



## Review Article

# Implications of the revised cervical cancer FIGO staging system

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**The 2018 revised International Federation of Gynaecology and Obstetrics (FIGO) staging of cervical cancer has brought about a paradigm shift by offering the option of adding imaging and pathology to clinical staging. This makes it applicable to all types of resource situations across geographies with implications for all stakeholders, including gynaecologists, gynaecologic oncologists, radiologists, pathologists and radiation and medical oncologists. The new staging classification has more granularity, with three sub-stages of stage IB and a new category of stage IIIC for all cases with lymph node (LN) involvement. The major limitations of clinical staging were inaccurate assessment of tumour size and inability to assess pelvic and para-aortic LNs with the limited investigations permitted by FIGO to change the stage. This resulted in understaging of stages IB-III, and overstaging of stage IIIB, which has been largely overcome by incorporating imaging findings. Although any imaging modality can be used, magnetic resonance imaging appears to be the best imaging modality for early-stage disease owing to its better soft-tissue resolution. However, the use of contrast-enhanced computed tomography or ultrasonography are also feasible options, depending on the availability and resources. But wherever pathological evaluation is possible, it supersedes clinical and radiological findings.**

**Key words** Cervical cancer - implications - FIGO - oncologists - pathologists - radiologists - revision - staging

## Introduction

Staging systems of any cancer need to be revisited in a timely manner with periodic revision and modifications when there are new data to inform the impact of advancements in diagnostic tools and treatment strategies on oncological outcomes<sup>1,2</sup>. Cervical cancer is predominantly a disease of low- and middle-income countries (LMICs) where resources are constrained, hence to maintain global uniformity

the International Federation of Gynaecology and Obstetrics (FIGO) continued to recommend clinical staging till 2009, with only a few basic investigations allowed to change the stage<sup>3</sup>. However, the last decade witnessed rapid changes because of significant developments in imaging, surgical and radiotherapy techniques and new drug development, which had an enormous impact on the management of cervical cancer, including fertility preserving and minimally

invasive approaches, improved radiation techniques, addition of biologically targeted therapies, *etc*<sup>4</sup>. A review of the published oncological outcomes led to the latest revision of the FIGO staging for carcinoma cervix in 2018, which is unique in that it offers flexibility to the user to choose clinical, radiological or pathological findings as the basis for stage assignment, depending upon the availability of resources, and thus takes into account the problems faced in LMICs. The revised classification system thus affects all members of the multi-disciplinary team involved in the care of women with cervical cancer, including gynaecologists, oncologists, radiologists and pathologists. This article looks at the main revisions from different viewpoints.

### The revisions

The 2018 staging of cervical cancer was presented at the XXII FIGO World Congress at Rio de Janeiro, Brazil after a collaborative effort of nearly three years by the FIGO Gynaecologic Oncology Committee, working with all major societies<sup>5</sup>. Due to some concerns raised by pathologists regarding alignment with TNM classifications of malignant tumours, a corrigendum was agreed upon and published soon thereafter<sup>6</sup> (Table I).

The main changes in the revised staging are as follows:

(i) For microinvasive disease (stage IA), the horizontal dimension is no longer considered; (ii) In Stage IB, the sub-stages have been revised according to greatest tumour dimension (Stage IB1: invasive carcinoma up to 2 cm; Stage IB2: >2 cm and ≤4 cm and Stage IB3: invasive carcinoma >4 cm); (iii) The involvement of lymph nodes (LNs) according to either imaging (*r*) or pathology (*p*) is now assigned stage IIIC, irrespective of tumour size and extension (stage IIIC1: pelvic LN metastasis only; stage IIIC2: paraaortic LN metastasis), however, the pathological staging, if available, takes priority over findings on imaging; (iv) The presence of micrometastases allocates the case to stage IIIC. This is one of the changes in the corrigendum, which aligns it with the TNM classifications of both the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC). The presence of isolated tumour cells (ITCs) does not change the staging, but a note should be made of this finding. As with other aspects of the revised staging, centres that do not have the pathological facilities to assess micrometastases are not mandated to do so; (v) While the definition of stages II and IV remain the

same, their allocation can be changed by imaging, *e.g.*, observation of parametrial infiltration, *etc*; (vi) When documenting the findings, it is important to indicate whether these are derived based on clinical findings (no additional notation), or radiological or pathological findings (notation of '*r*' or '*p*' where these have changed the findings).

