A retrospective analysis comparing clinical staging with magnetic resonance imaging staging in patients with cervical cancer

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Abstract

This single-institution retrospective study compares the accuracy of clinical and magnetic resonance imaging (MRI) staging of cervical cancer. For patients who underwent surgery, MRI and clinical staging were compared to final pathological stage. Pathological stage was utilised as the reference standard.

One hundred and twenty-eight patients underwent MRI and 45 proceeded to surgery. There was concurrence between MRI staging and pathological stage in only 29.3% of patients. MRI overestimated staging in 53.6% of the patients, and underestimated staging in 17.1%. The comparison between clinical staging and pathological stage indicated concurrences in 43.9% of the patients. Stage was overestimated in 19.5% and was underestimated in 36.6%. There was no statistically significant difference between the two staging options.

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Introduction

Cervical cancer is a common malignancy in developing countries, in particular those with a high prevalence of human papillomavirus and human immunodeficiency virus (HIV).[1] According to the South African National Cancer Registry's 2001 published report, cervical cancer was the third most common malignancy (16%) after breast cancer (19%) and basal cell carcinoma of the skin (17%) in female patients, and the most common malignancy in black African women (31%).[2]

Approximately 250 patients are seen every year with newly diagnosed cervical cancer at our institution. The majority present with locally advanced and inoperable disease, owing in part to a lack of awareness of screening programmes, especially in the poorer socio-economic groups. Only 40-50 patients are suitable for surgical treatment per year.

A multidisciplinary team, consisting of a radiation oncologist, as well as a member of the gynaecology oncology team, evaluates all new patients. Patients are staged using the International Federation of Gynecology and Obstetrics (FIGO) clinical classification.[3] The FIGO clinical staging remains the gold standard and subsequent surgical findings do not impact on the final recorded stage. In addition to a clinical examination, use is made of radiological investigations, which include a chest radiograph, a pelvic and abdominal ultrasound, and computed tomography (CT) or magnetic resonance imaging (MRI).

The two main treatment modalities in cervical cancer are surgery and primary chemoradiation (CRT). Options regarding treatment depend upon the stage of the patient, fertility plans and underlying medical conditions. Accurate staging is crucial for appropriate treatment selection. The aim is to avoid having to use bimodality treatment in the early-stage group (surgery followed by CRT), as it is associated with greater acute toxicity and late morbidity, compared to single-modality treatment.[4-7]

In an effort to more accurately stage patients, the use of CT or MRI has been employed. Internationally,

MRI is routinely used to evaluate patients with early-stage cervical cancer. The use of MRI for the staging of cervical cancer at Tygerberg Hospital was introduced in 2004, based on literature that demonstrated improved pretreatment staging. Prior to this, all treatment decisions were based solely on clinical examination.

This study will compare the accuracy of clinical staging and MRI staging of cervical cancer, using pathological stage as the reference standard. In addition, we evaluated the agreement between clinical staging and MRI staging in patients who did not undergo surgery.

Method

Study design

This was a retrospective analysis of all newly diagnosed patients with clinical stage I-IIB cervical cancer at Tygerberg Hospital, who underwent pelvic MRI as part of their staging investigations. Data were obtained from the Division of Radiodiagnosis MRI register, the Unit of Gynaecological Oncology and Division of Radiation Oncology clinical database.

Collected data included variables of age, clinical stage and MRI stage. Multidisciplinary treatment decisions, as well as pathological stage for those patients who underwent surgery, were captured.

Prior ethics approval was obtained from the Stellenbosch University Ethics Committee.

Descriptive statistics were used for demographic variables. Sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) were calculated. Appropriate 95% confidence intervals (CI) were calculated for these values. In addition, the association between the clinical and MRI methods was compared using the McNemar's chi-squared test for dependent proportions. The odds ratio (OR) of a correct result, relative to surgical assessment, was calculated for clinical and MRI methods separately. The software that was used was Statistica®, version 10 (2011) and SAS version 9.1.3.

Results

During the period June 2004 to May 2011, 201 pelvic MRIs were performed. One hundred and twenty-eight patients were clinical stage I-IIb. Of these, 45 patients underwent surgery, and in four patients no tumours were detected pathologically after hysterectomy [previous large loop excision of the transformation zone (LLETZ) procedure] and were excluded from the final analysis.

The patients had a median age of 46 years (range 44-55 years). Squamous cell carcinoma was the most common histological type, occurring in 86.7% of cases.

A summary of clinical staging, MRI staging and pathological stage in the subgroup of patients who underwent surgery is reflected in Table I. The majority of patients were clinically staged as IBi. The majority of patients staged by MRI were IIB.

