T2-Weighted Fast Spin-Echo MR Findings of Adenocarcinoma of the Uterine Cervix: Comparison with Squamous Cell Carcinoma

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──── Abstract ────

The purpose of this study was to investigate the differences in MR findings of adenocarcinoma (AC) and squamous cell carcinoma (SCC) of the uterine cervix and to compare MR findings with pathologic findings. MR images of 17 patients with pathologically proven AC, using a fast spin-echo (FSE) T2-weighted image (T2WI) with pelvic phased-array coil on a 1.5-T unit, were retrospectively evaluated. After measurement of the signal intensity (SI) ratios of the region of interest between tumors and gluteus maximus muscle, we compared the ratios of AC with those of 16 patients with SCC. AC showed relatively high SI on FSE T2WI with multiseptated lesions in four cases and hydrometrocolpos in three cases. The mean SI ratio was 3.82 ± 1.68 in AC and 2.35 ± 0.42 in SCC ($p < 0.0001$, t-test). Multiple tumorous glands with cytoplasmic and intraglandular mucin or serous fluid were pathologically found in AC, but SCC revealed the compact cellularity of stratified squamous tumor cells. The cervical AC showed higher SI than SCC on FSE T2WI with occasional multiseptated lesions and hydrometrocolpos. If the SI ratio of the tumor was more than 3.0, AC could be diagnosed with a sensitivity of 68.8% and a specificity of 100%.

Key Words: Uterine neoplasms, uterine neoplasms-MR, uterine neoplasms-diagnosis, magnetic resonance (MR)-comparative studies

INTRODUCTION

Adenocarcinoma (AC) of the uterine cervix is the second most common carcinoma of the uterine cervix after squamous cell carcinoma (SCC).[1] The relative frequency of AC has increased in recent years compared to that of SCC, accounting for 34% of all cervical malignancies.[2-4]

AC of the cervix usually originates from the endocervical canal and the endocervical growth of this tumor with involvement of the lower uterine segment likely results in a larger tumor volume, but about 15% of patients with AC have no visible lesion because the carcinoma is either within the endocervical canal or it is infiltrative and small. This

tumor has been known to show a poorer prognosis when compared stage for stage with SCC[5] due to delayed tumor detection because of invisibility and a poor response to radiation therapy. As a result, it is clinically important to distinguish AC from SCC of the uterine cervix before determining a treatment plan.

Computed tomography (CT) and sonography could not differentiate endocervical AC from SCC,[6,7] so the authors investigated whether T2-weighted magnetic resonance (MR) images obtained with fast spin-echo (FSE) technique were helpful in differentiating these tumors, and if they were helpful, what the histopathological findings causing the differences in MR findings were.

MATERIALS AND METHODS

Seventeen patients with pathologically proven AC of the uterine cervix ranging in age from 32 to 75 years (mean, 48.7 years) were evaluated in a consecutive series for three years. Five of these 17 patients underwent radical abdominal hysterectomy

(RAH) with bilateral salpingo-oophorectomy (BSO) and the remaining 12 patients were pathologically confirmed by dilatation and curettage (D & C), or by punch biopsy. The clinical stages of 17 patients with AC were Ib in seven, IIa in two, IIb in five, and IIIb in three cases. Five patients who underwent surgery were four cases of stage Ib and one case of stage IIa.

Regardless of clinical stage, 16 patients with SCC who had a mean age of 50 years and mean mass size of 3 cm (similar to the mean size of AC) were selected for comparison with AC patients. Among them, eight patients underwent RAH with BSO. The remaining eight patients were confirmed by D & C or punch biopsy. The tumor size was expressed as the greatest diameter in at least two dimensions on axial, coronal and sagittal MR images.

In both AC and SCC groups, the patients with stage Ib or beyond underwent radiation therapy, not surgery. Even if a patient was in stage Ib, the choice of treatment modality was dependent on the clinician.

