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Clinical and imaging findings in cervical cancer and their impact on FIGO and TNM staging – An analysis from the EMBRACE study

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HIGHLIGHTS

- Local stage of advanced cervical cancer changes in 27% comparing MRI and clinical examination.
- For treatment allocation important clinical stages IB1-IIA2 changed to IIB on MRI in 31%.
- Pelvic wall/bladder infiltration vary considerably, likely due to different definitions for clinical and imaging findings.
- 50% of this cohort are allocated to stage IIIC with FIGO 2018, obscuring local tumour extent.
- TNM offers the most differentiated stage allocation with 26 subgroups in this cohort.

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ABSTRACT

Objective. To investigate differences in local tumour staging between clinical examination and MRI and differences between FIGO 2009, FIGO 2018 and TNM in patients with primary cervical cancer undergoing definitive radio-chemotherapy.

Methods. Patients from the prospective observational multi-centre study "EMBRACE" were considered for analysis. All patients had gynaecological examination and pelvic MRI before treatment. Nodal status was assessed by MRI, CT, PET-CT or lymphadenectomy. For this analysis, patients were restaged according to the FIGO 2009, FIGO 2018 and TNM staging system. The local tumour stage was evaluated for MRI and clinical examination separately. Descriptive statistics were used to compare local tumour stages and different staging systems.

Results. Data was available from 1338 patients. For local tumour staging, differences between MRI and clinical examination were found in 364 patients (27.2%). Affected lymph nodes were detected in 52%. The two most frequent stages with FIGO 2009 are IIB (54%) and IIIB (16%), with FIGO 2018 IIIC1 (43%) and IIB (27%) and with TNM T2b N0 M0 (27%) and T2b N1 M0 (23%) in this cohort.

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Conclusions. MRI and clinical examination resulted in a different local tumour staging in approximately one quarter of patients. Comprehensive knowledge of the differential value of clinical examination and MRI is necessary to define one final local stage, especially when a decision about treatment options is to be taken. The use of FIGO 2009, FIGO 2018 and TNM staging system leads to differences in stage distributions complicating comparability of treatment results. TNM provides the most differentiated stage allocation.

1. Introduction

Surgery or radio-chemotherapy are the cornerstones in the curative treatment of cervical cancer. The decision regarding which treatment is used is determined primarily by the stage of disease. Precise staging is therefore a crucial aspect in the management of cervical cancer. Relevant information for treatment allocation includes the tumour size, the local tumour extension including infiltration of surrounding tissues and organs (vagina, parametria, pelvic wall, ureter, bladder, rectum), and presence of lymph node metastasis and systemic disease. The Fédération Internationale de Gynécologie et d'Obstétrique (FIGO) system and the Tumour, Node, Metastasis (TNM) system as proposed by Union Internationale Contre le Cancer (UICC)/ American Joint Committee on Cancer (AJCC) are the most commonly used staging systems for cervical cancer. The FIGO system has a long tradition (first appearance in 1929 as the League of Nations classification for cervical cancer [1]) and was for a long time mainly based on clinical findings and did not include nodal disease [2]. Therefore, in the recently published European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology "Guidelines for the Management of Patients with Cervical Cancer" (ESGO/ESTRO/ESP) guidelines [3] the use of the TNM staging system [4], which includes clinical, histopathologic and imaging information for local, nodal and distant disease, is recommended for cervical cancer staging. In the meantime, the FIGO system was updated in 2018 and now allows for imaging findings and incorporates nodal disease status [5]. The aim of this study is (1) to compare imaging and clinical findings for local tumour staging in a representative group of patients with primary cervical cancer undergoing definitive radio-chemotherapy, (2) to report TNM stages and (3) to compare to FIGO 2009 and FIGO 2018 systems.

