ORIGINAL ARTICLE

Retrospective study of pelvic and para-aortic lymph nodes positivity in stage 1A to 2A cervical cancer patients

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ABSTRACT

Background: The significance of pelvic and para-aortic lymph nodes (retroperitoneal lymph nodes) metastasis in the five-year survival of early stage cervical cancer (CC) patients is well established. The previous International Federation of Gynaecology and Obstetrics (FIGO) 2009 staging of CC was clinical and excluded advanced radiological assessment in assigning a stage. However, with the current FIGO 2018 staging, advanced radiological assessment and pathological findings were allowed to assign a stage which would alter the subsequent management. This pilot study aims to obtain local data on the correlation between radiological retroperitoneal lymph node positivity and histological lymph node positivity in early stage CC (stage 1A2 to 2A1) and seeks to correlate independent prognostic factors for recurrence to histological lymph node positivity.

Materials and Methods: In this retrospective cross-sectional analysis, clinical data, including clinical staging, Computed Tomography (CT) scan findings and histopathological results were collected and analysed in the Department of Obstetrics and Gynaecology, Hospital Ampang, Ministry of Health Malaysia.

Results: A total of 31 patients had surgery for CC from 1st August 2018 till 31st August 2020. Radical hysterectomy was done on 23 of them as primary treatment for early stage cervical cancer. Both pelvic and para-aortic lymph node dissection was done in 6 patients while 17 patients had only pelvic lymph node dissection. All patients had thoraco-abdomino-pelvic CT scans done preoperatively. Among the 82.6% patients with no enlarged pelvic lymph nodes on CT scan, all were confirmed by histology to be negative of malignancy. In the remainder 17.4% of patients with enlarged pelvic nodes on CT scan, three quarters had histology positive pelvic nodes for malignancy (p=0.002). Among patients with no enlarged para-aortic lymph nodes on CT scan, 83.3% had histologically negative para-aortic nodes. Among patients with clinical tumour diameter 2- 3.9 cm, 14.3% had positive pelvic nodes while a quarter of patients with clinical tumour diameter ≥ 4cm had histological positive pelvic nodes. None of the patients with tumour diameter < 2cm had positive pelvic nodes (p=0.993). Positive pelvic lymph nodes involvement was present in 37.5% of those with positive lymphovascular space invasion (LVSI). All patients with negative LVSI had no histological positive pelvic nodes (p=0.103). Among patients with tumour invasion involving the inner third of the stroma, 16.7% had histological positive pelvic nodes while 18.2% with outer third stromal invasion had positive nodes (p=0.977). None of the patients had histologically positive para-aortic lymph nodes with negative pelvic lymph nodes. Among patients with clinical stage 1B2, 20% would have been upstaged to stage 3C based on radiological imaging and final histology confirmation.

Conclusion: This study shows that in early stage CC, there is a statistically significant correlation between CT scan findings of enlarged pelvic lymph nodes and histological positive pelvic lymph nodes.

KEYWORDS:
Cervical cancer, radical hysterectomy, para-aortic lymph nodes, pelvic lymph nodes, computed tomography, FIGO staging

INTRODUCTION

In Malaysia, CC is ranked the third most common cancer in women after breast and colorectal with an age-standardised incidence rate per 100,000 of 6.2%.[1] Between 2011-2016, 3,981 cases of CC was reported with 59% detected in stage 1 and 2.1 In 2018, approximately 570,000 new cancer cases were diagnosed with more than 300,00 death reported worldwide.[2] Approximately 85% of new cases and 90% of deaths occur in low-resource countries or among people from low socioeconomic sections of society.[3] The occurrence of metastatic lymph nodes is an important factor that has implication on treatment and therapeutic outcomes in cervical cancer patients.[4] Therefore, accurate detection of lymph nodes metastases is paramount as it is correlated with a reduction in the five-year survival rate, despite of adjuvant radiotherapy to the surgery.[4]

The FIGO 2009 staging mainly depends on clinical and radiographic examination.[3] This staging was recently revised by FIGO Gynaecologic Oncology Committee to enable imaging and pathological findings, where available, to determine the stage and was presented in FIGO XXII World Congress of Gynaecology and Obstetrics in Rio de Janeiro in October 2018.[3] In FIGO 2009 staging, radiological node status did not determine stage. However, pre-treatment staging has shown that 18% of patients with stage 1B to 4A CC had para-aortic lymph node metastasis.[3,5] With the new FIGO 2018 staging, nodes positive patients was assigned to Stage 3C as lymph node involvement confers a worse prognosis.[3,6] Patients with pelvic lymph nodes positive and para-aortic lymph nodes positive was assigned to stage 3C1 and stage

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3C2 respectively.[3] Thus, stage 3C has been added and defined as the presence of nodal metastases on histology or advanced imaging such as CT scan, Magnetic Resonance Imaging (MRI), or Positron Emission Tomography(PET).