FSE MR imaging was performed on a 1.5-T Signa imager (GE Medical Systems, Milwaukee, WI, USA) with a pelvic phased-array coil for all patients. T2-weighted $(3,000-5,000/92, 108/2$ [TR/TE$_{eff}$/ excitations]) axial and sagittal images with a 256×256 matrix and a $16-20$ cm field of view (FOV) were obtained with a 5 mm section thickness and a 1.5

mm intersection gap.

On axial images, a region of interest (ROI) was drawn along the tumor margin by MR scanner and another ROI was delineated on the neighbouring gluteus maximus muscle with as much of the same size and shape as possible (Fig. 1). The gluteus maximus muscles revealed relatively homogeneous signal intensity (SI) in all cases. Then the signal intensity ratio (SIR) of AC mass to the gluteus maximus muscle was measured. The same method was performed in SCC. SIR of AC was compared with that of SCC, which was verified by t-test.

The SI, size, location, longitudinal extent, histological subtype of tumor, and associated findings on MR images were analyzed. We also observed the histopathological findings of five patients with RAH and BSO, and investigated the causes of the difference in the image findings between the AC and SCC on FSE T2-weighted imaging (T2WI).

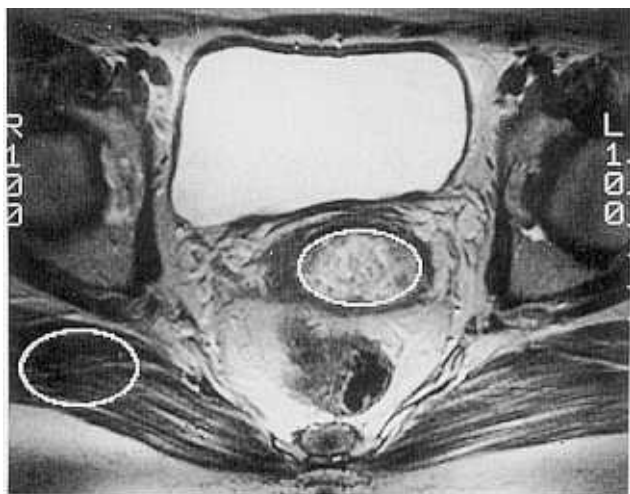## RESULTS

All 17 cases of AC showed higher SI than the

Fig. 1. Adenocarcinma (AC) of the uterine cervix shows heterogeneous and high signal intensity on fast spin-echo T2-weighted axial image. Two oval-shaped solid lines of region of interest are seen in both the uterine cervix and right gluteus maximus muscle, and the square measures of which are the same. We calculated the signal intensity ratio of the AC mass to the gluteus maximus muscle.
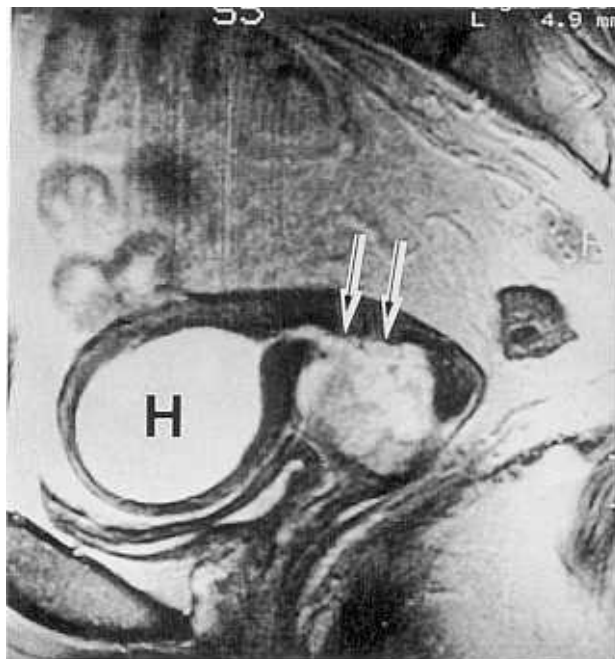

Fig. 2. AC in a 61-year-old woman. Large mass (arrows) with higher signal intensity than the myometrium is noted in the endocervical canal on fast spin-echo T2-weighted sagittal image. A large amount of hydrometrocolpos (H) is seen due to occlusion of the endocervical canal by the tumor mass.