2. Material and methods

2.1. Patients and study design

All patients from the EMBRACE I study based on data dump 08/2017 were considered for this analysis. The EMBRACE I study is a prospective multicentre observational trial reporting the key treatment and outcome parameters in cervical cancer patients. Patients with newly biopsy-proven squamous cell carcinoma, adenocarcinoma or adenosquamous carcinoma of the uterine cervix, FIGO (2009) stage IB, IIA, IIB, IIIA, IIIB, IVA and with para-aortic metastatic nodes (stage IVB) to the level of L2 were included in the study. Patients with further dissemination were not eligible. All patients received external beam radiotherapy up to 45-50.4 Gy in 25-28 fractions +/- concomitant chemotherapy (cisplatin 40 mg/m^2 weekly) followed by MRI-guided brachytherapy according to the Groupe Européen de Curiethérapie-ESTRO (GEC-ESTRO) guidelines [6,7]. Data assessment included collection of patient and tumour characteristics, treatment details and outcome related parameters. In total >6000 parameters were collected per patient. A modified FIGO 2009 classification was used for tumour staging. The modification implied classification of patients with hydronephrosis detected by any imaging modality as FIGO IIIB and classification of patients with paraaortic lymph node metastasis detected by any imaging modality or lymphadenectomy as FIGO IVB.

A diagnostic MRI of the pelvis and a gynaecological examination at diagnosis were mandatory for local tumour assessment. Evaluation of MRI in regard to local tumour extension was performed at the discretion of the centre either by radiologists or by radiation oncologists experienced in the treatment of gynaecologic malignancies. Both modalities were performed unblinded and in order of every centre's regimen. The following parameters were used for assessment of local tumour extension: tumour width, height and thickness in millimetres, presence of hydronephrosis, presence and extent of infiltration of vagina (upper vs middle vs lower third), invasion into left and right parametrial tissue (proximal vs distal), extension to pelvic wall, rectum and bladder. Endoscopy of bladder (cystoscopy) or rectum (rectoscopy) could be performed at the discretion of the treating physician. In case of visible tumour infiltration of the mucosa on endoscopy, stage was considered as T4. On MRI, any involvement of bladder or rectum was considered as infiltration and therefore as stage T4.

In addition to a pelvic MRI, an abdominal CT and X-ray of the chest were the minimum requirements for nodal staging and exclusion of distant metastasis beyond paraaortic lymph node metastasis. Thoracic CT, PET-CT and pelvic or paraaortic lymphadenectomy were optional according to institutional practice. The following parameters were used for the recording of nodal status: location (parametrial, external/internal iliac, common iliac, inguinal, paraaortic nodes), positivity (yes/no) and level of confirmation (CT/MRI vs PET-CT vs histology). Only the modality with the highest diagnostic accuracy was reported in the database for lymph node staging (lymphadenectomy > PET-CT > CT/MRI).

2.2. Methodology

Based on the above clinical, imaging and histological parameters TNM, FIGO 2009 and FIGO 2018 stages were retrospectively derived.

The TNM stage was calculated according to TNM 8th edition, 2017. To differentiate between clinical and imaging findings the T-stage was subdivided into a clinical T-stage (T_{clin}) and an MRI based T-stage (T_{MRI}). Tclin was defined based on the clinical examination ± endoscopy only and TMRI was defined based on MRI imaging only. For example, a patient with a 4.5cm maximum diameter tumour with infiltration of the proximal parametrial tissue on MRI and a 5cm maximum diameter tumour and no infiltration of parametrial tissue on clinical examination and negative lymph nodes was defined as TMRI 2b N0 M0 but Tclin 1b2 N0 M0. The nodal status was used as reported in the database. In addition, landmarks of local tumour extension relevant for T-staging (parametrial invasion, pelvic wall infiltration, vaginal infiltration, bladder/rectum infiltration) were compared separately.

A non-modified FIGO 2009 stage was calculated based on clinical parameters ± endoscopy only. As exemption modification, any imaging was used to test for hydronephrosis, rather than specific need for urography.

The FIGO 2018 stage was calculated based on clinical parameters ± endoscopy only for local tumour staging and imaging and histopathologic findings for nodal staging.

Descriptive statistics within Microsoft Excel 2016 were used to summarize and compare Tclin vs. TMRI and TNM stages. Cross tables are presented to evaluate differences in local staging and to describe nodal status. Diagnostic accuracy (true positive + true negative/all), sensitivity (true positive/true positive + false negative), specificity

(true negative/true negative + false positive), positive predictive value (true positive/true positive + false positive; PPV) and negative predictive value (true negative/true negative + false negative; NPV) of MRI for bladder mucosa infiltration, rectal wall infiltration and vaginal wall infiltration were calculated and compared to cystoscopy, rectoscopy and clinical examination, respectively.