### Implications for gynaecologic and radiation oncologists

The primary aim of staging for the treating oncologist is an accurate assessment of locoregional and distant extent of the disease for appropriate management, accurate prognostication and comparison among institutions<sup>7</sup>. Previously, cervical cancer was staged clinically with only a few imaging modalities being allowed to change the staging<sup>4</sup>. The main drawback of this approach was the high probability of inaccuracies, especially with respect to nodal staging, which was known to change the prognosis but did not change the stage. According to a multivariate analysis of prognostic variables, conducted by the Gynaecologic Oncology Group as far back as 1991, tumour size and LN status, both pelvic and paraaortic, were shown to be significantly associated with progression-free survival<sup>8</sup>. Using the 2009 staging system, it was seen that a large number of cases who were operated based on clinical findings later needed adjuvant therapy; hence, such inaccuracies also had an adverse impact on treatment-related morbidity. Finally, in LMICs, this also meant inappropriate use of scarce resources<sup>2</sup>.

Tumour size across all stages has previously been shown to have an impact on cause-specific survival (CSS) and overall survival (OS)<sup>8</sup>. When the hazard ratio (HR) for CSS in Stage I tumour with size <2 cm was taken as 1.00, the corresponding values were 3.26 [95% confidence interval (CI), 2.64-4.04] for tumours measuring 2-4 cm, and 6.65 (95% CI, 5.45-8.12) for tumours >4 cm<sup>9</sup>. Accrual of data from oncological outcomes of fertility-sparing surgery (FSS) has greatly informed the tumour size cut-offs in stage IB in the FIGO 2018 staging and will, in turn, influence management decisions in this group of patients<sup>10-12</sup>. Tumour size was found to be an important independent prognostic factor, associated with increased risk of recurrence<sup>10,11</sup>. Fertility sparing surgery (FSS) is presently recommended for tumours <2 cm in diameter as the risk of recurrence is relatively lower (6%). On the other hand, for tumours >2 cm, the risk of recurrence is unacceptably high (17%) and

**Table I.** International Federation of Gynecology and Obstetrics (FIGO) 2018 revised staging of cervical carcinoma<sup>6</sup>

Stage I	The carcinoma is strictly confined to the cervix (extension to the corpus should be disregarded)
IA	Invasive carcinoma that can be diagnosed only by microscopy with a maximum depth of invasion $\leq 5$ mm <sup>a</sup>
IA1	Measured stromal invasion $\leq 3$ mm in depth
IA2	Measured stromal invasion $>3$ mm and $\leq 5$ mm in depth
IB	Invasive carcinoma with measured deepest invasion $>5$ mm (greater than Stage IA); lesion limited to the cervix uteri with size measured by maximum tumour diameter <sup>b</sup>
IB1	Invasive carcinoma $>5$ mm depth of stromal invasion and $\leq 2$ cm in greatest dimension
IB2	Invasive carcinoma $>2$ cm and $\leq 4$ cm in greatest dimension
IB3	Invasive carcinoma $>4$ cm in greatest dimension
Stage II	The cervical carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall
IIA	Involvement limited to the upper two-thirds of the vagina without parametrial invasion
IIA1	Invasive carcinoma $\leq 4$ cm in greatest dimension
IIA2	Invasive carcinoma $>4$ cm in greatest dimension
IIB	With parametrial invasion but not up to the pelvic wall
Stage III	The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or paraaortic lymph nodes
IIIA	Carcinoma involves lower third of the vagina, with no extension to the pelvic wall
IIIB	Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)
IIIC	Involvement of pelvic and/or paraaortic lymph nodes (including micrometastases) <sup>c</sup> , irrespective of tumour size and extent (with <i>r</i> and <i>p</i> notations) <sup>d</sup>
IIIC1	Pelvic lymph node metastasis only
IIIC2	Paraaortic lymph node metastasis
Stage IV	The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous oedema, as such, does not permit a case to be allotted to Stage IV
IVA	Spread of the growth to adjacent organs
IVB	Spread to distant organs

