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STAGE REDISTRIBUTION FOLLOWING 2018 FIGO STAGING FOR CARCINOMA CERVIX- A SINGLE INSTITUITIONAL STUDY

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ABSTRACT Cancer cervix is one of the leading causes of cancer related deaths in low and middle income countries. The FIGO 2018 staging system has brought in various pathological and radiological parameters for stage classification to guide treatment-related decision-making and for better prognostication

Objective: The purpose of this study is to analyse the results of stage redistribution by applying 2018 International Federation of Gynecology and Obstetrics (FIGO) staging system for cervical cancer patients in a tertiary care cancer centre.

Patients & Methods: For this study, we re-staged all patients based on the FIGO 2018 staging system of patients diagnosed at our centre with carcinoma cervix from Jan 2014 to Dec 2018. Stage by stage comparison to the previous version (FIGO 2009) was done.

Results: The most significant change was from stage IIB and stage IIIB to IIIC1. Upstaging occurred significantly in stage IIIB (54.1% upstaged) followed by stage IIB(33.7% upstaged). Stage IIIC1 emerged out to be the most populous stage(36.73%) followed by stage IIIB (19.36%)& IIB(14.84%). Downstaging occurred only in stage IVB ie to stage IIIC.

Conclusion: The current FIGO 2018 staging system for cervical cancer appears to be useful for predicting survival in patients considering radiological and pathological variables. As per our study, majority of the cancer cervix patients fall into a single subgroup – III C1; this, in a country were already most patients present with advanced disease, will skew the data further. Stage III C1 cervical cancer is not homogenous; sub classification within stage IIIC1 may result in better prognostication.

KEYWORDS : Carcinoma cervix, FIGO, staging system, 2009, 2018

Background

Globally, cervical cancer continues to be one of the most common cancers among females, being the fourth most common after breast, colorectal, and lung cancer[1]. In low- and middle-income countries (LMICs), it is more common, being the second most common cancer in incidence among women and the third most common in terms of mortality. The majority of new cases and deaths (approximately 85% and 90%, respectively) occur in low-resource regions or among people from socioeconomically weaker sections of society.

New initiatives for prevention and early detection have been undertaken. The two major approaches for control of cervical cancer involve: prevention of invasive cancer by HPV vaccination; and screening for pre-cancerous lesions. However, these have not yet been implemented on a large scale in many LMICs due to lack of efficient and effective intervention programs. WHO has recently given a call to action for elimination of cervical cancer. This is foreseeable, if implemented in earnest through successful public health programs achieving high coverage.

With widespread implementation of screening programs worldwide, there has been an increase in the number of early cervical cancers being detected. For patients with early stage cervical cancer, radical hysterectomy plus pelvic lymphadenectomy is considered the treatment of choice. The oncologist determines the adjuvant treatment after radical surgery according to the risk factors of patients. For locally advanced cervical cancer, concurrent chemo-radiotherapy is the standard of care. [6]

The FIGO staging [2] of all gynaecologic cancers was initially clinical. Endometrial and ovarian cancers were revised to a surgico-pathological system, but until the last staging of cervical cancer in 2009 it continued to be a clinical one. Only certain basic investigations were allowed to change the staging. The reason was the fact that the vast majority, about 85%, occur in low- and middle-income countries (LMICs) which have limited availability of imaging and pathology facilities [2]. However, clinical assessment of staging has several drawbacks—notably, assessment of tumour volume is inaccurate; parametrial involvement may be misdiagnosed; most importantly, lymph node involvement cannot be evaluated by clinical examination.

The FIGO 2018 staging system has brought in various pathological and radiological parameters for stage classification to guide treatment related decision making and for better prognostication.

OBJECTIVE:

The purpose of this study is to analyse the results of stage redistribution by applying 2018 International Federation of Gynecology and Obstetrics (FIGO) staging system for cervical cancer patients in a tertiary care cancer centre, who were previously staged according to FIGO 2009.

PATIENTS & METHODS:

Data of all cervical cancer patients who underwent various forms of treatment at our institute including surgery, radiotherapy and chemotherapy from Jan 2014 to Dec 2018 were collected from the Medical Records Department. All patients were staged by the FIGO 2009 criteria, which is based on clinical and imaging criteria (including chest X-ray, CT abdomen & CT or MRI pelvis) and cystoscopy/ sigmoidoscopy as indicated. For this study, we re-staged all patients by the FIGO 2018 staging system of patients diagnosed at our centre with carcinoma cervix from Jan 2014 to Dec 2018. Patients with incomplete data were excluded from the study. A total of 1907 patients for whom complete records were available were included in the study.