Studies using the sentinel lymph node mapping technique, confirms that any of the pelvic or para-aortic lymph nodes groups, may contain the first draining lymph node and resulting it to be the first site of nodal metastasis.[7,8,9] This demonstrates the possible occurrence of skipped lymph nodes involvement where there are para-aortic lymph nodes involvement without the involvement of pelvic lymph nodes. Clinical tumour size, depth of stromal invasion (DSI) and LVSI are independent prognostic factors for recurrence.[10] Increasing DSI is proportionate with the risk of pelvic lymph node metastasis. The risk of pelvic lymph node involvement is as high as 7% for stage 1A2 disease.[11] The incidence of LVSI was positively associated with DSI and lymph node metastasis. Lymph node metastasis is an independent factor that affects postoperative overall survival.[12] Survival is correlated with retroperitoneal lymph node involvement.[10] Early stage CC patients without pelvic nodes involvement treated with surgical treatment have five years' survival of 90%.[10] Pelvic lymph nodes involvement decreases the survival rate to 50-60% while para-aortic lymph nodes involvement decreases the rate further to 20-45%.[10]

The purpose of this pilot study was to obtain local data with regards to the correlation between radiological lymph node positivity versus histological proven lymph node positivity. It also seeks to correlate independent prognostic indicators for recurrence with histologically proven pelvic node positivity as well as the percentage of skipped para-aortic lymph nodes positivity without involvement of pelvic lymph nodes. Lastly, this study also seeks to determine the percentage of patients with stage 1A2 to 2A1 CC who are upstaged to stage 3C (FIGO 2018) based on radiological and histological results.

MATERIALS AND METHODS

Study design and population

This is a retrospective cross-sectional study conducted in a tertiary hospital, Hospital Ampang (HA), Ministry of Health Malaysia, Selangor. The medical records of patients with histologically proven cervical squamous cell carcinoma, adenocarcinoma or adenosquamous carcinoma who had undergone primary radical or modified radical hysterectomy and bilateral pelvic lymphadenectomy including dissection up to the level of para-aortic lymph nodes were reviewed. Patients with pre-operative FIGO 2009 stage 1A2 to 2A1 CC were included while patients with pre-operative staged as 1B3 following FIGO 2018 were re-staged to 1B2 and were included. These patients were operated in HA during the study period between 1st August 2018 till 31st August 2020.

The preoperative diagnosis of CC was obtained via cervical punch biopsy, Large Loop Excision of Transformation Zone (LLETZ), Loop Electrosurgical Excision Procedure (LEEP) biopsy or cone biopsy. Patients with previous neoadjuvant chemotherapy or radiotherapy (including haemostatic radiotherapy), known HIV infection, concurrent pregnancy on diagnosis, recurrent cervical cancer, palliative nodal debulking, inadvertent diagnosis of CC post-surgery where the surgery was done for a seemingly benign condition as well as those with neuroendocrine or sarcoma of cervix as final histopathological result were excluded.

Clinical data including CT scan reports and histopathological reports of patients fulfilling the criteria above were obtained from the electronic-hospital information system (e-HIS) using standardized data collection forms. This study was conducted in compliance with Malaysian Good Clinical Practice Guideline and was registered with the National Medical Research Register, Malaysia. The ethical approval for this study was obtained from the Medical Research and Ethical Committee (MREC), Ministry of Health Malaysia (NMRR-20-1457-55599).