*Source:* Reproduced with permission from Ref 65. <sup>a</sup>Imaging and pathology can be used, when available, to supplement clinical findings with respect to tumour size and extent, in all stages, pathological findings supercede imaging and clinical findings; <sup>b</sup>The involvement of vascular/lymphatic spaces should not change the staging. The lateral extent of the lesion is no longer considered; <sup>c</sup>Isolated tumour cells do not change the stage, but their presence should be recorded. <sup>d</sup>Adding notation of *r* (imaging) and *p* (pathology) to indicate the findings used to allocate the case to stage IIIC.

FSS is not recommended<sup>10</sup>. Thus, the division of stage IB into three sub-stages in the FIGO 2018 staging allows for better prognostic discrimination and enables gynaecologic oncologists to identify women in stage IB1 who are most suitable for fertility-sparing, those in stages IB1 and IB2 who are likely to be cured by surgical treatment alone without the need for adjuvant therapy, and those in stage IB3 who are best treated by chemoradiation because of the increased likelihood of requirement of post-operative adjuvant therapy<sup>13</sup>.

Although lymph node (LN) involvement was not included in the FIGO 2009 staging, it has always

been a major factor in treatment planning<sup>14</sup>. Patients found to have positive nodes were not considered suitable for surgery regardless of tumour size and other characteristics and were directly referred to chemoradiation<sup>15,16</sup>. In many parts of the world, surgico-pathological assessment of paraaortic nodes is considered necessary before offering extended field radiation to women with locally advanced disease, recognizing the side-effects of this treatment<sup>15,17</sup>. In recent years, assessment of LNs by minimally invasive techniques had become the standard of care in many institutions<sup>17</sup>. Addition of a separate sub-stage IIIC

for cases with LN metastasis was a major change in the 2018 staging, segregating patients who would be deemed operable based on clinical examination but would need subsequent adjuvant therapy because of positive LNs. This would prevent morbidity associated with multimodality therapy for a large majority of cases<sup>13,15</sup>. According to the current staging system, patients staged as IIIC (C1/C2) will directly receive chemoradiation, with the field of radiation planned according to the sub-stage assignment, which has profound implications for radiation oncologists<sup>15</sup>.

Following the publication of the 2018 revised staging, several centres reviewed their data retrospectively and observed a significant stage shift and impact on prognosis across all stages (Tables II and III)<sup>18-22</sup>. Tumour size and LN involvement were the two main variables responsible for this stage shift in 23 and 32 per cent cases, respectively<sup>21</sup>. An analysis by Narayan *et al*<sup>23</sup> demonstrated a significant stage shift which was proportionate to tumour size. Tumour volume was assessed by magnetic resonance imaging (MRI) with or without positron emission tomography (PET) among 853 patients who had received non-surgical management. Among 69 patients with tumour diameter <2 cm (4 cm<sup>3</sup> volume), 42 per cent remained confined to the cervix and were node negative, 10 per cent upstaged to stage IIB, and 29 per cent to stage IIIC. Among 307 cases with tumour diameter 2-4 cm (<33 cm<sup>3</sup>), 28 per cent retained the same stage, 23 per cent upstaged to stage IIB and 35 per cent to stage IIIC. In 423 women with tumour diameter >4 cm (>33 cm<sup>3</sup>), the disease remained confined to cervix in only nine per cent of cases, while 26 per cent upstaged to stage IIB and 53 per cent to stage IIIC. Overall, 43 per cent patients upstaged to the newly created stage IIIC<sup>23</sup>.