Table 1. Summary of the 17 Patients with Adenocarcinoma of Uterine Cervix

	Age	Size (cm)	Stage	SIR*	Confirmation	Histologic subtype	Differentiation	Special MR findings
1	61	3.0×3.0	IIa	5.43	hysterectomy	endocervical	well	fluid in endometrial cavity
2	59	3.3×3.0	IIIb	4.99	D & C†	no subtype	moderate	fluid in endometrial cavity
3	43	3.2×2.8	Ib	6.23	hysterectomy	mixed endometrioid & mucinous	well	multiple cysts in tumor
4	39	4.0×3.0	Ib	3.29	D & C	endocervical	well	
5	48	4.0×3.0	Ib	4.53	punch biopsy	no subtype	well	
6	37	4.0×2.0	IIb	2.16	punch biopsy	endocervical	moderate	
7	49	7.0×6.0	IIb	7.26	D & C	endocervical	well	multiple cysts in tumor
8	75	3.0×2.8	IIIb	1.97	punch biopsy	no subtype	moderate	fluid in endometrial cavity
9	65	2.0×1.5	IIb	1.51	D & C	no subtype	well	
10	34	1.7×1.5	Ib	3.55	hysterectomy	adenocarcinoma-in-situ	well	multiple cysts in tumor
11	56	3.0×2.8	Ib	3.81	hysterectomy	endometrioid	well	
12	61	2.5×2.5	IIIb	2.84	punch biopsy	no subtype	moderate	
13	39	2.0×2.0	Ib	5.45	punch biopsy	no subtype	moderate	
14	48	1.5×1.2	IIb	3.05	punch biopsy	endocervical	moderate	
15	32	2.0×2.0	IIb	3.89	punch biopsy	endometrioid	moderate	multiple cysts in tumor
16	41	2.5×2.5	IIa	3.13	punch biopsy	no subtype	well	
17	41	3.0×3.0	Ib	1.86	hysterectomy	endocervical	moderate	

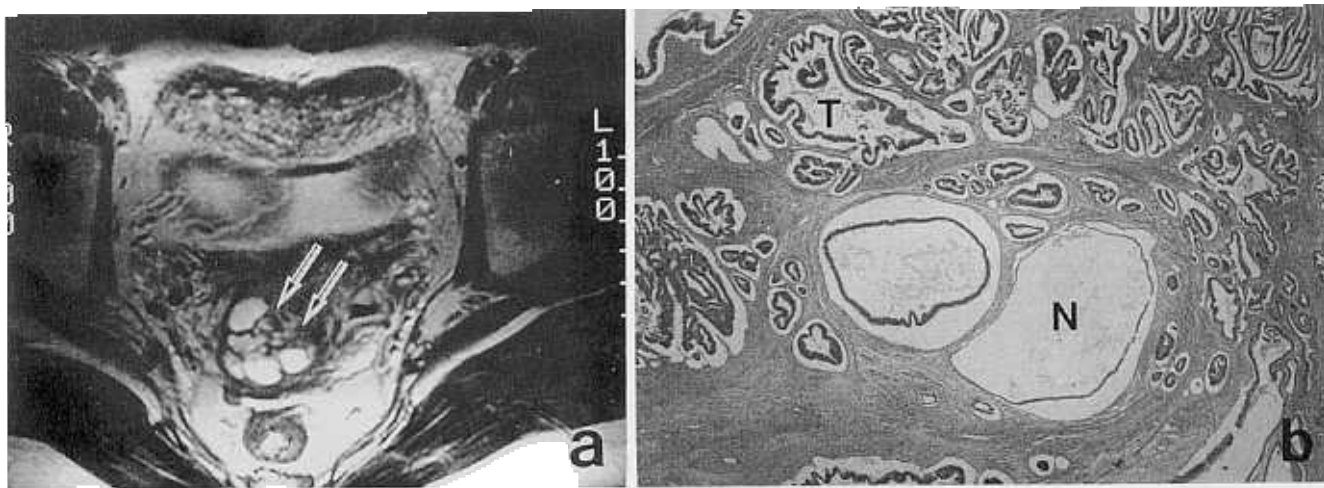*SIR, signal intensity ratio; † D & C, dilatation and curettage.