3. Results

3.1. Patient cohort

1416 patients were included in the EMBRACE I study. 78 were excluded for the following reasons: not fulfilling inclusion criteria, no patient information, missing tumour characteristics. 1338 patients were available for this analysis. A pelvic MRI at diagnosis and gynaecological examination at diagnosis was available in all patients. Cystoscopy was performed on 548 patients (41%), and 156 patients (12%) had a rectoscopy. Lymphadenectomy was performed in 365 patients (27.3%). Median time interval between MRI and gynaecological examination was 4 days. 65% of the patients underwent MRI before the gynaecological examination.

3.2. T-stage

Tclin and TMRI stages are presented in Table 1. Differences between Tclin and TMRI are shown in Table 2. In short, differences in T-stage were found in 364/1338 (27.2%) patients. 141 patients (10.5%) had a lower T-stage on MRI than on clinical examination, whereas 223 patients (16.7%) had a higher stage on MRI. Change of stage between clinical examination and MRI varies between the different stages from a minimum of 9.3% in T2b to maximum 69.2% in T2a1. Centre-specific differences (for centres accruing >30 patients) were in the range from 17% to 43%. In patients undergoing MRI before gynaecological examination, significantly fewer differences were observed than when the MRI followed the gynaecological examination (25% vs. 31%, p = 0.019).

3.3. Vaginal infiltration

Vaginal infiltration was reported by clinical examination in 599/1338 (44.8%) of the patients. Similarly, vaginal wall infiltration was identified on MRI in 578/1338 (43.2%). The accuracy for detecting vaginal wall infiltration on MRI (with clinical examination as reference) in our cohort is 87.8%. Sensitivity, specificity, PPV and NPV are 84.6%, 90.4%, 87.7% and 87.9%, respectively.

3.4. Parametrial and pelvic wall infiltration and hydronephrosis

Parametrial infiltration without pelvic wall infiltration was found in 775/1338 (57.9%) patients clinically and in 926/1338 (69.2%) patients on MRI. The most frequent reason that T_{MRI} was increased over T_{CLIN} was a change from Ib2 to 2b on the basis of parametrial invasion on MRI (40 patients) (Table 2).

Table 1
Distribution of clinical T-stages based on clinical findings + urography (derived from imaging) ± endoscopy only (Tclin) and T-stages based on MRI only (TMRI).

	T_{clin} (n=1338)	T_{MRI} (n=1338)
T1b1	141 (10.5%)	105 (7.9%)
T1b2	121 (9.0%)	102 (7.6%)
T2a1	39 (2.9%)	28 (2.1%)
T2a2	44 (3.3%)	47 (3.5%)
T2b	728 (54.4%)	834 (62.3%)
T3a	15 (1.1%)	12 (0.9%)
T3b	220 (16.4%)	125 (9.3%)
T4	30 (2.2%)	85 (6.4%)

Table 2
Cross table showing all EMBRACE I patients evaluable (n = 1338) with clinical-only and MRI-only T-stages as re-staged by investigators based on clinical findings only (Tclin) and MRI findings only (TMRI): stage and change of stage are indicated in absolute numbers in detail and overall.

	TMRI								
Tclin		1b1	1b2	2a1	2a2	2b	3a	3b	4	Change of stage/total
	IB1	70	24	4	0	43	0	0	0	71/141 (50.4%)
	IB2	9	66	0	4	40	0	2	0	55/121 (45.5%)
	IIA1	4	0	12	15	8	0	0	0	27/39 (69.2%)
	IIA2	1	4	4	17	15	1	0	2	27/44 (61.4%)
	IIB	22	8	7	8	660	2	6	15	68/728 (9.3%)
	IIIA	0	0	1	1	3	8	0	2	7/15 (46.7%)
	IIIB	0	0	0	2	62	1	115	40	105/220 (47.7%)
	IVA	0	0	0	0	2	0	2	26	4/30 (13.3%)
										364/1338 (27.2%)

Pelvic wall infiltration was found in 211/1338 (15.8%) patients clinically and in 123/1338 (9.2%) patients on MRI. The most frequent reason that T_{MRI} was decreased over T_{CLIN} was a change from T_{CLIN} IIIB to T_{MRI} 2b on the basis of lack of MRI correlate for pelvic wall infiltration (60 patients) (Table 2).

Unilateral tumour extend to parametrial tissue or pelvic wall was diagnosed in 531/1338 patients (39.7%) clinically (to the left side in 349/1338 patients (26.1%) and to the right side in 182/1338 patients (13.6%)), bilateral extent was seen in 455/1338 patients (34.0%). On MRI, 454/1338 patients (33.9%) were diagnosed with unilateral infiltration of parametrial tissue/pelvic wall (to the left side in 296/1338 patients (22.1%) and to the right side in 158/1338 patients (11.8%)), and bilateral infiltration was seen in 595/1338 patients (44.5%).