In the entire early-stage (IB1–IIA2) dataset of 464 patients, MRI upstaged 65 (14%) patients to stage IIB, while addition of PET upstaged 186 (40%) to stages IIIC1 and IIIC2 (32.9% and 7.1%, respectively). Of those originally in stage IIB, 75/221 (34%) patients remained in stage IIB, 25 (11%) were downstaged to stage IB, while 116 (51%) patients were upstaged to stages IIIC1-IVB. Of 111 cases originally in stage IIIB, only 16 (13.5%) remained in the new stage IIIB, 21 (19%) were downstaged to stage IIB, while 74 (66%) were upstaged to stages IIIC1-IVB<sup>23</sup>. Lymph node metastasis (stage IIIC) was seen in 43 per cent, contributed from all stages. Contribution to pelvic nodal disease (stage IIIC1) was 31, 41, 29, 30, 32, 33 and 34 per cent from stages IB1, IB2, IB3, IIA1, IIA2,

IIIA and IIIB, respectively of FIGO 2009 staging<sup>23</sup>. The corresponding contribution to paraaortic nodes (stage IIIC2) was 5, 6, 16, 15, 15 and 24 per cent, respectively. Nodal metastasis was similar in the following groups: stages IB1 and IIA1 (36-40%), stages IB2, IIA2 and IIB (40-50%) and stages IIIB and IVA (47-50%)<sup>23</sup>.

Interestingly, it was observed that patients with corpus invasion had a significantly higher risk of LN involvement (61 vs. 30%;  $P < 0.001$ ). In both the 2009 and 2018 staging systems, uterine corpus involvement does not change the stage; nevertheless in this retrospective analysis, the stage changed in two-thirds of these cases because of concomitant involvement of LNs<sup>23</sup>.

Regarding oncological outcomes, the retrospective analyses showed that reassignment according to FIGO 2018 staging allowed better prediction of disease-free survival and OS in stages I, II and III (Table III). The analysis by Matsuo *et al*<sup>24</sup> also found a good discriminatory value with five-year survival rates for revised stages IB1, IB2 and IB3 of 97, 92.1 and 83.1 per cent, respectively. The 2018 staging system was an independent prognostic variable for CSS: risk of death due to cervical cancer was two-fold higher in stage IB2 and four-fold higher in stage IB3 than stage IB1 (IB2: HR 1.98, 95% CI 1.62-2.41; IB3: HR 4.07, 95% CI 3.33-4.97): for stage IB3 was also two-fold lower than for stage IB2 (HR 2.11, 95% CI 1.80-2.47). However, the survival of women in stage IIIC1 was found to be higher than of those in stages IIIA or IIIB (five-year CSS: 46.0, 42.6, and 62.1% in stages IIIA, IIIB and IIIC1, respectively). This could be because tumour size is an independent variable for disease control, as the five-year CSS was found to decrease from 75 per cent for T1, 59 per cent for T2 and 39 per cent for T3 tumours<sup>24</sup>. Yan *et al*<sup>19</sup> also observed the heterogeneity within stage IIIC1 and relationship between the survival and number of positive pelvic LNs; however, its significance is not yet established and needs further investigation. The survival in stage IIA1 was better than in stage IB3. Thus, there are some clinical scenarios that still remain to be explored<sup>25</sup>. Stage IIIC1 disease especially is a heterogeneous group where the present staging classification does not take tumour size into account.

### Implications for radiologists

Previous FIGO staging systems were based on clinical assessment and only basic imaging techniques were allowed to change the staging. However, the