Fig. 3. (a) AC in a 43-year-old woman. Intratumoral multiseptated lesion (arrows) with high signal intensity is noted in the uterine cervix on fast spin-echo T2-weighted axial image. The remaining central portion of slightly high signal intensity is also a tumorous component. (b) Multiple large tumorous glands (T) with mucinous fluid and neighbouring small nabothian cysts (N) are histologically demonstrated in the intratumoral multiseptated lesion (hematoxylin/eosin; × 40).

myometrium on FSE T2WI (Fig. 2), and the mean tumor size was 2.9 cm in diameter (Table 1). The endocervical canal was the most common location (n=10, 58.8%) and the remaining seven cases (41.2%) showed a downward extension into the ectocervix. When the 17 cases were classified according to the subtypes of AC, they were divided into six cases of endocervical type, two cases of endometrioid type, one case of AC-in-situ, one case of mixed endometrioid and endocervicioid type, and seven cases of non-classified subtype. All seven cases of non-classified subtype were pathologically proven by punch biopsy or D & C. There were nine cases of well-differentiated AC and eight cases of moderately-
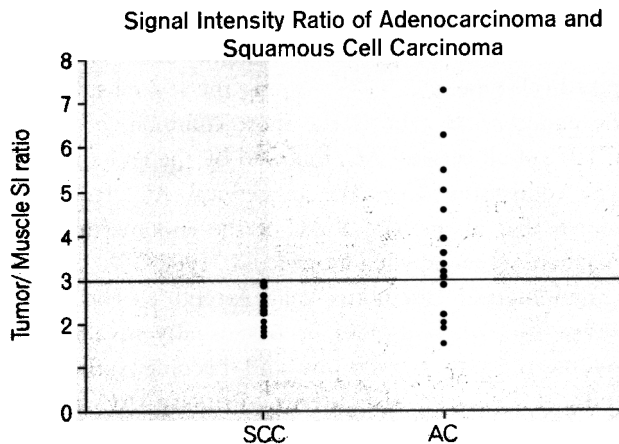
Signal Intensity Ratio of Adenocarcinoma and Squamous Cell Carcinoma

Fig. 4. Signal intensity ratios (SIR) of region of interest in two tumors are 3.82 ±1.68 in adenocarcinoma (AC) and 2.35 ±0.42 in squamous cell carcinoma (SCC), respectively (p <0.0001, t-test).

Fig. 6. Microscopic finding of squamous cell carcinoma reveals the stratified squamous tumor cells with compact cellularity, showing no glandular structures or cytoplasmic mucinous fluid (hematoxylin/eosin; ×20).
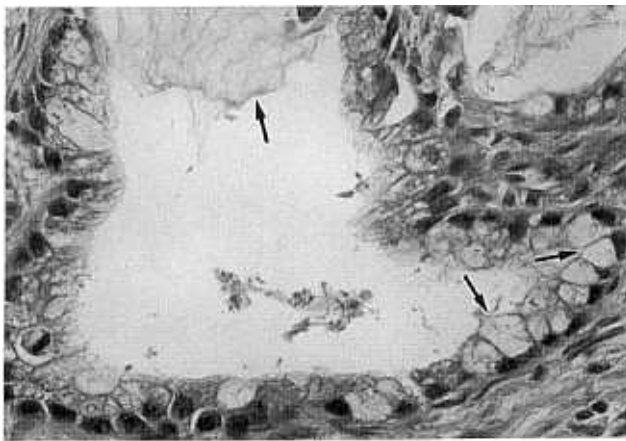

Fig. 5. Microscopic finding of adenocarcinoma shows the adenomatous acini with single-layered, tall columnar cells with cytoplasmic and intraglandular mucin (arrows), large and basal nuclei, and hyperchromacia (hematoxylin/eosin; ×400).

differentiated AC without a single case of poorly-differentiated AC. The SI of well-differentiated AC is usually higher than that of moderately-differentiated AC. Intratumoral multiseptated lesions with high SI (Fig. 3, a and b) were noted in four patients (23.5%) and hydrometrocolpos caused by occlusion of the endocervical canal was seen in three patients (17.6%).