Patient selection and surgery

The medical records of 31 patients who had surgery done for CC cancer was reviewed. Eight patients were excluded from the study due to the following reasons. Three had cervical neuroendocrine carcinoma and one had cervical carcinosarcoma as the final histopathological diagnosis. Two patients had exenteration and were staged as 3A and 4A respectively. One patient had neoadjuvant chemotherapy and was staged as stage 3A while another had extrafascial hysterectomy done for stage 2A2 with ovarian metastasis. The records of the remainder 23 patients were reviewed and were all clinically staged by trained Gynae-oncology Fellows and Consultant. Clinical staging was done either in the clinic or in the operation theatre under anesthesia. All patients had pre-operative histologically confirmed diagnosis of CC obtained either from certified pathologists in Hospital Serdang (HS), Ministry of Health Malaysia, Selangor or pathologists from private laboratories in Malaysia. All patients had either Type B or C radical hysterectomy according to Querleu and Morrow classification.[3] All post-operative specimens were sent to HS for histopathological analysis.

Radiological lymph node positivity

The preoperative CT scan reports of the thorax, abdomen and pelvis of the patients were reviewed. All reports were done either by in-house certified radiologists or radiologists from private medical centers in Malaysia. Lymph node positivity was taken as a short axis diameter ⩾10mm, single or multiple occurring either unilaterally or bilaterally with or without central necrosis.[13,14]

DSI and LVSI

The formal histopathological report of the patients was reviewed. DSI and LVSI were obtained after microscopic examination by certified pathologists and were reported as depth of invasion over the cervical wall thickness in millimeters. Accordingly, the depth of invasion was then categorised into inner third, middle third, and outer third infiltration. The lymphovascular space invasion was classified as either positive or negative based on the report.

Statistical Analyses

All analyses of the collected data were carried out using the statistical software Statistical package for Social Science (SPSS) Version 25. Armonk, NY: IBM Corp. Categorical data

were expressed as frequencies and percentages. Cross tabulation was used to demonstrate the association between the variables. Additionally, Fisher's exact test, Phi coefficient and Cramer's V were calculated to indicate, in quantitative terms, the extent of the association. Parametric testing was not feasible as the sample size was below 50. All p-values are two-sided and p values <0.05 were considered statistically significant.

RESULTS

The median age of the 23 patients was 56 years (range, 31-69 years). Majority of the patients were Malaysian Chinese (78.3%) followed by Malays (17.4%). There was a solitary patient of Thai descent in this study. Overall, 95.7% of the patients were parous. Following FIGO 2009 staging, stage 1B2 disease was the most common (65.2%), followed by stage 1B1 (21.7%) and stage 2A1 (13.0%). There were no patients with stage 1A2 in this cohort. Squamous cell carcinoma was the most common histologic cell type (56.5%), followed by adenocarcinoma (39.1%) and adenosquamous carcinoma (4.3%) (Table I). The median number of pelvic lymph nodes removed was 27 bilaterally (range 2- 52).

All 23 patients had pelvic lymph nodes dissection done as part of the radical hysterectomy inclusive of 6 patients with additional para-aortic lymph nodes dissection. No enlarged pelvic lymph nodes were noted on CT scan in 82.6% of them. All the patients with no enlarged pelvic lymph nodes had no histological pelvic lymph nodes involvement. Among those with enlarged pelvic nodes on CT scan, three quarter had histologically confirmed malignancy spread to the lymph nodes (p=0.002). The False Positive Value (FPV), False Negative Value (FNV), Positive Predictive Value (PPV), Negative Predictive Value (NPV), Sensitivity and Specificity are 5%, 0%, 75%, 100%, 100% and 95% respectively. Among the six patients with both pelvic and para-aortic lymph node dissection done, none had enlarged para-aortic lymph nodes on CT scan. Subsequently, 83.3% (5/6) of them were confirmed by histology to be negative of malignancy. The NPV for para-aortic nodes on CT scan is 83.3% (Table II).

In patients with clinical tumour diameter 2- 3.9 cm, 14.3% had positive pelvic nodes on histology. In contrast, 25% of patients with clinical tumour diameter ≥ 4cm had histological positive pelvic nodes. None of the patients with tumour size < 2 cm had histology positive pelvic nodes (p=0.993). In this study, 37.5% of patients with positive LVSI had histological pelvic lymph node involvement. All the patients with negative LVSI had no pelvic lymph node involvement (p=0.103). The NPV, PPV and specificity is 100%, 75% and 83.3% respectively. With regards to DSI, 16.7% and 18.2% of those with inner and outer third stromal involvement respectively had histological pelvic lymph node involvement (p=0.977) (Table III).