Table II. Correlation of stage allocation by the International Federation of Gynecology and Obstetrics (FIGO) 2009 and revised FIGO 2018 staging systems in retrospective analyses													
Author, number of cases, FIGO stage	FIGO 2009		FIGO 2018 stage										Overall stage shift to IIIC n (%)
	FIGO stage	IA n (%)	IB1, n (%)	IB2, n (%)	IB3, n (%)	IIA1, IIA2 n (%)	IIB, n (%)	IIIA, n (%)	IIIB, n (%)	IIIC1p, n (%)	IIIC2p, n (%)		
Ayhan <i>et al</i> <sup>18</sup> n=425, stages IB and IIA	IB1 (n=294)	-	53 (18.2)	127 (43.2)	29 (9.8)	-	-	-	-	70 (23.8)	15 (5.1)	35.3% (150/425)	
	IB2 (n=131)	-	0	0	66 (50.4)	-	-	-	-	44 (33.6)	21 (16.1)		
Yan <i>et al</i> <sup>19</sup> n=662, stages IB and IIA	IB1 (n=336)	-	149 (44.3)	122 (36.3)	0	0	-	-	-	58 (17.3)	7 (2.1)	28.2% (187/662)	
	IB2 (n=99)	-	-	-	52 (52.5)	0	-	-	-	44 (44.5)	3 (3.0)		
	IIA1 (n=130)	-	-	-	-	93 (71.5)	-	-	-	33 (25.4)	4 (3.1)		
	IIA2 (n=97)	-	-	-	-	59 (60.8)	-	-	-	36 (37.1)	2 (2.1)		
Wright <i>et al</i> <sup>20</sup> n=62,212, stages I-IV	IA1 (n=2858)	2812 (98.4)	-	-	-	-	-	-	-	-	46 (1.6)	16.7% (6914/41,364)	
	IA2 (n=893)	844 (94.5)	-	-	-	-	-	-	-	49 (5.5)	459 (9.3)		
	IB1 (n=10,547)	-	4480 (42.5)	-	-	-	-	-	-	1000 (19.5)	-		
	IB2 (n=4847)	-	-	4120 (85.0)	-	3790	-	-	-	1545 (29.0)	-		
de Gregorio <i>et al</i> <sup>21</sup> n=265, stages IA1-III B	IB3	-	-	-	-	-	-	-	-	-	-		
	IIA1 (n=899)	-	-	-	-	-	742 (82.5)	-	-	157 (17.5)	-		
	IIA2 (n=1593)	-	-	-	-	-	1101 (69.1)	-	-	492 (30.9)	-		
	IIB (n=11,487)	-	-	-	-	-	8904 (77.5)	-	-	NA	-		
	IIIA (n=1385)	-	-	-	-	-	-	954 (68.8)	-	431 (31.1)	-		
de Gregorio <i>et al</i> <sup>21</sup> n=265, stages IA1-III B	IIIB (n=7912)	-	-	-	-	-	-	5177 (65.4)	-	2735 (34.6)	-		
	IA1 (n=10)	9 (90)	-	-	-	-	-	-	-	1 (10)	-	32% (85/265)	
	IA2 (n=13)	13 (100)	-	-	-	-	-	-	-	-	-		
	IB1 (n=96)	-	48 (50)	34 (35.4)	2 (2.1)	-	-	-	-	10 (10.4)	2 (2.1)		
	IB2 (n=37)	-	-	-	25 (67.6)	-	-	-	-	12 (32.4)	-		
	IIA1 (n=5)	-	-	-	-	-	3 (60)	-	-	2 (40)	-		
de Gregorio <i>et al</i> <sup>21</sup> n=265, stages IA1-III B	IIA2 (n=11)	-	-	-	-	6 (54.5)	-	-	-	5 (45.4)	-		
	IIB (n=93)	-	-	-	-	-	40 (43.1)	-	-	43 (46.2)	10 (10.7)		

**Table III.** Summary of studies showing the impact of revised staging on stage-wise prognosis

FIGO stage	Ayhan <i>et al</i> <sup>18</sup> (n=425)		Yan <i>et al</i> <sup>19</sup> (n=662)		Wright <i>et al</i> <sup>20</sup> (n=62,212)	Liu <i>et al</i> <sup>22</sup> (n=586)
	5 yr DFS (%)	5 yr OS (%)	5 yr PFS (%)	5 yr OS (%)	5 yr OS (%)	3 yr DFS (%)
<b>IA</b>						
2009	-	-	-	-	93.4	-
2018	-	-	-	-	94.1	-
<b>IB1</b>						
2009	81	88	-	-	85.5	-
2018	91.5	95.2	94	-	91.6	-
<b>IB2</b>						
2009	61.7	73.5	-	73.2	70.9	73.2
2018	81.9	89.3	91	-	83.3	-
<b>IB3</b>						
2009	NA	NA	NA	NA	NA	NA
2018	67.6	84.2	88.5	-	76.1	-
<b>IIA1</b>						
2009	-	-	-	63.7	68.0	63.7
2018	-	-	91.4	-	70.3	-
<b>IIA2</b>						
2009	-	-	-	-	61.7	-
2018	-	-	86.4	-	65.3	-
<b>IIB</b>						
2009	-	-	-	66.7	61.3	66.7
2018	-	-	-	-	63.9	-
<b>IIIA</b>						
2009	-	-	-	64.7	40.5	64.7
2018	-	-	-	79.9	40.7	79.9
<b>IIIB</b>						
2009	-	-	-	59.6	38.4	59.6
2018	-	-	-	70.4	41.4	70.4
<b>IIIC1</b>						
2009	NA	NA	NA	NA	NA	NA
2018	75.2	79.0	79.5	66.3	60.8	66.3
<b>IIIC2</b>						
2009	NA	NA	NA	NA	NA	NA
2018	45.3	67.2	43.8	29.8	37.5	29.8

