Accuracy of MRI for diagnosing pelvic and para-aortic lymph node metastasis in cervical cancer

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Abstract. The current study aimed to evaluate the accuracy of diffusion-weighted imaging and morphological aspects at 3 Tesla (T) and 1.5T MRI for diagnosing metastatic lymph nodes (LN) in cervical cancer. A retrospective study was conducted at the Barretos Cancer Hospital. A total of 45 patients with cervical cancer who underwent MRI examination and pelvic and/or para-aortic lymphadenectomy as part of surgical procedure were included. Data regarding LN images included size (short-axis diameters), morphology (usual, rounded or amorphous), appearance (homogeneous or heterogeneous), limits (regular, irregular or imprecise), presence or absence of necrosis, diffusion (normal or greater restriction than expected for normal tissue) and aspect (suspected, undetermined or normal). These findings were compared with histopathological results. According to histology results, among the 45 patients, 14 (31.1%) LNs were tested positive for metastasis and 31 (68.9%) LNs were tested negative. A total of 41 metastatic positive LNs were detected from a total of 976 resected nodes. Twelve patients from the 45 (26.7%) had LN classified as metastatic by histology and suspected by MRI, 26 (57.8%) as negative in both evaluations, 2 (4.4%) as positive by histology and negative by MRI and five (11.1%) as negative by histology and positive by MRI. Based on these results, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were 85.7, 83.9, 70.6, 92.9 and 84.4%, respectively. The Cohen's κ test exposed a general outcome of 0.657 (P<0.05), demonstrating that the two variables (histology and MRI) have substantial concordance. The κ test results between histological and MRI data for paraaortic and pelvic LNs were found to be 1 and 0.657, respectively. Finally, short axis >10 mm, T2 hypointensity, rounded morphology and greater restriction than expected for normal tissues are the four most common MRI findings associated with metastatic LN. The concordance between MRI and histology was substantial, indicating that this method using MRI for diagnosing suspected LN metastasis is reliable. The results of the current study revealed that the most important aspects to be evaluated in MRI include: Short axis >10 mm, T2 hypointensity, rounded morphology and greater restriction than expected for normal tissues. If these four characteristics are present in MRI, histological evaluation is likely to reveal positive lymph node metastasis.

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Introduction

According to the American Cancer Society, 13,240 new cases of cervical cancer were registered in the United States in 2018 (1). When regional or distant metastases are detected, survival rates within four years are 57 and 17%, respectively (1). The involvement of the lymphatic system is one of the most important predictors of poor prognosis (2) and the standard method used to determine the presence of lymph node (LN) involvement with precision is histological examination (3). MRI was subsequently developed for pre-operative evaluation and post-operative follow-up. Through morphological and functional tools, LN metastasis can be detected, categorized and staged using MRI (4,5).

An important tool in MRI is diffusion-weighted imaging (DWI), which randomizes molecular movement and provides insight into how tumors behave in the tissue environment (6). DWI uses the apparent diffusion coefficient (ADC) to analyze the magnitude of diffusion by measuring the diffusion of water molecules inside the tissue (5). In cancer tissues, ADC is normally low due to the high cancer cellularity and abundance of membranes (2,7-9). As the size, shape, extension of tumor outside the tissue and presence of necrosis can impact directly on treatment, these aspects must be evaluated to detect the existence of metastatic LNs (10,11).

Therefore, it is important to discriminate which LN has a higher chance of being metastatic, based on its morphological

and functional aspects, to avoid complications of lymphadenectomy as well as to define an optimal radiotherapy plan, without having to irradiate healthy tissue unnecessarily (12).

The current study evaluated morphological characteristics and DWI results of pelvic and paraaortic LNs using MRI in patients with cervical cancer and compared these results to histological analysis. To the best of the authors' knowledge, previous studies did not successfully compare imaging examinations of metastatic LNs in detail. The current study was designed to identify metastatic LNs with a higher precision compared with histopathological findings, and obtain more specific and sensitive results. The aim of the present study was to evaluate the accuracy of DWI and morphological features at 3 Tesla (T) and 1.5T MRI for diagnosing metastatic LNs in cervical cancer.