The lateral tumour extent to parametrial tissue ± pelvic wall (infiltration vs. no infiltration) changed in 448/2676 sites (16.7%) comparing clinical examination and MRI. 12.2% were diagnosed as infiltrated on MRI but not on clinical examination, whereas 4.6% were diagnosed as infiltrated clinically but not on MRI.

Unilateral hydronephrosis was found in 84/1338 patients (6.3%), bilateral hydronephrosis was diagnosed in 23/1338 patients (1.7%) on MRI.

3.5. Urinary bladder and rectal infiltration

548/1338 patients (41%) underwent cystoscopy. 26/548 (4.8%) presented with involvement of the bladder mucosa. The accuracy to detect bladder wall infiltration (involvement of mucosa) for MRI in our cohort with cystoscopy as reference is 93.6%, sensitivity, specificity, PPV and NPV are 96.2%, 93.5%, 42.4% and 99.8%, respectively.

Regarding the whole study population, 79/1338 (5.9%) patients had bladder wall infiltration on MRI. Of those, 20/79 (25%) had no cystoscopy, in 22/79 (28%) no involvement of the mucosa was seen during cystoscopy, 12/79 (15%) had an edema of the mucosa and 25/79 (32%) were diagnosed with infiltration of the mucosa during cystoscopy.

Rectoscopy was performed in 156/1338 patients (12%). Of those, one had rectal wall infiltration which was also seen on MRI.

In 4/1338 patients, clinical examination revealed a directly palpable tumour in the rectum (one was also seen as rectal wall infiltration on MRI and later confirmed with rectoscopy, three were not seen as rectal wall infiltration on MRI and had no rectoscopy).

On MRI, 10/1338 patients were reported with rectal wall infiltration. Of those, 7/10 had no rectoscopy, 1/10 had no rectal wall infiltration, 1/10 had an impression of the rectal wall without infiltration and 1/10 was diagnosed with rectal wall infiltration during endoscopy. Digital rectal examination was not done in 2/10, showed no rectal infiltration in 5/10, a palpable impression in 2/10 and a directly palpable tumour in 1/10.

3.6. N-Stage

In total, 697/1338 (52.1%) patients had affected pelvic and/or paraaortic nodes on images and/or at lymphadenectomy. 101/1338 (7.6%) patients had affected paraaortic nodes. 27.3% of the patients underwent lymphadenectomy. Patterns of regional and paraaortic lymph node disease in this patient cohort are described in a previous publication [8].

3.7. TNM and FIGO stages

Utilizing the TNM system, 26 subgroups are at hand in this patient cohort (figure 1). Differences between FIGO 2009 and FIGO 2018 (local staging based on Tclin) are presented in figure 2. The two most frequent stages with FIGO 2009 are IIB (54%) and IIIB (16%), with FIGO 2018 IIIC1 (43%) and IIB (27%) and with TNM T2b N0 M0 (27%) and T2b N1 M0 (23%) in this cohort.

4. Discussion

In this study differences between clinical examination and MRI for local tumour staging were assessed in a multicentre patient cohort with primary cervical cancer undergoing definitive radio-chemotherapy. T-stage-relevant information comprises the tumour size, parametrial infiltration, pelvic wall infiltration, vaginal infiltration and bladder/rectal infiltration, which are discussed in the following:

Assessment of tumour size is necessary to differentiate between IB1 and IB2 and between IIA1 and IIA2. In particular, a change of stage between IB1 and IB2 is relevant as it has the potential to change treatment decisions. In this study, 50% of patients with FIGO 2009 Tclin IB1 were allocated to a higher stage on MRI and of those, 33% were allocated to IB2 due to larger tumour size. The prospective ACRIN 6651/GOG 183 Intergroup study showed in 208 patients with histopathologic confirmation that MRI is superior to clinical examination for measuring the tumour size [9]. A review by Sala et al reports an MRI accuracy >90% for detecting tumour size in comparison to 60% with clinical examination [10]. Furthermore, a recent retrospective analysis on 1016 patients with clinical stage IB1-IIA2 undergoing surgery and preoperative MRI confirmed a significantly increased accuracy for the assessment of maximal tumour diameter with MRI. In this study, 20% of the patients with clinical IB1 were allocated to a higher stage on MRI (of those 40% to IB2) [11].