DFS, disease-free survival; OS, overall survival; PFS, progression-free survival; NA, not applicable

major limitations of clinical staging are under-staging in stages IB-III (up to 20-30% patients) and over-staging in stage IIB (in nearly 64% patients)<sup>26</sup>. To overcome these limitations, the revised FIGO staging has incorporated diagnostic imaging for assessment of loco-regional spread of the disease and identification of distant metastases. This will help in tailoring

treatment for optimum disease control with minimum treatment-related morbidity. The incorporation of radiological features in staging has placed additional responsibility on radiologists to provide an accurate assessment of primary tumour size, spread to parametria and vagina, lymph nodal involvement and metastatic spread. In case of discrepancy between



clinical and radiological findings, and in the absence of pathological confirmation, the stage allocation is based on radiology.

The FIGO 2018 staging allows the use of any imaging techniques to allocate the stage<sup>6</sup>. However, considering difference in available resources globally, FIGO does not mandate any particular imaging modality, the choice of which is based on availability and expertise. While this recommendation is practical, it is unclear whether it would have the potential to assign a different stage to the same patient if a different type of modality is used. Therefore, it is recommended to specify imaging techniques used for staging the patient to allow for meaningful understanding of the data in the future.

Cross-sectional imaging can demonstrate loco-regional extent of the disease as well as distant metastases. In clinically early-stage disease with small masses, MRI is the imaging modality of choice owing to its better soft-tissue resolution. It is significantly better than clinical staging for the estimation of tumour size in early stage cancers and in patients with endocervical growths. In a study by Zhang *et al*<sup>27</sup>, the mean diameter was reported to be  $2.97 \pm 1.39$ ,  $2.78 \pm 1.24$  and  $1.97 \pm 1.70$  cm, respectively ( $P < 0.0001$ ) in the final histopathology, MRI and clinical examination, respectively. The correlation of tumour size with final histopathology reported size was better with MRI than clinical examination with a correlation coefficient of 0.481 and 0.362, respectively. An MRI is also more accurate in determining parametrial infiltration as compared to clinical assessment with a sensitivity of 84 per cent (vs. 40%) and specificity of 92 per cent (vs. 93%)<sup>28</sup>. Assessment of tumour diameter may be affected by inflammatory oedema or haemorrhage, particularly following biopsy. The addition of newer imaging techniques such as diffusion-weighted image and dynamic contrast-enhanced sequence (DCE) enhances the efficacy of conventional MRI in tumour size estimation, LN detection, parametrial infiltration and depiction of recurrence<sup>29,30</sup>.

Contrast-enhanced computed tomography has a comparable accuracy to MRI in detecting parametrial infiltration and LN detection<sup>31</sup>. However, it has its own fallacies in terms of poor soft-tissue resolution, which makes differentiation of a bulky cervix from carcinoma cervix difficult. It is more readily available, cost-effective and less time-consuming than MRI and is preferred in patients with advanced stage, large tumour

and in resource-constrained settings as it enables fast acquisition of chest and abdomen images<sup>31</sup>.

Positron Emission Tomography (PET) is a non-invasive imaging modality which assesses molecular functioning by demonstrating a degree of uptake of the radiotracer by the diseased sites<sup>32</sup>. The most commonly used radiotracer is <sup>18</sup>F-2-fluoro-2-deoxy-D-glucose (FDG) which gets accumulated in the tumour and metastatic sites. Hybrid imaging involves the acquisition of CT along with PET and has been shown to improve the accuracy in both LN detection and local disease spread, as compared to either CT or PET used as stand-alone modalities<sup>32</sup>. FDG uptake can be seen in primary cervical cancers larger than 7 mm in size, thus improving the tumour detection rates; however, it is limited in cases of necrosis, ulceration, accumulation of fluid or blood in endocervical or endometrial canal<sup>33</sup>. The sensitivity and specificity of LN detection with PET-CT vary with stage of the disease; ranging from 53-73 upto 90-97 per cent, respectively in early-stage disease. In more advanced disease, the sensitivity improves to 75 per cent but specificity remains the same *i.e.* 95 per cent<sup>34</sup>.