Materials and methods

Patient data. The present study was entirely based on the review of patients' medical records, and no human samples were used. Approval was obtained from the Ethics Committee of Barretos Cancer Hospital (approval no. 1150/2016; Barretos, Brazil). All patients consented to the use of their medical records in the current study. Medical records of patients with cervical cancer who attended the Gynecologic Oncology Department between January 2013 and December 2016 were retrospectively reviewed to obtain patient demographics, imaging findings, surgical-pathological data and follow-up information after treatment. The present study included 45 female patients (age range, 26-74 years) with stage IA1 to IVB who also had lymph vascular space invasion, who had an MRI examination for primary local tumor staging. This group of patients belong to a group that underwent pelvic and/or paraaortic lymphadenectomy as part of surgical staging or primary treatment. Patients who did not undergo MRI examination or pelvic and/or paraaortic lymphadenectomy were excluded from this study. These patients were followed up after treatment until December 2019.

Recently, the International Federation of Gynecology and Obstetrics (FIGO) staging systems for cervical cancer have been revised and two new sub-categories were included to classify the stage by LN involvement, including IIIC1 (pelvic LN metastasis) and IIIC2 (para-aortic LN metastasis) (13). Since the information for the current study was collected before the update, patients were reclassified according to the new FIGO recommendations.

Histological analyses. Histological analyses were made on LNs resected in pelvic and/or paraaortic chains. All the LNs were cut into 3-mm thickness before they were embedded into paraffin cubes and cut using microtomes. The final thickness measured 4 μm and the LNs were visualized using an optical microscope.

Image analyses. At the Barretos Cancer Hospital the inferior abdomen of patients with cervical cancer is evaluated though MRI scans, since the analysis of tumor and its relation to adjacent structures using MRI can yield superior visualization compared with that by abdominal CT. When evaluating pelvis and its structures, including those of suspected LNs, MRI scans exhibit superior accuracy compared with CT. However, renal veins are evaluated using contrasted CT at the Barretos Cancer Hospital. The public health system in Brazil does not cover positron emission tomography-CT (PET-CT) analyses in patients with cervical and endometrial cancer. In addition, since the Barretos Cancer Hospital is a public institution, CT technology was not available between January 2013 and December 2016.

The standard protocol performed at The Radiology Department of Barretos Cancer Hospital to obtain the pelvic MRI images for cervical cancer included T2-weighted images (WI) in different planes (axial, sagittal and coronal) and T1-WI (slice thickness, 3 mm; slice gap, 0.3-mm). Images were acquired from the superior portion of the antero-superior iliac spine to the inferior portion of inferior pubic branches. High resolution T2-WI sequences were taken of the axial plane at 3 mm slice thickness, which were adjusted by sagittal and coronal planes (acquired in the same exam), with 3 mm slice thickness and no gap. The diffusion weighted sequence is acquired by using the same axial plane and slice thickness in the T2-weighted sequence with high resolution. This protocol also includes an additional T2-weighted sequence, with slice thickness of 3 and 0.3 mm gaps, which were acquired from the left renal vein until the lower pubic branches. Although these MRI images were captured to visualize pelvic LNs, the final sequence in the T2-WI aforementioned, which were taken using the same protocols, was also used to evaluate paraaortic LNs, since this sequence has higher cutting thickness and possible artifacts imaging (for instance intestinal gases and movement), which could reduce the analysis accuracy of the paraaortic LN.

Lymph node status was classified by the impression of the radiologists (R.R.S and M.D.S), according to the chain removed, including right pelvic (RP), left pelvic (LP) and paraaortic (PA) and its quality: Diagnostic and non-diagnostic samples were classified according to the subjective impression of the radiologists. Non-diagnostic samples were excluded from the analysis. All images were captured at baseline assessment using Achieva 3.0T (Philips Healthcare) or a Signa™ 1.5T HDxT (GE Healthcare). PACS software (version 3.3.36) inside packages with PixViewer and Viewer MPR (year 2019; version 19.9.0; Pixeon Medical Systems SA) was used to visualize the images.