All 16 cases of SCC also showed slightly higher SI than myometrium on FSE T2WI, but not as high as AC on gross observation. Neither multiseptated lesions nor hydrometrocolpos were demonstrated in any patients with SCC. Twelve of the 16 cases of SCC

were noted in the ectocervix and four cases extended upward to the endocervix.

SIRs of ROI in two tumors were 3.82 ± 1.68 in AC and 2.35 ± 0.42 in SCC, respectively (p < 0.0001, t-test). If SIR was over 3.0, the AC was diagnosed with a sensitivity of 68.8% and a specificity of 100% (Fig. 4). According to the subtypes of AC, SIRs of two cases of endocervical type and three cases of non-classified subtype were lower than 3.0. The mean SIRs of well-differentiated AC (nine patients) and moderately-differentiated AC (eight patients) were 4.36 and 3.28, respectively with disregard to the histological subtypes, which were not statistically significant (p > 0.05).

Histopathologically, the AC showed multiple tumorous glands composed of adenomatous acini with single-layered, tall columnar cells. Cytoplasmic and intraglandular mucin was demonstrated in the branching glands and papillary structures of AC (Fig. 5). Serous, not mucinous, fluid was often seen in the tumorous glands of AC. In SCC, stratified squamous tumor cells were noted with compact cellularity, showing no mucinous or serous fluid in the cytoplasms or surrounding stroma (Fig. 6). The causes of higher SI in AC than in SCC were probably cytoplasmic mucin and intraglandular mucinous or serous fluid in the multiple tumorous glands with sparse density.

DISCUSSION

MR has been reported to be useful in the diagnosis and staging of uterine cervical neoplasms.[7,8] However, it is very difficult to distinguish AC from SCC by conventional MR images, because the appearance on MR imaging and the patterns of spread of AC are similar to those of SCC.[7]

FSE sequence permitted the use of longer repetition and echo times to increase SI and contrast with a larger matrix and more signal averaging, which was three-to-four times faster than conventional SE T2WI, resulting in decreased ghosting artifacts from respiration, vascular pulsation or bowel peristalsis.[9-12]

AC of the uterine cervix usually arises from the endocervical canal with a barrel-shaped mass. But AC often reveals a false negative on a Pap smear due to its high location in the endocervical canal, so the exact punch biopsy, D & C or conization should be required to make a correct diagnosis.[13]

Recent studies have revealed that human papillomavirus (HPV) type 18 was present in 40% of patients with AC and in 70% of patients with adenocarcinoma in situ. Nulliparous and diabetic women have also shown an increased incidence of AC. Clear cell carcinoma, a subtype of AC, of the cervix and/or vagina rarely develops in girls or young women who were exposed, in utero, to diethylstilboestrol (DES).[3,14] AC-in-situ is a precursor of invasive AC, and two tumors can often coexist. Squamous neoplasia, intraepithelial or invasive, occurs in 30−50% of cervical AC.[15]

In our study, AC showed multiple, variable-sized tumorous glands with cytoplasmic and intraglandular mucin in the branching glands. Serous fluid was often seen in the tumorous glands of AC. In SCC, stratified squamous tumor cells with compact cellularity showed no mucinous or serous fluid in the cytoplasms or surrounding stroma. We believe that the causes of higher SI in AC than in SCC could be cytoplasmic mucin and intraglandular mucinous or serous fluid in the multiple tumorous glands with sparse density. Intratumoral multiseptated lesions in four AC patients were pathologically multiple, large tumorous glands with mucinous fluid and neighbouring small nabothian cysts (Fig. 3b).