Considering all these factors, many authors have studied the feasibility of transvaginal (TVS) and transrectal ultrasonography (TRUS) for the evaluation of early-stage tumours. Both these modalities have shown comparable efficacy as compared to the gold standard MRI in tumour detection, size estimation and parametrial infiltration<sup>35</sup>. With large, friable tumours, TVS may induce bleeding and may also prove an impediment. Transrectal US (TRUS) does not have this disadvantage. The diagnostic accuracy of ultrasound being comparable to MRI and CT scan has led to its use even in good-resource settings<sup>36</sup>. Centres in Europe have reported results for local tumour assessment with TVS and TRUS<sup>37</sup>. Thus, in resource-limited settings, a TVS or TRUS with a high-frequency transducer can be recommended as an alternative to MRI for local tumour characterization. Screening with transabdominal ultrasound along with TRUS/TVS may be considered to rule out enlarged LN and hydronephrosis at the same time. The detection of metastatic LNs on imaging would up-stage the case to stage IIIC1(r) or C2(r) regardless of local tumour size and spread. The main concern has been of determining whether LN enlargement is caused by inflammation or metastasis. Conventionally, if the node is with a short-axis dimension of more than 10 mm or shows necrosis should be considered suspicious for metastasis. An MRI can detect such LN

metastases with an accuracy of 76-100 per cent and sensitivity of 36-89.5 per cent<sup>38</sup>. Since PET determines the metabolic activity within the tissue, it is found to be more accurate than MRI in detecting LN involvement in carcinoma cervix with the positive predictive value and specificity reaching up to 100 per cent; however, the latter is better in demonstrating the local tumour spread<sup>39</sup>. Many areas of the world where there is a high incidence of cervical cancer are also endemic for tuberculosis and HIV infection, which are also associated with necrotic or enlarged LNs. This may pose a diagnostic dilemma in patients with equivocal imaging features<sup>40,41</sup>. Hence it is imperative that radiologists develop consensus standards and criteria for image acquisition, interpretation and standardized reporting format. At the same time, clinicians should be aware of and weigh the strengths and limitations of various imaging modalities and correlate the clinical presentation along with imaging findings.

### **Implications for pathologists**

Pathologists have always held the final diagnosis especially in cancer. In the revised system too, the final stage allocation is based on pathologic findings in case of any discordance between clinical, radiological and pathologic features<sup>6</sup>.

The extent of horizontal spread has been omitted from stage IA in the current staging for the following reasons: poor reproducibility, insufficient data on correlation with nodal involvement or prognosis and was apparently arbitrary. But removal of the horizontal spread has implications both for clinicians as well as the pathologists. A small number of patients who would have been assigned stage IB1 based on >7 mm spread in FIGO 2009 will now be down-staged to stage IA. Although the extent of horizontal spread does not affect the staging, pathologists are nevertheless required to report the exact size and extent of horizontal spread to inform future revisions. Here, it is also important to mention the number of sections or blocks that are involved by the tumour. The chief concerns regarding removal of horizontal spread as a criterion include underreporting of the spread and the possibility of missing out vaginal involvement in superficially spreading tumours<sup>15</sup>. However, this is unlikely to have any significant impact as the superficially spreading squamous cell carcinomas of the uterine cervix are less common<sup>42</sup>. Moreover, a careful gross and meticulous microscopic evaluation of sections from the vaginal cuff in the specimen would detect any such spread.