RESULTS:

The data of patients with carcinoma cervix diagnosed in the 5 years between 2014 & 2018 was tabulated according to both 2009 FIGO staging as well as 2018 FIGO staging. Significant up-staging to Stage IIIC1 & IIIC2 was noted. (Table 1& 2)

Table 1: Stage Distribution as per FIGO 2009 System:

FIGO 2009	2014	2015	2016	2017	2018
I A1	1	2	1	0	1
I A2	3	3	2	2	1
I B1	11	10	7	12	16
I B2	39	50	45	47	38
II A1	8	7	9	16	15
II A2	15	11	8	15	18
II B	139	69	52	96	69
III A	22	14	19	12	12
III B	122	211	204	139	129
IV A	5	7	3	23	8
IV B	12	32	26	30	32
Total	**377**	**416**	**373**	**392**	**349**

Table 2: Stage Distribution as per FIGO 2018 System:

FIGO 2018	2014	2015	2016	2017	2018
I A1	1	2	1	0	1
I A2	3	3	2	2	1
I B1	5	5	5	5	6
I B2	4	4	2	5	7
I B3	24	27	32	30	28
II A1	7	6	8	14	13
II A2	10	9	7	11	11
II B	89	42	37	66	48
III A	8	6	7	6	6
III B	42	81	101	79	65
III C1	154	183	139	114	108
III C2	15	13	7	11	8
IV A	5	7	3	23	8
IV B	10	28	25	26	29
Total	**377**	**416**	**373**	**392**	**349**

Table 3: Stage Distribution comparison:

Stage	FIGO 2009 (as percentage of total)	FIGO 2018 (as percentage of total)
1A1	0.26	0.26
1A2	0.57	0.57
1B1	2.93	1.36
1B2	11.48	1.15
1B3	NA	7.42
IIA1	2.88	2.52
IIA2	3.51	2.52
IIB	22.28	14.84
IIIA	4.14	1.73
IIIB	42.21	19.36
IIIC1	NA	36.73
IIIC2	NA	2.84
IVA	2.41	2.42
IVB	6.92	6.21

The most significant change was from stage IIB and stage IIIB to IIIC1. Upstaging occurred significantly in stage IIIB (54.1% upstaged) followed by stage IIB (33.7% upstaged). Stage IIIC1 emerged out to be the most populous stage (36.73%) followed by stage IIIB (19.36%) & IIB (14.84%). Downstaging occurred only in stage IVB ,i.e, to stage IIIC. (Table 3)

The contributions to the new stages IIIC1 is mainly from stages IIIB, IIB & IB2(old). The new stage IB3 is formed from the patients previously classified as IB2. Most of the data was based on radiological consideration of enlarged pelvic and para- aortic nodes as metastatic even in the absence of histological proof.

DISCUSSION:

Table 4 Changes in cervical cancer staging system.[3]

Characteristics	2014 FIGO system	2018 FIGO system
Stage IB1	Tumor size ≤4 cm	Tumor size ≤2 cm
Stage IB2	Tumor size >4 cm	Tumor size >2cm & < 4cm
Stage IB3	n/a	Tumor size ≥4 cm
Stage IIIC1	n/a	Pelvic lymph node metastasis only
Stage IIIC2	n/a	Para-aortic lymph node metastasis

FIGO does not specify the modality to be used for imaging, the choice of which is to be based on the available resources and expertise. If it is based on the pathology report (whether cytology or histology), a notation of 'p' is added (i.e. C1p or C2p). The pathological staging supersedes other findings.

The presence of isolated tumour cells (ITCs) does not change the staging but the presence of micrometastases will change the staging to stage IIIC.

Based upon a recent validation analyses of Matsuo et al. [5] using the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program between 1988–2014, the revised FIGO staging system for cervical cancer is useful to distinguish survival groups. Applying the new system, stage IB1 and stage IB2 disease have distinct characteristics and outcomes, e.g., stage IB1 disease is more likely to be low-grade, and have adenocarcinoma histology, whereas stage IB2 disease is more likely to be high-grade and have squamous histology. Patients with stage IB2 disease are more likely to undergo pelvic lymphadenectomy and radical hysterectomy, while women with stage IB1 disease are less likely to have received postoperative radiotherapy. [7] Additionally, patients with stage IB2 disease have a nearly 2-fold increased risk of cervical cancer death compared to those with stage IB1 disease. Based on this new classification, risk-stratification will be very useful when applied to the treatment algorithm for tumors less than 4 cm.