There were no patients with positive para-aortic lymph nodes with negative pelvic lymph nodes. In patients who were initially staged as 1B1 and 1B2 (FIGO 2009), 20% (1/5) and (3/15) had histological positive pelvic lymph nodes respectively (p=0.614). None of the patients staged 2A1 had positive pelvic nodes (Table IV). The incidence of patients with clinical stage 1B2 with enlarged pelvic lymph nodes on CT scan and histological positive pelvic lymph nodes were 20% (Table V).

DISCUSSION

Our data is consistent with the latest Malaysia National Cancer Registry 2012-2016 with regards to the highest incidence of CC between age 50-65 years and among Malaysian Chinese followed by Malays.[1] Squamous cell carcinoma was the most common histology followed by adenocarcinoma and adenosquamous which was also consistent with published data.[15]

Published meta-analysis regarding the diagnostic performance of CT scan showed that the specificities were more than 90% (high specificity) in the detection of lymph nodes metastases but has a sensitivity of less than 60% (low sensitivity).[4] In our data, the correlation between CT finding of enlarged pelvic nodes and histological proven metastasis to the pelvic lymph nodes are statistically significant with a specificity of 95% (p=0.002). However, compared to the published data on CT scan imaging in predicting pelvic lymph nodes metastasis, our data differed in NPV (90.1% vs 100%), sensitivity (51.4% vs 100%) and PPV (41.3% vs 75%).[14] The difference compared to our data is mainly attributed to skewed representation as none of the patients in this cohort with no enlarged CT pelvic lymph nodes had positive pelvic node on histology. However, our results of the high specificities and NPV do concur with the available data.

The correlation between CT findings of enlarged para-aortic nodes to histological involvement of para-aortic nodes could not be computed because in this smaller sample size of six patients, none of the patients had enlarged para-aortic nodes resulting in absence of false positive and true positive values.

Our results indicate that larger diameter tumours are associated with an increased risk of lymph node metastasis although it did not achieve statistical significance. As these clinical tumour diameters of 2-3.9cm and ≥ 4cm correspond to FIGO 2018 stages 1B2 and 1B3 respectively, it can be implied that the incidence of pelvic lymph node metastasis in stage 1B2 and 1B3 is 14.3 - 25%. This corresponds to available literature where the risk of pelvic lymph nodes metastasis in cervical stage 1B to 2A is 16-25%.[10] The absence of patients at stage 2A1 with histology positive lymph nodes indicates that patients with larger tumour volume has higher risk of pelvic lymph nodes involvement compared to clinical stage alone.

The presence of LVSI and DSI is known to be positively associated with lymph node metastasis.[12] Although our data has shown correlation with regards to DSI and pelvic lymph node positivity, it has failed to achieve statistical significance due to sample limitations.

There were no patients with histological para-aortic lymph node involvement skipping the involvement of the pelvic lymph nodes. Taking the data on sentinel lymph nodes into consideration, it is expected that a larger sample of patients may yield a result reflective of the actual occurrence demonstrated by available studies.