Clinical assessment of tumour size is highly subjective and is often inaccurate<sup>43</sup>. Division of stage IB disease into three sub-stages based on pathological or radiological assessment is expected to improve the accuracy of tumour size measurement compared to clinical assessment alone. In patients who undergo radical surgery, the final stage assignment will be based on pathological dimensions and not on clinical or radiological assessments. An accurate assessment of all dimensions of primary tumour in a hysterectomy specimen will therefore be of utmost importance for staging and will require a greater degree of time and effort to ensure consistency and accuracy. Tumour size is generally evaluated in two dimensions and accurate assessment of tumour volume is practically not possible. Only the ectocervical tumour can be assessed in most cases. For instance, tumours which are more infiltrative and with greater endocervical extension cause indurated enlargement of the cervix, appearing at times like a barrel-shaped tumour which may indicate a larger volume<sup>44</sup>. There is a likelihood that the size of such tumours may be measured inaccurately. Hence, there is a need to arrive at a consensus about the size of tumour to accurately classify stage IB into the three sub-stages especially when the size ranges in the transition zone (2 and 4 cm respectively). This should typically be discussed by a multidisciplinary team involving a gynaecologist, radiologist and pathologist to avoid any gross under- or over-estimation of size. In the case of multifocal tumours, the size of the largest tumour is to be taken into consideration. In tumours that are predominantly exophytic and in tumours which have extensive ulceration of the surface epithelium, there may be limited deep invasion into the cervical stroma, or the assessment of depth may not be possible. The tumour thickness may be provided in such cases instead of depth, with a note explaining the reason for the inability to assess depth such as lack of proper orientation of the specimen at the time of embedding<sup>44</sup>.

In the FIGO 2018 staging, patients with LN metastasis including micro-metastasis (small clusters <0.2 mm in greatest dimension) are assigned stage IIIC(p). Pathologists are required to perform a meticulous dissection of all LNs, submit them for microscopic examination and provide a detailed report. Larger LNs should be cut into 2-3 mm thick slices perpendicular to the long axis and placed in the appropriate number of cassettes rather than being crammed into one. Smaller LNs <0.5 cm may,



however, be processed in totality. The method of detection of metastasis, *i.e.*, on LN biopsy or on fine-needle aspiration cytology must also be mentioned in the report. Increasing use of sentinel LN (SLN) and ultra-staging in the surgical management of early-stage cervical cancer has the potential to increase the detection of micro-metastases. Around 15 per cent additional metastases could be detected by ultra-staging and SLN biopsy, by this criterion<sup>45,46</sup>. Ultra-staging involves serial sectioning of each node at multiple levels and staining with pan-cytokeratin immunohistochemistry when routine haematoxylin and eosin (H&E) stains do not reveal any tumour. The method proposed by Cibula and McCluggage<sup>46</sup> involves slicing each SLN at 2 mm intervals, making paraffin blocks from all the slices, sectioning at 200  $\mu$  intervals and cutting at least 2 sections per level. One of the sections is for H&E staining and the other for pan-cytokeratin (immunohistochemistry), if no tumour is detected on the H&E stained slides. It is also recommended to keep additional unstained sections at each level. Various other protocols have been described for ultra-staging, but all are extremely time-consuming and laborious for the pathology laboratory. Clinicians need to be aware that there will be increased waiting time for the final report. A separate note should be made if metastasis is detected on ultra-staging because prognostic implications of LN micro-metastases and ITCs in cervical cancer are yet to be firmly established<sup>46,47</sup>. In developing countries, infection, especially tuberculosis, may be a cause of lymphadenopathy and this should be kept in mind in the appropriate clinical context. When suspected an aspiration cytology or biopsy of enlarged nodes may be warranted.

Overall, there are several merits to the FIGO 2018 staging system including tumour size and LN-based categorization and the incorporation of imaging and pathology. The revised staging system, therefore, requires meticulous and uniform assessment and reporting not only by clinicians but also by pathologists and radiologists. It provides a better distinction within stages and reflects survival outcome more accurately than the previous staging system with poorer outcome as the stage advances. Some issues still remain, *e.g.*, role of ITCs and uterine corpus involvement, poorer outcomes of parametrial involvement *vis-à-vis* LN metastases, *etc.* Standardized reporting will be of paramount importance for the treatment and prognostication of the patient and is the key for comprehensive cancer registries, epidemiological studies and research. Data

from LMICs are hence needed since the major burden of disease remains in these countries.

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