FIGO) advised that staging of endometrial cancer is on a basis of surgical pathology and comprehensive surgery that assist in measuring tumor extent<sup>8</sup>. Common disadvantages of SSS of endometrial tumors are injuries to major vessels, nerve injuries, lymphedema and cellulitis<sup>6, 9</sup>.

For cases with ovarian tumors, early surgery is beneficial in SSS and management. The SSS in ovarian tumors is helpful in diagnosis, prognosis and need for chemotherapy 10. The FIGO reported the significance of SSS, which involves peritoneal washing (ascites sample), hysterectomy with bilateral salpingo-oophorectomy, infracolic omentectomy, different peritoneal samples, pelvic and para-aortic lymphadenectomy and samples of lesions and adhesions 11.

Yearly, about 100,000 women are recorded with gynecologic malignancy and about 30 % of those women showed cancer recurrence, sometimes with a poor prognosis<sup>12</sup>. For endometrial cancer, 15% of the women showed recurrence and 50% of recurrent cases occurred within two years of primary management<sup>13</sup>. Regarding ovarian cancer, the recurrence is shown in about 25% of women with early stages and about 80% of women with highly advanced stages<sup>14</sup>. Large uterus, myometrial invasion, suboptimal debulking surgery and lack of MDT in management strategy are the main risk factors for high recurrence rates of these cancers<sup>15-17</sup>.

Although, FIGO guidelines reported that incomplete SSS was shown in 98% of gynecological tumor cases globally<sup>18, 19</sup>. Many authors related these incomplete staging cases to the absence of MDT, and knowledgeable unskilled and poorly specialists, which has led to improper inspection and interpretation of SSSresults<sup>18</sup>-<sup>20</sup>. Gynecological tumors are prevalent in Iraq, especially ovarian and endometrial carcinomas<sup>21</sup>. The annual incidence rates of all tumors are increased in the Kurdistan region specifically in Sulaymaniyah city in the last three decades<sup>22</sup>. The incidence rate of gynecological tumors was elevated among women in Sulaymaniyah due to sedentary lifestyle, obesity, smoking, oral contraceptive pills and human papillomavirus infection<sup>23</sup>.



Although these high national rates regarding gynecological tumors, there was a scarcity in literatures discussing the importance of SSS that urged to conduct this study that aimed to know the difference between standard surgical staging (SSS) and no standard surgical staging (NSSS) in gynecological cancers in terms of recurrence rate in Sulaymaniyah city.

## **Patients and methods**

The design of the present study was a retrospective cross-sectional study implemented in both Maternity Teaching Hospital and Hiwa Hospital in Sulaymaniyah city-Kurdistan region/Iraq over two years from 1st of June 2020 to 30th of June 2022. The studied population was all women with gynecological cancers admitted to Maternity Teaching Hospital and Hiwa Hospital. Inclusion criteria were women diagnosed with endometrial and ovarian cancers with complete follow-up information. Exclusion criteria were other gynecological malignancies, incomplete missing or women's data and those who had no follow-

The proposal of the research was approved by the Ethical Committee of Kurdistan Higher Council of Medical specialist-Gynecology & Obstetrics Department with approval number 1182 at 11/9/2021, then approval was taken from the Sulaymaniyah Health Directorate before the commencement of the study. A verbal consent taken from each patient.

A sample of eighty-six women with gynecological cancer divided into two study groups (42 women underwent SSS during 2019 and 2020 and 44 women underwent NSSS during 2015 and 2016) was enrolled in the present study.

Information on women was collected retrospectively by the researchers by reviewing saved data of women in the hospitals and filling a prepared questionnaire

The designed by the researchers. questionnaire included women's sociodemographic characteristics (age, marital status, parity, race, residence and smoking), women's menstrual and clinical history (age at menarche, menopause, age at menopause, past medical history and family history of cancer), cancer characteristics (type of cancer, histopathological types, staging and mode of the treatment) and outcomes of cancers (recurrence, stage at recurrence, time at recurrence, site of lymph node involvement, recurrence, planned recurrence treatment, distant metastasis and mortality). The cancer diagnosis was done by Specialists in the hospitals according to histopathological examination results.