The MRI images were analyzed before surgery by two experienced radiologists (RRR and MDS) in a blinded manner. The final report was through consensual analyzes and each LN was classified as normal or suspect. For correct distribution, all statistical analyses considered the following criteria for assessing the signal sequences of the MRI: i) Appearance, homogenous or heterogenous; ii) presence of necrosis, yes or no; and iii) T2 intensity, low broadcast, areas with low signal or normal signal. For assessing the morphological aspects using the conventional sequences of MRI, for following criteria were used: i) Size, short-axis diameter >10 mm; ii) morphology, usual, rounded or amorphous, iii) limits, regular, irregular or imprecise; iv) diffusion, normal or greater restriction than expected for normal tissue; and v) aspect, suspected or normal. Patients with ≥1 LN classified as suspect using MRI were considered positive, since the chain analyzed in MRI was the same chain that was removed in posterior surgery and then identified as positive by histology.

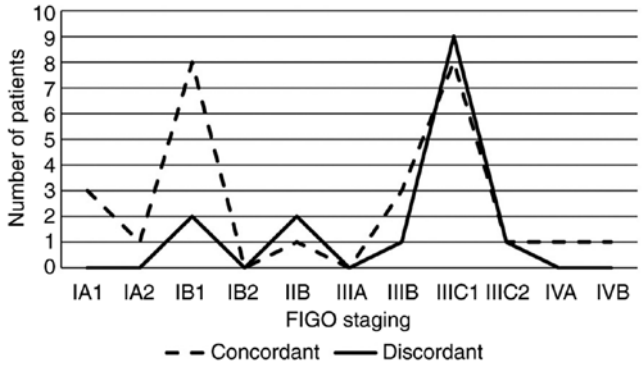

Figure 1. Number of patients exhibiting concordance and discordance according to FIGO staging and the presumed FIGO staging by MRI analysis.

Statistical analysis. Statistical analyses were performed using the SPSS software (version 21; IBM Corp.). Quantitative criteria (symmetric and non-symmetric) were presented as the mean ± standard deviation and categorical data were presented as n (%) in tables. The κ and concordance test were used to evaluate if the variable MRI had a link with histopathology results, where values closer to 1 was considered to indicate higher degrees of concordance between the MRI and histopathology data. $P<0.05$ was considered to indicate a statistically significant difference. Sensitivity (S), specificity (E), positive predictive value (PPV) and negative predictive value (NPV) were used to determine the accuracy of MRI images. Study data will be collected and managed using Redcap software version 9.5.14 (Research Electronic Data Capture) electronic data capture tools hosted at MD Anderson (Texas) (14).

Results

General results. A total of 45 patients with cervical cancer who underwent pelvic and/or paraaortic lymphadenectomy were included in the current study. The median age was 50 years (age range, 26-74). Among these 45 patients, 34 (75.6%) had squamous carcinoma, 8 (17.8%) had adenocarcinoma and 3(6.6%) had other histological subtypes. According to the revised FIGO staging system 4 patients (8.9%) were categorized as IA1, 1 (2.2%) as IA2, 10 (22.2%) as IB1, 8 (18.8%) as IIB, 1 (2.2%) as IIIA, 3 (6.7%) as IIIB, 9 (20.0%) as IIIC1, 5 (11.1%) as IIIC2, 1 (2.2%) as IVA and 3 (6.7%) as IVB. In addition, FIGO stage diagnoses obtained by physical examination were compared with the FIGO stage prediction made using MRI before surgery. A total of 27 patients (60%) were concordant and 18 patients (40%) were discordant comparing histological FIGO stage and presumed FIGO stage by MRI, respectively. The number of concordant and discordant patients was determined at each FIGO stage (IA1-IVB; Fig. 1).

The MRI evaluated was before surgery (median, 43 days; range, 3-163 days). Among 45 patients, 14 (31.1%) and 31 (68.9%) had metastatic and negative LNs by histology, respectively. Among these 14 metastatic patients, 9 (64.3%) had positive LNs in both pelvic (RP and LP) and PA chains, 4 (28.6%) in PA and 1 (7.1%) in RP and PA. Among the 14 (31.1%) patients with positive LNs, 8 (57.2%) had no recurrence after treatment at the Barretos Cancer Hospital. However, recurrence was recorded in 6 (42.8%) patients. These recurrences were diagnosed by MRI. Two patients (33.3%) had recurrence in pelvic organs, 2 (33.3%) in the abdomen, 1 (16.7%) in pelvic LNs and 1 (16.7%) pelvic LNs and lungs. Recurrence in the same lymphatic chain that had prior lymphadenectomy was observed in 3 patients (50%). Among the 31 patients with negative LNs, 26 (83.8%) had no recurrence, whereas 5 (16.2%) had recurrence. A total of 4 (80%) of these patients were diagnosed only by MRI and one (20%) by MRI and tomography. Among the 5 patients with recurrence, 3 (60%) were in the abdomen, 1 (20%) in liver and lungs, and 1 (20%) in pelvic organs.