The presence of parametrial infiltration defines stage IIB, which is a clear indication for primary radio-chemotherapy as recommended by the ESGO-ESTRO-ESP guidelines [3]. Therefore - in particular for smaller sized tumours, which might be also candidates for a primarily surgical procedure– exclusion of parametrial infiltration is essential to avoid overtreatment. A meta-analysis of the assessment of parametrial invasion with more than 3200 patients with histopathologic reference revealed a specificity of >90% for clinical examination (95% CI 83-89) and MRI (95% CI 90-95), but a sensitivity of only 40% (95% Confidence interval (CI) 25-58) with clinical examination compared to 84% (95% CI 76-90) with MRI [12]. In accordance, in our cohort 31% of the patients with clinically staged IB1-IIA2 were upstaged to IIB with MRI, whereas 91% of the patients staged clinically as IIB were confirmed by MRI. Only 9% had discrepant findings; however, those ranged from IB1 to IVA.

There are very few published analyses on pelvic wall infiltration. A clear definition for pelvic wall infiltration is missing. Some define pelvic wall infiltration on MRI by at least 3mm infiltration of the internal obturator, piriform, or levator ani muscles, with or without a dilated ureter [13,14], whereas on clinical examination full thickness parametrium involvement to abut the vascular space just medial to the pelvic wall musculature up to fixation of the tumour against the pelvic wall is assessed. In our study, <60% of the patients with clinical pelvic wall infiltration had signs of infiltration on MRI, which is likely due to the different underlying definitions. It can be questioned for example whether tumour fixation to the pelvic wall as detected through clinical examination necessarily implies muscle infiltration e.g. of the internal obturator muscle. The prognostic value of these differences – especially in the setting of primary radio-chemotherapy - remains unclear.

Vaginal infiltration is a frequent characteristic in cervical cancer (>40% in our cohort of locally advanced tumours), which is (due to the even more frequent and dominant characteristic of parametrial infiltration) hardly represented by the various staging systems (7% were classified as IIA or IIIA in our study). Most authors report for the assessment of vaginal infiltration a higher accuracy with clinical examination than with MRI compared to histopathologic findings as gold standard [15–19]. Interestingly, in our study clinical examination and MRI had similar results for the detection of vaginal infiltration (accuracy of 88% with clinical examination as reference), which might be related to the more advanced tumours in our cohort with more obvious vaginal infiltration. However, despite the good agreement for the endpoint vaginal infiltration overall, the Tclin IIA1 and IIA2 showed the highest

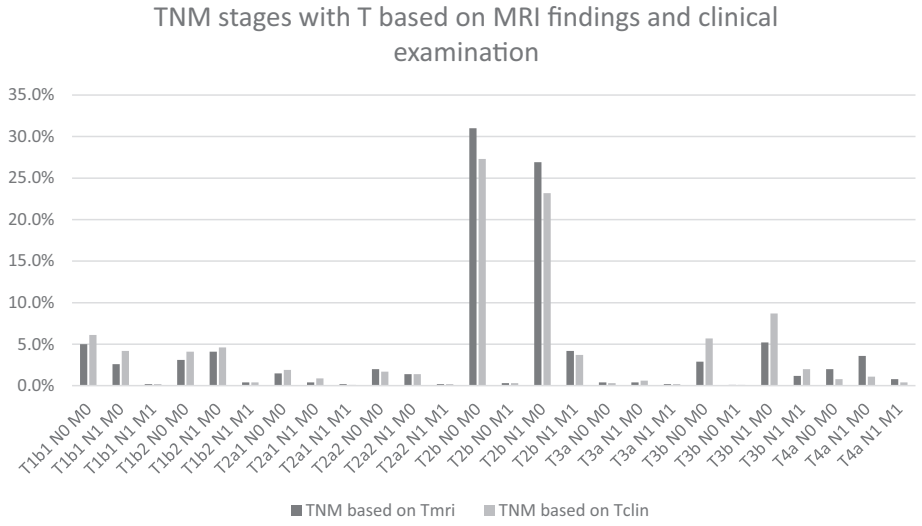

Fig. 1. Stage allocation to in total 26 subgroups based on TNM (8th edition, 2017) utilizing clinical T-stage only (Tclin) for local staging and (PET-)CT, ± lymphadenectomy results for nodal staging (light grey) or T-stage based on MRI only (TMRI) for local staging and (PET-)CT, ± lymphadenectomy results for nodal staging (dark grey).