Table I: Distribution of clinical, radiological and pathological stages in the 45 patients who underwent surgery

FIGO stage	Clinical stage		MRI stage		Pathological stage	
	n = 45	%	n = 45	%	n = 45	%
No tumour detected	-	-	6	13.3%	4	8.9%
In-situ	-	-	-	-	6	13.3%
Stage I						
IAi	-	-	-	-	2	4.4%
IAii	2	1.6%	-	-	2	4.4%
IBi	26	58.8%	10	22.2%	16	35.7%
IBii	8	17.8%	2	4.4%	8	17.8%
Stage II						
IIA	6	13.3%	9	12.5%	2	4.4%
IIB	3	6.7%	17	37.8%	4	8.9%
Stage III						
IIIA	-		-	-	-	-
IIIB	-		-	-	-	-
Stage IV						
IVA	-	0.6	1	2.3%	-	-
IVB	-		-	-	1	2.3%

FIGO: International Federation of Gynecology and Obstetrics, MRI: magnetic resonance imaging

A summary of the clinical stage and radiological stage for the group of patients who did not undergo surgery is reflected in Table II. The majority of patients were both clinically and radiologically staged as IIB.

Table II: Distribution of clinical and magnetic resonance imaging staging in patients who did not undergo surgery

FIGO stage	Clinical stage Number of patients, n = 83 (%)		MRI stage Number of patients, n = 83 (%)	
Stage I				
IAi	-	-	-	-
IAii	-	-	-	-
IBi	16	19.3%	2	2.4%
IBii	11	13.3%	2	2.4%
Stage II				
IIA	12	14.4%	7	8.5%
IIB	44	53%	65	78.3%
Stage III				
IIIA	-	-	-	-
IIIB	-	-	2	2.4%
Stage IV				
IVA	-	-	5	6%
IVB	-	-	-	-

FIGO: International Federation of Gynecology and Obstetrics, MRI: magnetic resonance imaging

Data were analysed and results were calculated for concordance, overestimation of stage and underestimation of stage for the final cohort of 41 patients. Because of the small sample size, neither a univariate nor a multivariate analysis could be performed (Table III). The results demonstrated that clinical, rather than MRI, staging, was more likely to be concordant with pathological stage. There was a concurrence rate of 43.9% and 26.8% respectively. The ORs for clinical staging and MRI staging accuracy were 0.78 and 0.41 respectively (p-value = 0.15).

In the group of patients who did not undergo surgery,

Table III: Concordance of staging method and pathological stage (n=41)

	Clinical versus MRI	MRI versus pathology	Clinical versus pathology
n	**41**	**41**	**41**
Concordant	11 (26.8%)	12 (29.3%)	18 (43.9%)
Non-concordant	30 (73.2%)	29 (70.7%)	23 (56.1%)
Upstaged	23 (56.1%)	7 (17.1%)	8 (19.5%)
Downstaged	7 (17.1%)	22 (53.6%)	15 (36.6%)

the treatment decision was changed in 24/83 (28.9%) patients as a result of the MRI. Patients were upstaged to a more advanced stage in all of the cases and the treatment decision was changed from surgery to chemoradiotherapy.

The remainder of the patients who showed discordance in staging between clinical examination and MRI had locally advanced disease. Treatment decisions remained unchanged. Radiologically, 5/83 (6%) patients were staged as IVA without histological confirmation of bladder or bowel involvement.

According to the FIGO staging criteria, histological confirmation is needed before a patient can be called a stage IV, thus in these patients, the clinical stage remains the definite stage and patients were treated accordingly.

A subgroup analysis was performed on the 41 patients who proceeded to surgery and where a tumour was found on histology. The MRI and clinical staging were compared to the histopathological staging of each patient.

Data demonstrated that the clinical examination had a higher specificity than MRI staging and a superior PPV in our small cohort. By contrast, MRI staging had an improved sensitivity in comparison to clinical staging. The NPV was comparable between the two staging methods (Table IV and V).

Table IV: Magnetic resonance imaging and clinical staging sensitivity and specificity

Parameter	Sensitivity		Specificity	
	MRI	Clinical	MRI	Clinical
Parametrial involvement	80%	40%	65%	90%
Vaginal involvement	75%	40%	68.3%	100%
Lymphadenopathy	0%	N/A	100%	N/A

MRI: magnetic resonance imaging

Table V: Magnetic resonance imaging and clinical staging positive predictive values and negative predictive values

Clinical	Positive predictive values		Negative predictive values	
	MRI	Clinical	MRI	Clinical
Parametrial involvement	22.2%	100%	96.3%	93.0%
Vaginal involvement	18.8%	33.3%	96.6%	92.3%
Lymphadenopathy	0%	N/A	80%	N/A