Table I: Demographic data, pre-operative stage and type of cervical cancer

Variable	Patients (n= 23)	Final Histology			p-value
		Adenocarcinoma	Squamous cell carcinoma	Adenosquamous carcinoma	
Age group					0.254
31-40	4 (17.4%)	1 (11.1%)	3 (23.1%)	0 (0)	
41-50	2 (8.7%)	2 (22.2%)	0 (0%)	0 (0)	
51-60	11 (47.8%)	3 (33.3%)	8 (61.5%)	0 (0)	
61-70	6 (26.1)	3 (33.3%)	2 (15.4%)	1 (100)	
Race					0.099
Chinese	18 (78.3%)	9 (100%)	9 (69.2%)	0 (0)	
Malay	4 (17.4%)	0 (0%)	3 (23.1)	1 (100)	
Others	1 (4.3%)	0 (0%)	1 (7.7)	0 (0)	
Parous					0.435
Yes	22 (95.7%)	1 (11.1%)	0 (0)	0 (0)	
No	1 (4.3%)	8 (88.9%)	13(100)	1 (100)	
Pre-Op Stage FIGO 2009					0.231
1B1	5 (21.7%)	2 (22.2%)	2 (15)	1 (100)	
1B2	15 (65.2%)	7 (77.8%)	8 (61.5)	0 (0)	
2A1	3 (13.0%)	0 (0%)	3 (23.1)	0 (0)	
CT Pelvic node					1.000
Negative	19 (82.6%)	7 (77.8%)	7 (77.8%)	1 (100)	
Positive	4 (17.4%)	2 (22.2%)	2 (15.4)	0 (0)	
CT Para-aortic node					-
Negative	6 (100%)	2 (33.3%)	4 (66.7%)	0 (0%)	
Positive	0 (0%)	0 (0%)	(0%)	0 (0%)	
LVSI					0.253
Negative	15 (65.2%)	4 (44.4%)	10 (76.9%)	1 (100%)	
Positive	8 (34.8%)	5 (55.6%)	3 (23.7%)	0 (0%)	
DSI					0.534
Inner	6 (26.1%)	2 (22.2%)	4 (30.8%)	0 (0%)	
Middle	6 (26.1%)	3 (33.3%)	3 (23.1%)	0 (0%)	
Outer	11 (47.8%)	4 (44.4%)	6 (46.2%)	1 (100%)	
Pelvic Node Status					0.392
Negative	20 (87.0%)	7 (77.8%)	12 (92.3%)	1 (100%)	
Positive	3 (13.0%)	2 (22.2%)	1 (7.7%)	0 (0%)	
Pelvic Nodes removed					0.868
1-10	1 (4.3%)	0 (0%)	1 (7.7%)	0 (0%)	
11-20	6 (26.1%)	2 (22.2%)	4 (30.8%)	0 (0%)	
21-30	6 (26.1%)	3 (33.3%)	2 (15.4%)	1 (100%)	
31-40	7 (30.4%)	3 (33.3%)	4 (30.8%)	0 (0%)	
41-50	2 (8.7%)	1 (11.1%)	1 (7.7%)	0 (0%)	
51-60	1 (4.3%)	0 (0%)	1 (7.7%)	0 (0%)	
Para-aortic Nodes					0.333
Negative	5 (83.3%)	1 (50%)	4(100%)	-	
Positive	1 (16.7%)	1 (50%)	0 (0%)	-	
Para-aortic nodes removed					0.983
< 5	4 (66.7%)	1 (50%)	3 (75%)	-	
> 5	2 (33.3%)	1 (50%)	1 (25%)	-	

n = frequency; % = percentage

Table II: Comparison between CT lymph nodes positivity with histological retroperitoneal lymph nodes positivity

	Histological pelvic node n= 23		Histological para-aortic node n= 6		Total	p-value
	Negative	Positive	Negative	Positive		
CT Pelvic Node						
Negative	19 (82.6%)	0 (0%)	0 (0%)	0 (0%)	19 (82.6%)	0.002
Positive	1 (4.3%)	3 (13.0%)	0 (0)%	0 (0%)	4 (17.4)	
Total	20 (87.0%)	3 (13.0%)			23(100)	
CT Paraortic Node						
Negative	0 (0%)	0 (0%)	5 (83.3%)	1 (16.7%)	6 (100%)	
Positive	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Total	0 (0%)	0 (0%)	5 (83.3%)	1 (16.7%)	6 (100%)	
FPV	0.05		-			
FNV	0.0		-			
Sensitivity	1.0		-			
Specificity	0.95		-			
PPV	0.75		-			
NPV	1.0		0.833			

n = frequency; % = percentage

Table III: Prognostic factors in comparison with histologic pelvic nodes

	Histological pelvic node n= 23		Total	p-value
	Negative	Positive		
Clinical tumor size				0.993
<2 cm	5 (21.7%)	0 (0%)	5 (21.7%)	
2-3.9 cm	12 (52.2%)	2 (8.7%)	14 (60.9%)	
≥4 cm	3 (13.0%)	1 (4.3%)	4 (17.4%)	
Total	20 (87.0%)	3 (13.0%)	23 (100%)	
LVSI				0.103
Negative	15 (65.2%)	0 (0%)	15 (65.2)	
Positive	5 (21.7%)	3 (13.0%)	8 (34.8)	
Total	20 (87.0%)	3 (13.0%)	23 (100)	
DSI			0.977	
Inner	5 (21.7%)	1 (4.3%)	6 (26.1)	
Middle	6 (26.1%)	0 (0%)	6 (26.1)	
Outer	9 (39.1%)	2 (8.7%)	11 (47.8)	
Total	20 (87.0%)	3 (13.0%)	23 (100)	

n = frequency; % = percentage

Table IV: FIGO 2009 cervical cancer stage in comparison with histological pelvic nodes