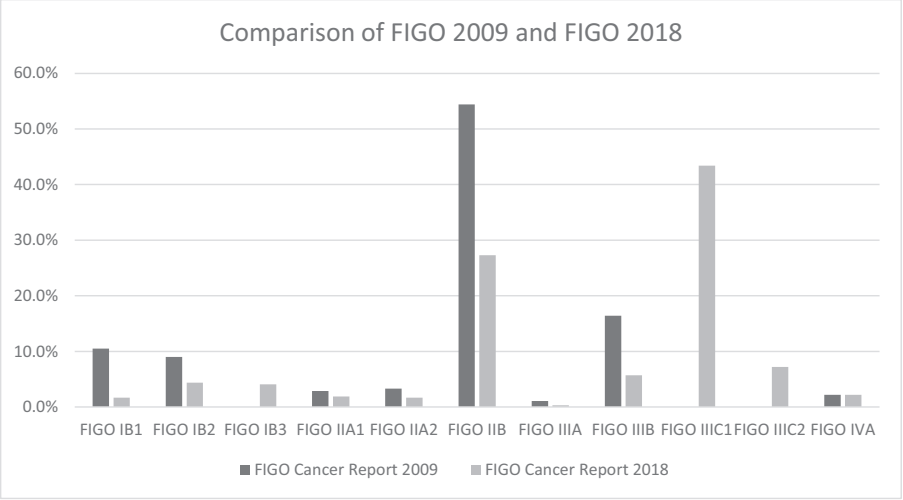

Fig. 2. Comparison of FIGO stages based on FIGO Cancer Report 2009 (dark grey) and FIGO Cancer Report 2018 (light grey).

variability – mainly in regard to the extent of vaginal infiltration or suspicion of additional parametrial infiltration on MRI.

Urinary bladder infiltration has been investigated by Rockall et al comparing MRI to cystoscopy with an NPV of 100% for bladder wall infiltration on MRI compared to cystoscopy results in 115 patients, but a PPV of only 10% [20]. Our results seem to confirm these findings that MRI overestimates the incidence of bladder wall infiltration compared to cystoscopy. However, with regard to the different histological layers of the bladder wall, MRI may better visualize other aspects of bladder infiltration such as infiltration of mucosa on cystoscopy or bladder wall involvement without direct mucosal invasion on MRI. Therefore, in contrast to the statement above, cystoscopy might underestimate overall bladder involvement instead. Rectal infiltration was observed much less frequently. Due to the small number of events, no clear conclusion can be drawn.

Overall, in the present study, approximately one quarter of patients had discrepant local tumour stages between clinical examination and MRI. Such differences can have a major impact on the overall management of patients, in particular to decide whether patients are candidates for surgery or radio-chemotherapy which is beyond the scope of this investigation. Currently, it is not clear how to weight the discrepant clinical and imaging findings. With regard to the above-mentioned literature, tumour size (at least in limited sized tumours) and parametrial infiltration seems to be more precisely assessed with MRI. Vaginal infiltration is generally considered as a clinical domain. For bladder wall infiltration, differences between cystoscopy and MRI seem to be large which is likely due to the variation in the underlying definitions. Also, for the diagnosis of pelvic wall infiltration and the allocation to stage T3b or T2b (IIIB or IIB) the differences between MRI and clinical examination are pronounced. The radiologic definition for pelvic wall infiltration (true pelvis muscle infiltration) seems to correspond only partly to the clinically palpated fixation of the tumour to the pelvic wall. These issues need to be clarified in the oncological community regarding their relative clinical and prognostic impact. A thorough gynaecological examination (e.g. at diagnosis) and documentation is especially relevant for brachytherapy treatment planning to ensure proper coverage of certain structures within the initial tumour extent such as vagina and pelvic wall. Altogether the differential values of the clinical and imaging assessment should be comprehensively appreciated and discussed. A combination of a detailed clinical examination and MRI findings (quantifying e.g. proximal/distal parametrial or uterine infiltration which are currently not reflected by TNM or FIGO) into one final quantitative score for local tumour assessment ("T-score") was recently suggested by Lindegaard et al and seems to be valuable for prognosis [21].