The diagnosis of cancer recurrence was done either by Oncologists in Hiwa Hospital during their follow-up or when they presented to Gynecologists with new clinical symptoms.

The data of women who underwent NSSS extrapolated from saved records of the women with ovarian or endometrial cancers in Hiwa Hospital and those who had SSS were collected from saved records of women with ovarian or endometrial cancers in Maternity Teaching Hospital and all of them were subjected to MDT management. The MDT Meetings are regular meetings held between a team of gynecologists, general oncologists, radiologists surgeons, histopathologists. These meetings were started in 2019 and occur at a two-week in Sulaymaniyah interval Maternity-Teaching Hospital. The purpose of these meetings is to discuss gynecological cancer cases including details of their history, examinations, investigations, clinical radiological findings and results of any biopsy if taken and to propose a plan of action to better manage the cases by preventing the spread and stage development of the tumor,



reducing the recurrence and controlling the need of been re-operated with its relevant surgical complications.

Technically, SSS for both endometrial and ovarian cancers included midline laparotomy, peritoneal washout or taking peritoneal fluid for cytology, samples taken from the right and left sub-diaphragmatic surfaces, infracoloic Omentectomy, total abdominal hysterectomy (TAH)& bilateral salpingo-oophorectomy (BSO), abdominal and pelvic peritoneal sampling with any peritoneal deposits and pelvic and para-aortic Lymphadenectomy in maternity hospital and the data of the cases whom underwent NSSS (including unilateral or bilateral ovarian cystectomy or oophorectomy or salpingooophorectomy or hysterectomy or THA and BSO) taken from Hiwa hospital data system. all the operations for NSSS were done previously in maternity hospital collected data were entered and interpreted statistically by the SPSS program<sup>26</sup>. Suitable statistical tests (Chi-square and Fishers exact tests) for data were implemented accordingly and a p-value of  $\leq 0.05$  was regarded as significant.

## **Results**

This study included eighty-six women with gynecological cancer divided into two study groups (42 women arranged through MDT and underwent SSS and 44 women underwent NSSS). No significant differences were observed between women of both study group regarding age (p=0.37), marital status

(p=0.6), parity (p=0.16), race (p=0.18) and smoking (p=0.22). There was a significant association between rural residents and women who underwent SSS (p=0.01), Table 1.

No significant differences were observed between women of both study groups regarding age at menarche (p=0.13), menopause (p=0.32), age at menopause (p=0.65), past medical history (p=0.2) and family history of cancer (p=0.67), Table 2. No significant differences were observed between women of both study groups regarding the type of cancer (p=0.15), histopathological types (p=0.38), staging (p=0.16) and surgery (p=0.16). A significant association was observed between chemotherapy management and women underwent SSS (p=0.01). There was a significant association between radiotherapy management and women underwent NSSS (p=0.05), Table 3. There was a significant association between a high recurrence rate those women underwent NSSS (p=0.009). A significant association was observed between advanced cancer stages at recurrence and women underwent NSSS (p=0.03). No significant differences were observed between women of both study groups regarding the time at recurrence (p=0.65), site of recurrence (p=0.28), lymph (p=0.15),involvement planned recurrence treatment (p=0.8), and distant metastasis (p=0.3). Although no significant difference in death outcome between both study groups (p=0.09), no woman who underwent SSS with recurrence died, while the death rate of women underwent NSSS with recurrence was (63.6%), Table 4.

**Table (1):** Distribution of women's general characteristics according to study groups.

Variable	Study groups		p value
	SSS	No SSS	



	No.	%	No.	%	
Age	0.37				
<40 years	1	2.4	3	6.8	
40-49 years	18	42.9	14	31.8	
50-59 years	9	21.4	15	34.1	
≥60 years	14	33.3	12	27.3	
Marital status				l	0.37 0.6 0.16 0.18 0.01
Single	5	11.9	4	9.1	
Married	37	88.1	40	90.9	
Parity	0.16				
Nulliparous	13	31.0	8	18.2	
Multiparous	29	69.0	36	81.8	
Race					0.18
Kurdish	41	97.6	40	90.9	
Arabic	1	2.4	4	9.1	
Residence					0.01
Urban	18	42.9	31	70.5	
Rural	24	57.1	13	29.5	
Smoking	0.22				
Smoker	10	23.8	6	13.6	
Non-smoker	32	76.2	38	86.4	

Table (2): Distribution of women's menstrual and clinical history according to study groups.