Comparison between data obtained using histology and MRI. Comparing between histology and MRI findings, 12 patients (26.7%) had suspected LN metastasis by MRI and were tested positive by histological analysis, 26 (57.8%) were tested negative for LN metastasis by both MRI and histology, five (11.1%) were tested negative by histology and positive by MRI and two (4.4%) were tested positive by histology and negative by MRI (Table I). Based on these results, further analysis revealed the sensitivity, specificity, PPV, NPV and accuracy to be 85.7, 83.9, 70.6, 92.9 and 84.4%, respectively. The κ test exposed a general outcome of 0.657 ($P<0.05$), suggesting that the data obtained using histology and MRI have substantial concordance. According to the κ test, the value for data obtained using histology and MRI was calculated to be 1 for paraaortic LN and 0.657 for pelvic LN (both $P<0.05$).

To identify possible errors, the false negative and false positive cases were analyzed further to verify the concordance between data obtained by histological and MRI examinations. A total of two false negative cases were found, of which one (50%) did not reveal suspected LN metastasis by MRI and was subsequently admitted for pelvic and paraaortic lymphadenectomy. This patient had an important difference in the short axis diameter by pre-operative MRI (6 mm) compared with that revealed by histological analysis (23 mm), possibly due to the 41-day gap between MRI to surgery. The other false negative case had suspected LN metastasis in the bilateral pelvic chains as revealed by MRI and was admitted for paraaortic lymphadenectomy 15 days after MRI. Among the five false positive cases, three (60%) had suspected bilateral pelvic LN metastasis as revealed by MRI, one (20%) metastasis was detected in the right pelvic LN and one (20%) in the left pelvic LN. All five patients were admitted for pelvic and paraaortic lymphadenectomy. The MRI method used to analyze paraaortic LN is a one-sequence scan that was performed without good resolution and therefore could be the reason for underdiagnosis. The medical records of the five false positive cases were reviewed to examine the follow up status up until October 2019. In total, four (80%) patients were alive without disease and one (20%) died in 2015 as a result of cervical cancer.

Among the 12 true positive cases, four (33.3%) had suspected bilateral pelvic LN metastasis by MRI and were admitted for pelvic and paraaortic surgery, three (25.0%) had suspected right pelvic LN metastasis and received pelvic and paraaortic surgery, two (16,7%) had suspected bilateral pelvic and paraaortic LN metastasis and received paraaortic surgery, one (8.3%) had suspected right pelvic LN metastasis and was admitted for right pelvic and paraaortic surgery, one (8.3%) had suspected left pelvic LN metastasis and received pelvic

Table I. Patients with suspect and non-suspect lymph nodes by MRI comparing to histopathological results.

MRI	Positive by histological analysis N (%)	Negative by histological analysis N (%)	Total N (%)
Positive for suspected metastasis	12 (26.7)	5 (11.1)	17 (37.8)
Negative for suspected metastasis	2 (4.4)	26 (57.8)	28 (62.2)
Total	14 (31.1)	31 (68.9)	45 (100)

Table II. Distribution of number of analysis regarding number of lymph nodes encountered, according to lymphadenectomy performed and pre-operative MRI evaluation.