The nodal status -which is another relevant parameter for treatment allocation - was not reflected by the FIGO staging system until the 2018 revision. In our cohort, 52% of the patients presented with affected lymph nodes. Interestingly, but likely due to selection bias (only patients undergoing radio-chemotherapy), the involved lymph node regions for patients with affected lymph nodes were relatively well-balanced for all Tclin stages (and TMRI stages) except for inguinal lymph nodes (higher rates in patients with Tclin T3a and T4) and for paraaortic lymph nodes (higher rates for all T3 and T4 patients) [Appendix]. The incidence of affected paraaortic nodes in 560 patients who all underwent PET-CT has been reported in 9%, 21%, 17%, 25%, 33% and 27% of clinically staged IB2, IIA, IIB, IIIA, IIIB and IVA patients, respectively [22]. Patients with PET negative paraaortic nodes still had surgical affected paraaortic nodes in 12% [23]. In our cohort, only 8% of patients were diagnosed with affected paraaortic nodes (perhaps due to the variation in diagnostic tools), but the majority of nodal failures took place in the paraaortic region [8]. Therefore, an under-reporting can be assumed. With the FIGO 2018 system, patients with affected pelvic and paraaortic lymph nodes are classified as IIIC1 and IIIC2, respectively, which is helpful to treatment selection as the prognostically relevant nodal information is taken into account. Unfortunately, the local tumour stage which is also prognostically highly relevant is obscured by the nodal status in these patients [24]. In our cohort, the majority contributing to the FIGO 2018 IIIC1 and IIIC2 stages are from FIGO 2009 IB1, IIB and IIIB and make these groups rather limited in size. The TNM system allows for a more comprehensive representation of the individual tumour status. In our cohort, the most frequent stages were T2b N0 M0 (27%), T2b N1 M0 (23%), T3B N1 M0 (9%), T1B1 N0 M0 (6%) and T3b N0 M0 (6%). All other stages were observed in less than 5%. Overall, 26 subgroups were noted. This high number of subgroups and the relatively small number of patients per subgroup however may limit its clinical and scientific value. It appears that the optimal tumour classification system for cervical cancer still needs to be developed. The proposed comprehensive quantitative "T-score" [21] in combination with the nodal status may offer possible discussion pathways.

The main limitation of this work can be found in the unblinded assessment of clinical examination and MRI. Therefore, some influence of the MRI on clinical examination and subsequently on the respective Tclin and TMRI stages has to be assumed. Nevertheless, under these "real-world-conditions" one quarter of patients were still reported with discrepant findings. A blinded comparison might reveal even

higher differences. Furthermore, there is a variability in the diagnostic performance within MRI (e.g slice thickness, field strength, use of diffusion-weighted sequences and application of vaginal gel) and within clinical examination (examination under anaesthesia, clinical experience) which is unknown. The degree of experience in clinical assessment and image interpretation by the specialized centres within this study could also have an impact on the results.

5. Conclusion

Local tumour staging based on MRI results in a different classification in approximately one quarter of the patients compared to clinical findings only. With MRI, upstaging is more frequent than downstaging. Comprehensive knowledge of the differential value of clinical examination and MRI is necessary to integrate them into one final local stage as suggested by the recent ESGO/ESTRO/ESP recommendations, especially when treatment decisions have to be taken. The use of FIGO 2009 and FIGO 2018 staging system leads to very different stage distributions in a given cohort, as over 50% of patients present with lymph node metastases. TNM stage distribution is again different from both FIGO 2009 and 2018, but provides the most comprehensive information on tumour, nodal and also distant metastatic status.

Declaration of Competing Interest

None.

The following are the supplementary data related to this article.
Table S1. Vaginal infiltration on MRI (top row) and as seen clinically (left column) in total numbers and in percent.
Table S2. All 548 patients with cystoscopy. Bladder wall infiltration on MRI (top row) and mucosa infiltration on cystoscopy (left column) in total numbers and in percent.
Table S3. Lymph node metastases for every local clinical T-stage (Tclin) distributed to the different locations (parametrial, internal and external iliac, common iliac, inguinal, paraaortic) in numbers and in percent.
Table S4. Lymph node metastases for every local T-stage as seen on MRI (TMRI) distributed to the different locations (parametrial, internal and external iliac, common iliac, inguinal, paraaortic) in numbers and in percent.Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2020.07.007.

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