Variable	Study groups				p value
	SSS		No SSS		
	No. %		No.	%	



Age at menarche		0.13			
11-13 years	23	54.8	31	70.5	
14-16 years	19	45.2	13	29.5	
Menopause					0.32
Yes	30	71.4	27	61.4	
No	12	28.6	17	38.6	
Age at menopause					0.65
<50 years	12	38.7	12	44.4	
≥50 years	19	61.3	15	55.6	
Past medical history					0.2
No	18	42.9	25	56.8	
HT	14	33.3	14	31.8	
DM	4	9.5	5	11.4	
HT & breast cancer	1	2.4	0	-	
HT & DM	4	9.5	0	-	
DM & breast cancer	1	2.4	0	-	
Family history of cancer					0.67
No	19	45.2	19	43.2	
Ovarian	10	23.8	7	15.9	
Endometrial	3	7.1	6	13.6	
Cervical	1	2.4	3	6.8	
Breast	4	9.5	6	13.6	
Colorectal	3	7.1	3	6.8	
Ovarian & breast	1	2.4	0	-	
Endometrial & colorectal	1	2.4	0	-	

**Table (3):** Distribution of cancer characteristics according to study groups.

Variable	Study groups				
	SSS		No SSS		
	No.	%	No.	%	
Type of cancer	·	·	·	·	0.15



Ovarian	30	71.4	25	56.8		
Endometrial	12	28.6	19	43.2		
Histopathological types						
Papillary serous carcinoma	24	57.1	15	34.1		
Granulosa cell tumor	1	2.4	2	4.5		
Endometroid endometrial carcinoma	15	35.7	20	45.5		
Ovarian teratoma	1	2.4	1	2.3		
Ovarian invasive adenocarcinoma	0	-	2	4.5		
Ovarian mucinous cyst adenocarcinoma	1	2.4	2	4.5		
Ovarian epithelial carcinoma	0	-	1	2.3		
Ovarian yolk sac tumor	0	-	1	2.3		
Staging		<u>'</u>			0.16	
1a	3	7.1	10	22.7		
1b	7	16.7	4	9.1		
1c	3	7.1	7	15.9		
2a	8	19.0	3	6.8		
2b	5	11.9	5	11.4		
3a	8	19.0	4	9.1		
3b	5	11.9	8	18.2		
3c	2	4.8	3	6.8		
4a	1	2.4	0	-		
Surgery					0.16	
Yes	42	100.0	42	95.5		
No	0	-	2	4.5		
Chemotherapy						
Yes	32	76.2	22	50.0		
No	10	23.8	22	50.0		
Radiotherapy	·	<del>.</del>	•	·	0.05	
Yes	1	2.4	6	13.6		
No	41	97.6	38	86.4		

Table (4): Distribution of outcomes according to study groups.

Variable	Study groups S	udy groups SSS No SSS			p value
				Recurrence	0.009
Yes	2	4.8	11	25.0	



No	40	95.2	33	75.0	
	0.03				
Stage 2	1	50.0	0	-	
Stage 3	1	50.0	4	30.8	
Stage 4	0	-	7	69.2	
	Time	at recurrence	1		0.65
<2 years	2	100.0	10	90.9	
≥2 years	0	-	1	9.1	
	I	I	Si	te of recurrence	0.28
Peritoneum	2	100.0	3	27.3	
Vulva	0	-	1	9.1	
Ovary	0	-	5	45.4	
Vault	0	-	2	18.2	
	Lymph n	ode involvem	ent		0.15
Yes	0	-	6	54.5	
No	2	100.0	5	45.5	
	Planned re	currence treat	ment		0.65
Surgery	1	50.0	6	54.5	
Chemotherapy	1	50.0	4	36.4	
Radiotherapy	0	-	1	7.7	
	0.3				
Yes	0	-	4	36.4	
No	2	100.0	7	63.6	
	0.09				
Yes	0	-	7	63.6	
No	2	100.0	4	36.4	

# **Discussion**

Nowadays, there is an increase in the recurrence rate of gynecological cancers and this could be justified by lack of screening, delayed diagnosis, lack of MDT therapy,

poor compliance to guidelines, and improper use of chemical therapy, failed radical resection and absence of qualified radiotherapy facilities<sup>24</sup>.