Another major change in the current staging system is incorporation of lymph node (LN) status into stage III disease. Patients who have documented pelvic and/or para-aortic LN metastasis are specifically designated as stage IIIC. Under the revised system, radiographic and/or histological findings are allowed to assign stage IIIC disease. Stage IIIC1 is designated when only pelvic LN metastasis is detected, while stage IIIC2 is designated when para-aortic LN metastasis is documented by either method. Matsuo et al. [5] performed a validation analysis of this new system for classification of stage III disease by utilization of the SEER database. In stage III disease, survival of women with stage IIIC1 disease is greater for those patients with stage IIIA or stage IIIB disease. The analysis showed 5-year cervical cancer specific survival rates of 46.0% for stage IIIA disease, 42.6% for stage IIIB disease, and 62.1% for stage IIIC1 disease. It is essential to note that stage IIIC1 disease reflects a heterogeneous group of tumors with a wide range of survivals based on local tumor factors: 5-year cervical cancer-specific survival rates were 74.8% for T1, 58.7% for T2, and 39.3% for T3 with a 35.3% difference in absolute survival. Stage IIIC1 cervical cancer is not a single disease entity, and local tumor factors remain the primary determinant of survival. Nishio et al. [4] showed that the prognosis of women with cervical cancer with extra-pelvic metastasis varies based on metastatic sites outside of the pelvis. Specifically, outcomes for metastatic cervical cancer solely in the para-aortic LNs are superior when compared to cervical cancer metastasized to other extra-pelvic sites. This implies the necessity of distinguishing para-aortic LN metastasis from other metastasis, which is reflected in the 2018 staging system.

In a study[8] from Zhejiang cancer hospital , Hangzhou, China 662 cervical cancr patients who underwent surgery where restage as per 2018 guidelines. On re-staging of patients, 17.3%, 44.5%, 25.4%, and 37.1% of the patients with FIGO 2009 stage IB1, IB2, IIA1, and IIA2, respectively, were upgraded to FIGO 2018 IIIC1P stage, and 2.1%, 3.0%, 3.1%, and 2.1% patients, respectively, were upgraded to IIIC2P stage.

Several controversial issues continue to remain unresolved in the absence of substantial data on their impact on survival, e.g. including the prognostic value of ovarian metastases, presence of isolated tumor cells in nodal metastases & lymphovascular invasion.[3]

More importantly, in the revised staging system, assessment of lymph node involvement by radiological methods remains a very subjective decision. This is especially relevant in regions where there is a high burden of infections including tuberculosis , HIV & pelvic inflammatory diseases, which are common in regions with high cervical cancer prevalence, in which patients may develop non metastatic lymph node enlargement. It is upto the clinician to consider it as tumor spread or not.[3]

We recognize several limitations in our study. First, this was a retrospective study and had all the inherent limitations of this form of research. Second, consideration of radiological enlargement of pelvic nodes as pathological. Third, all patients were from a single centre and so the results may not be generalizable to all patients.

CONCLUSION:

The most important function of a good staging classification is to discriminate survival differences as the stage advances. As a corollary, this correlates with prognosis and is used to plan the best management strategy.

In conclusion, the current FIGO 2018 staging system for cervical cancer appears to be useful for predicting survival in patients considering radiological and pathological variables.As per our study majority of the cancer cervix patients fall into a single subgroup (IIIC1); this in a country were already most patients present with advanced disease, will skew the data further.

Stage IIIC1 cervical cancer is not homogenous; survival in stage

IIIC1p varies with the number of metastatic lymph nodes.[8] Efforts should be made to further improve the FIGO staging system. Therefore, we suggest that during the next revision of the staging system, the FIGO committee should take into account the influence of the number of lymph node metastases on survival and prognosis of IIIC1P patients. Also the local advancement (T size) of the disease should be taken into account and stage IIIC1 should be further sub classified. Establishment of pathological staging on a broader scale would definitely add more prognostic value to the current staging system.

Physicians who work in the LMICs are notoriously poor at data keeping. The end result is that an enormous amount of data is not available for contribution to evidence-based medicine. Now more than ever before it has become important to collect and report data that will determine the validity of the current staging and assist future revisions.

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