Chain	MRI=histology N (%)	MRI > histology N (%)	MRI < histology N (%)	Total N (%)
False positive				
LP	1 (6.7)	4 (26.7)	0 (0.0)	5 (33.3)
RP	1 (6.7)	4 (26.7)	0 (0.0)	5 (33.3)
PA	4 (26.7)	0 (0.0)	1 (6.7)	5 (33.3)
Sub. Total	6 (40.0)	8 (53.3)	1 (6.7)	15 (100.0)
False negative				
LP	0 (0.0)	1 (16.7)	1 (16.7)	2 (33.3)
RP	1 (16.7)	1 (16.7)	0 (0.0)	2 (33.3)
PA	1 (16.7)	0 (0.0)	1 (16.7)	2 (33.3)
Sub. Total	2 (33.3)	2 (33.3)	2 (33.3)	6 (100.0)
True positive				
LP	9 (25.0)	3 (8.3)	0 (0.0)	12 (33.3)
RP	5 (13.9)	4 (11.1)	3 (8.3)	12 (33.3)
PAs	8 (22.2)	0 (0.0)	4 (11.1)	12 (33.3)
Sub. Total	22 (61.1)	7 (19.4)	7 (19.4)	36 (100.0)
Total	30 (52.6)	17 (29.8)	10 (17.5)	57 (100)

LP, left pelvic; RP, right pelvic; PA, paraaorta; MRI=histology, number of analyses equal in both evaluations; MRI > histology, number of analyses higher in MRI than histology; MRI < histology, number of analyses smaller in MRI than histology.

and paraaortic surgery, one (8.3%) had suspected paraaortic LN metastasis and had paraaortic surgery.

As aforementioned, five cases (11.1%) were considered false positive, two (4.4%) as false negative and 12 (26.7%) as true positive, totaling 19 patients. These 19 patients had three possible outcomes comparing both MRI and histological analyses: i) The number of LN metastases encountered by MRI were equal to that by histology; ii) MRI revealed more LN metastases compared with histology; and iii) MRI encountered less LN metastases compared with histology. Therefore, a total of 57 possible analytical combinations were found for these 19 patients. This combination was subsequently divided according to the three groups as listed above and to the associated lymphadenectomy chains (LP, RP and PA). Of the 57 possible combinations, there were 30 (52.6%) cases in which had MRI and histology revealed an equal number of metastatic LNs, 17 (29.8%) cases where MRI diagnosed a greater number of LN metastases and 10 (17.5%) cases in which MRI diagnosed a lower number of LN metastases compared with histology (Table II).

Among all lymphadenectomies (pelvic and/or para-aortic) performed, a total of 976 LNs were resected. Of these, 41 (4.2%) were confirmed to be positive by histological analysis for metastasis whilst 935 (95.8%) were considered negative by histology. Further analysis revealed that from the 41 positive LNs, three (7.3%) were encountered in the LP, 10 (24.4%) in the RP, 18 (43.9%) in the PA, four (9.8%) in both LP and RP and six (14.6%) in pelvic (LP and/or RP) and PA.

MRI analyses. In terms of exam quality, examination of all 45 patients (100%) resulted in a successful diagnosis. A total of 44 LNs were analyzed using MRI, of which 42 (95.5%) were suspected to be metastatic by MRI and two (4.5%) were considered to be negative for metastasis. Among the 44 cases, two (4.5%) were found in the LP, eight (18.2%) in the RP, two (4.5%) in the PA, 19 (43.2%) in both LP and RP, and 13 (29.5%) in pelvic (left and/or right) and PA.

The morphological characteristics of the 42 (95.5%) suspected LN metastases as determined by DWI in MRIs were then compared against their corresponding histology

Table III. Association between suspect lymph nodes in morphological and functional features revealed using MRI that were subsequently found to be positive for metastasis by histological analysis.

MRI finding	Metastasis-positive lymph nodes by histology N (%)
Short-axis >10 mm	38 (90.5)
T2 hipointensity	34 (81.0)
Rounded morphology	33 (78.6)
Greater restriction than one would expect	32 (76.2)
Heterogeneous appearance	29 (69.0)
Presence of necrosis	20 (47.6)
Irregular limits	17 (40.5)

data, which is considered to be the golden-standard. It was found that those with short axes >10 mm had an major impact in determining the probability of an LN being metastatic in subsequent histological analyses, as 90.5% of the metastatic LNs found using MRI that were >10 mm were subsequently found to be metastatic in histological analysis. LN metastases with T2 hypointensities had an association of 81.0%, rounded morphology had an association of 78.6%, greater restriction than one would expect for this tissue had an association of 76.2%, heterogenous appearance had an association of 69%, presence of necrosis had an association of 47.6% whilst LN metastases with irregular limits had an association of 40.5% (Table III). When investigating the smallest diameter of the short axis in suspected metastases in LNs using MRI, it was concluded that the median size of all suspected metastases in LNs was 16.8 mm (5-50 mm), with a standard deviation of 0.96.