The current study indicates a significant association between high recurrence rate and



women who underwent NSSS (p=0.009), 25% of women underwent NSSS had recurrence as compared to a 4.8% recurrence rate in women who underwent SSS. These findings are parallel to reports of both Rungruang et al. and Swift et al., which documented the importance of SSS of endometrial and ovarian cancers decreasing the recurrence rate of these cancers<sup>6, 25</sup>. It was shown that SSS not only recognized metastasis but also detected women with high-risk factors of endometrial cancer recurrence like large size, deep myometrial invasion, lymphovascular invasion, cervical extension and positive peritoneal cytology<sup>26</sup>. Similarly, Trimbos et al. in their long-term analysis study revealed that SSS in women with ovarian carcinoma is essential in acquiring better outcomes of management specifically low recurrence rate and longer survival<sup>27</sup>.

A study conducted by Romero et al. on 46 women with borderline ovarian tumors showed that SSS is important in reducing the risk of recurrence in women with ovarian cancer<sup>28</sup>.

In recent years, the use of MDT in treatment including SSS had improved the quality of life and prognosis for women with gynecological cancers<sup>29</sup>. Unfortunately, diagnostic and management plans for gynecological cancers in Iraq are primitive with a lack of MDT in most Iraqi cancer centers except in the Kurdistan region<sup>30</sup>. Additionally, the SSS of gynecological cancers in these national centers needs updated qualifications and implementation specific guidelines<sup>30</sup>.

The present study showed a significant association between advanced cancer stages at recurrence and women underwent NSSS (p=0.03). This finding coincides with reports of Concin et al<sup>31</sup> who stated that the SSS is important in reducing the recurrence rate of endometrial carcinoma, especially in women

with advanced staging. Lheureux et al. revealed the absence of specific symptoms for earlier stages of ovarian cancer leading to the diagnosis of more than 70% of women with this cancer in the advanced stage accompanied by a high recurrence rate and low survival rate<sup>32</sup>. Wang et al <sup>33</sup>found that the recurrence rate in women at advanced stages of ovarian cancer was high, hence this again emphasizes the result of our study.

In the present study, there was a significant association between rural residents and women who underwent SSS (p=0.01). This finding is inconsistent with the results of Zahnd et al<sup>34</sup>, which showed that rural women with endometrial carcinoma are less likely to be subjected to SSS than urban women with endometrial carcinoma<sup>34</sup>. This inconsistency might be because our study is retrospectively collecting data from previous years and the rural women were more likely subjected to SSS after its implementation.

In our study, a significant association was observed between chemotherapy management and women who underwent SSS (p=0.01). This finding is consistent with the results of Kanno et al35, which documented that adjuvant chemotherapy of endometrial cancer is with SSS accompanied by low recurrence rates and improved quality of life<sup>35</sup>. On other hand, our study found a significant association between radiotherapy management and women underwent NSSS (p=0.05). This finding is similar to the results of Foerste et al<sup>36</sup> which reported that standard was rarely used in women with endometrial carcinoma subjected to adjuvant radiotherapy and this led to poor prognosis<sup>36</sup>. A small sample size has reduced the statistical power of the survey study, this could be justified by the limited duration of the time, the pandemic of COVID-19, and poor data documentation in the cancer center having greater impact on the data collection.



This study concluded that the SSS in women with gynecological cancer is an important factor that affects the outcomes of the recurrence rate of these cancers. Lack of MDT and SSS is associated with advanced stages gynecological cancer recurrence at diagnoses with more mortality and morbidity. SSS is accompanied by adjuvant chemotherapy, while accompanied is by adjuvant radiotherapy. This study recommends that every case with gynecological cancer should be discussed in MDT and planned for SSS to achieve a better outcome, in addition to further national longitudinal studies on the outcome of SSS should be supported.

#### **Conclusions**

The standard surgical staging in women with gynecological cancer is important in the recurrence rate of these cancers.

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