MRI: magnetic resonance imaging

The identification of pathological lymphadenopathy had a sensitivity of 0% and a specificity of 100%, with a PPV of 0% and a NPV of 80% (CI: 68.3-91.7%) as seen in Table IV and V. The reason for this is unclear as the same criteria were used at our institute as described in the literature to define a pathological node (10 mm). [3]

Discussion

Our small cohort study shows that in the surgical group of patients, there was limited concordance between MRI staging and pathological stage and a large percentage were inaccurately staged by MRI. This is in contrast to the literature, where a review by Boss et al showed that a change to an earlier stage occurred infrequently following MRI, in the region of 10-15%.[8]

The ORs for the accuracy of clinical staging and MRI staging were not significantly different in this study. There are multiple variables that might influence the accuracy of MRI reporting, for example, not having a dedicated radiologist to report pelvic MRIs and the difference in level of experience of individual consultants within the department. Further pitfalls leading to staging errors with MRI include difficulties in differentiating foci of cancer from surrounding tissue oedema, and excluding vaginal involvement in the presence of a bulky tumour.

In the group of patients who did not undergo surgery, it was found that there was limited agreement between the clinical stage and MRI stage. The treatment decision was changed in a third of patients, based on the result of the MRI. Compared to the literature, in their study population, Stenstedt et al found that treatment decisions were altered in only 8% of patients, based on the results of the MRI.[9] Imaging with MRI and the resultant change in clinical stage could potentially spare this population of patients the toxicity of bimodality treatment. However, following the results of this study, we questioned whether or not, in our cohort, some patients might have been inaccurately "upstaged". This assumption is based on the results of the analysis that the sensitivity for MRI in detecting parametrial involvement was at least 80%.

The sensitivity and PPV for parametrial involvement and vaginal involvement reported by MRI in our cohort of patients was also lower than that reported by Sheu et al, but the NPV was more comparable.[10] It would appear that MRI inaccurately overstaged disease in some of our patients, but it is difficult to draw a conclusion based on the large CIs. A reason for this is the small study population. The lower sensitivity and PPV of MRI detection of lymphadenopathy was clearly evident in our cohort, compared to the findings of both Shue et al and Hricak et al.[10,11] This may be because of the fact that MRI is only able to evaluate pathologically enlarged nodes ≥ 1 cm in size, whereas surgically positive nodes may have a small microscopic focus. Once again, these parameters are potentially inaccurate as demonstrated by the large CIs.

The comparison of clinical, with pathological, staging, in our cohort of patients showed there was a 43.9% concurrence. This value is lower than that reported by Boss et al.[8] Hricak et al reported higher accuracy for clinical staging, but the authors suggested that this was because of the fact that in 85% of patients, final staging was only documented after the radiology findings were reported.[11] They reported a 100% PPV for parametrial involvement and 92.3% NPV for vaginal involvement. This is contrary to most findings in the literature, where clinical staging was generally poor. When comparing MRI staging versus surgical stage, and clinical staging versus surgical stage, there appears to be a trend in our institution to show that clinical staging was more accurate than MRI in detecting parametrial and vaginal involvement. In addition, the specificity values of clinical staging were higher than MRI staging in our cohort. The German group of Hancke et al reported results similar to our own findings: that clinical staging was superior to MRI.[12] However, the majority of published studies found this not to be the case.

At the 45th annual meeting of the American Society of Clinical Oncology, the complexity of oncological care was discussed and recommendations presented that cancer care requires interdisciplinary collaboration that is provided through the development of multidisciplinary teams.[13] The multidisciplinary forum provides members of the patient care team with the opportunity to discuss face-to-face clinical, pathological and radiological findings, decide on the stage of the patient disease and devise an appropriate treatment plan that is relevant to the patient's situation. All major international centres have a dedicated radiologist for pelvic MRI interpretation as part of the multidisciplinary team.

Following the completion of our study, we recommend that there should be a dedicated radiologist on the multidisciplinary team for pelvic MRI. This will lead to consistency and most likely improved accuracy in reporting MRIs.

The strengths of this study include the fact that all patient data were available for those who met the inclusion criteria. Furthermore, there was a long study period during which experienced surgical and radiotherapy clinicians were consistent. Limitations include the small number of patients with early-stage cervical cancer who underwent surgery. As a consequence of the small study population, multivariate and univariate analysis could not be performed.

Results of this cohort study suggest a trend that clinical staging is more accurate than MRI staging. The international literature supports the hypothesis that MRI is the more accurate staging modality, rather than clinical staging. As stated above, the use of MRI at our institution had a number of limitations, which may have many commonalities with other resource-constrained institutions.

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