Cervical AC are histologically subtyped as mucinous (endocervical, intestinal, and signet-ring cell type) AC, endometrioid AC, adenosquamous carcinoma, clear cell carcinoma, adenoid cystic carcinoma, glassy cell carcinoma, minimal deviation AC (adenoma malignum), papillary villoglandular AC, and mixed-cell type, etc..[13,16,17] Among the several subtypes, the endocervical type is the most common, occurring in 70% of all cervical AC, followed by the endometrioid type comprising 15−20% of cervical AC. It is well known that about 5% of AC of the endometrium are mucinous (generally endocervicoid) type.[16]

Endometrial carcinoma may extend to the endocervix, but when it does, it has usually invaded the myometrium of the corpus and become sufficiently bulky to enlarge the uterus. Primary AC of the endocervix tends to expand the cervix, so if it, rather than the corpus, is enlarged, an endocervical primary site is clinically suggested.[17] A previous report suggested that AC of the uterine cervix may be suspected on MR imaging, when a cervical carcinoma is barrel-shaped along the endocervical canal and tends to involve lymph nodes in earlier stages.[18]

Microscopically, AC occurs in the mucus-secreting columnar epithelium on the cervical surface within the endocervical canal, or within endocervical crypts. AC reveals tumor glands of variable size and shape composed of single-layered, tall columnar cells, stromal reaction around the glands, some cellular stratification, loss of mucin secretion, large and basal nuclei, pale granular cytoplasm with vacuolization, hyperchromasia, and mitotic activity.[14,16]

Controversy has existed regarding the prognosis and the most effective method of management for cervical AC. Some investigators have observed similar survival rates, regardless of treatment modality.[2,19] However, most have reported superior survival rates with either radical surgery or combined treatment consisting of radiation therapy followed by extrafascial hysterectomy.[20] The frequency of pelvic lymph node metastasis in AC is known to be similar to that of SCC; about 20% of stage I AC at operation.[17] AC of the uterine cervix has been known to show a poorer prognosis than SCC due to delayed tumor detection because of its invisibility and a poor response to radiation therapy. It was reported that patients with stage I AC had a 60% five-year survival rate, compared with 90% for SCC,[21] therefore it is clinically important to distinguish AC from SCC of the uterine cervix before determining a treatment plan.

The independent drawing of ROI in all cases is necessary to the measurement of SIR, because the tumor size and shape are variable. The gluteus max-

imus muscle was chosen as a SI comparison, even though this muscle often showed mild fatty deposition in elderly patients. The obturator internus muscle is closer to the cervix and is less likely to undergo fatty infiltration, but it is too small and narrow to be compared with a larger tumor mass. Since the gluteus maximus muscle is the largest muscle with relatively homogeneous SI in the pelvic region, it is possible to draw ROI in the gluteus maximus muscle the same as in a large tumor mass. However, since the pelvic phased-array coil has higher sensitivity in the near field, the possibility of altered SI of the gluteus maximus muscle closer to the posterior coils may be present and the degree of alteration in SI would depend on the patients size.

The limitations of this study are the small number of patients with AC and the lack of a number of subtypes of AC. As well, the number of patients (five with AC and eight with SCC) who underwent surgery was too small. As a result, the biopsy results of the patients without surgery might be inaccurate in ruling out the presence of different subtypes of cervical carcinoma because the squamous neoplasia, intraepithelial or invasive, could occur in 30 – 50% of cervical AC.[15] Another limitation was that the number of SCC patients was not a true consecutive number during the same three-year period of accrual as the AC patients, but a chosen number according to the patient's age and tumor size.

In conclusion, cervical AC showed higher SI than SCC on FSE T2WI with occasional multiseptated lesions and hydrometrocolpos. If SIR of the tumor to the gluteus muscle was more than 3.0, AC could be diagnosed with a sensitivity of 68.8% and a specificity of 100%. We suggest that the pathologic findings of cytoplasmic mucin and intraglandular mucinous or serous fluid are the causes of higher SI in AC than SCC with compact cellularity on FSE T2WI.

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