	Histological pelvic node; n= 23			p-value
	Negative	Positive	Total	
Preop stage				
1B1	4 (17.4%)	1 (4.3%)	5 (21.7%)	0.614
1B2	12 (52.2%)	3 (13.0%)	15 (65.2%)	
2A1	3 (4.3%)	0 (0%)	3 (13.0%)	
Total	19 (82.6)%	4 (17.4%)	23 (100%)	

n = frequency; % = percentage

Table V: Pre-operative stage in comparison with radiologic and histologic pelvic lymph nodes positivity

n= 23	CT pelvic node positive + histological pelvic node positive	CT pelvic node positive + histological pelvic node negative	p-value
Pre-op stage			0.250
1B1	5 (22%)	0	0
1B2	15 (65%)	3	0
2A1	3 (13%)	0	1

n = frequency; % = percentage

Pre-op stage 1B2	n = 15	Total	p-value
CT positive pelvic node			
Negative	12 (80%)	15 (100%)	0.327
Positive	3 (20%)		
Histological pelvic node			
Negative	12 (80%)	15 (100%)	0.614
Positive	3 (20%)		

n = frequency; % = percentage

The incidence of positive pelvic lymph nodes in clinical stage 1B of 20% in this cohort corresponds with published data. The majority of patients in this cohort are in stage 1B2. Sub-analysing this sub-group of patients revealed that the incidence of patients with both enlarged pelvic lymph nodes on CT scan and positive histological involvement is 20% respectively. This implies that 20% of patients in this cohort with clinical stage 1B2 would be upstaged to 3C1 disease based on the CT scan imaging and the final histology of the pelvic lymph nodes. Our study also shows that in stage 1A2 to 2A1, based only on CT scan findings, 17.4% are upstaged to stage 3C1 (FIGO 2018). In comparison, based on final histology, 13.0% were upstaged to stage 3C1 and 4.3% were upstaged to stage 3C2 (FIGO 2018).

Stage 3C is classified as locally advanced disease which is associated with poorer survival outcome compared to those without lymph nodes involvement.[3] Concurrent chemoradiation is the standard contemporary treatment which consist of weekly cisplatin during the course of external beam radiation therapy.[3] Ongoing trial on additional adjuvant chemotherapy after chemoradiation are ongoing to assess the overall survival of this group of patients.[16] Although extended beam radiotherapy to these nodes is required together with chemotherapy to improve disease control, it has been proven that the benefit is minimal even with concomitant platinum-based chemotherapy as the rates of local and distant failure remain high in these patients.[17] Hence in our data, 4.3% of these patients would be at risk of recurrence or distant failure based on clinical staging versus the current staging.

Finally, our data also revealed the apparent deficiency of the FIGO 2009 staging which omitted the retroperitoneal lymph nodes as part of the staging. Based on our data, 17.4% of apparent stage 1A2 to 2A1 who should have been upstaged to stage 3C1 (FIGO 2018) would have been missed and thus omitted from adjuvant treatment which would have resulted in a higher risk of recurrence.

STUDY LIMITATIONS AND CONCLUSION

This study is limited by its retrospective nature and reduced sample size as the cohort of the study duration was at the transition between the FIGO 2009 and FIGO 2018 CC staging. Although the FIGO 2018 staging was published in October 2018, the change in surgical practice to include dissection of the para-aortic lymph nodes as part of radical hysterectomy for cervical cancer only started in November 2019 in HA. Hence a prospective study with similar objectives would be expected to yield a more accurate data representation. Looking forward, a follow-up study on the progression free survival and survival outcome of this cohort in this institution would be of importance.

Despite the limitations mentioned, this study has shown a statistically significant correlation between enlarged pelvic lymph nodes detected on CT scan and histological positive nodes. With the inclusion of radiological and histological retroperitoneal lymph nodes in the current FIGO 2018 staging, these patients would be up-staged to stage 3C. This has two main implications to clinical practice, namely the requirement to perform retroperitoneal lymph node dissection up to the level of the para-aortic which would necessitate retraining and establishment of the required dissecting skills to perform the procedure safely. The second implication is that the requirement to perform at least a thoraco-abdomino-pelvic CT scan for staging which may not be available in certain centers or affordable for some patients due to cost and availability especially in low resource countries.

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DISCLOSURES

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

CONFLICT OF INTEREST

All the authors declare no conflict of interests.

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