A representative case of a true positive patient with a metastatic LN as diagnosed by MRI and histological analysis, both in the RP chain is shown in Fig. 2. Morphological and functional characteristics that were associated with metastatic status were short-axis diameter measuring 21 mm, presence of necrosis associated with liquid level, areas with greater restriction than would be expected for this tissue, presence of round morphology and heterogenous appearance and irregular limits. For comparative purposes, a representative case of a false positive exam was also shown (Fig. 3). This patient was tested positive for LN metastasis in the RP by MRI and but negative by histological analysis. The morphological and functional characteristics that were associated with this image are short-axis diameter measuring 14 mm, areas with greater restriction than one would expect, rounded morphology, homogenous appearance and regular limits.

Discussion

In the present study the accuracy of MRI in diagnosing LN metastasis in patients with cervical cancer was compared against that of histological analysis, with emphasis on common morphological and functional (DWI) characteristics. By analyzing the combined morphological and functional characteristics of LN metastases, it was found that a substantial concordance between the data obtained using pre-operative MRI and histology can be achieved with high sensitivity and specificity. In addition, it was found that short axis >10 mm, T2 hypointensity, rounded morphology and greater restriction than one would expect were the most common characteristics encountered in metastatic LNs, which can be used as a diagnostic tool. A technical pelvic exam, performed in all steps with proper technique by a trained specialist, can also be used to predict FIGO staging, since the majority of the patients included in the present study exhibited concordant results between those obtained by physical and MRI examinations, especially for the presence of pelvic and para-aortic LN metastasis. Additionally, MRI was able to correctly identify the number of suspected LN metastases, specifically in >50% of the possible candidates for lymphadenectomy. These results potentially underline the important role of MRI in diagnosing LN metastasis, especially in the presence of the features aforementioned.

When comparing the number of patients tested positively for suspected LN using MRI, the present study revealed a sensitivity of 85.7% and NPV of 92.9%, when other previous studies (3,15,16) yielded 92, 86 and 92.1% for sensitivity and 98.2, 84 and 100% for NPV, respectively. Previous studies (2,17) also compared the importance of MRI images using DWI for diagnosing metastatic LN, resulting in values of 83.3 and 95.7% being deduced for sensitivity and 74.7 and 96.5% for specificity, respectively. Although the total number of patients in the present study was considered low, concordance with the current literature exist in terms of outcomes, as 85.7% was found for sensitivity and 83.9% was found for specificity in the present study. A previous meta-analysis performed by Liu *et al* (18) compared 67 studies which investigated MRI performance in diagnosing suspected LN metastasis in cervical cancer. The average of sensitivity and specificity were found to be 54 and 93%, respectively. Chou *et al* (19) showed that the moderate false-negative and false-positive rates found for MRI is due to some patients being staged as IA2-IIA, which can explain some lower sensitivities observed (19,20). Therefore, it is essential do use the ADC maps to address this issue (21-24).

It is generally considered that MRI exhibits higher degrees of diagnostic accuracy in patients with advanced disease, since the associated LNs are larger in size and has clearer defined features such as necrosis (25). Therefore, patients with early stage metastatic disease may be underdiagnosed using this method (25). This aspect may be considered to be a limitation in the results from the present study, combined with the low resolution in the paraaortic sequences.

Lymph node metastasis is one of the most important features to be categorized in cervical cancer, which serves as an important prognostic factor for patients with this disease. Therefore, it is important to differentiate healthy LNs from suspected metastatic LNs. Generally, healthy LNs tend to be ovoid in shape, homogenous in appearance, with intermediate signals in T2-weighted sequences and high signals in DWI sequences (26). In the present study, it was found that the four most common morphological and functional characteristics associated with the higher risk of malignancy in pelvic and/or para-aortic LN metastasis as diagnosed by MRI are, in decreasing order, short axis >10 mm, T2 hypointensity,

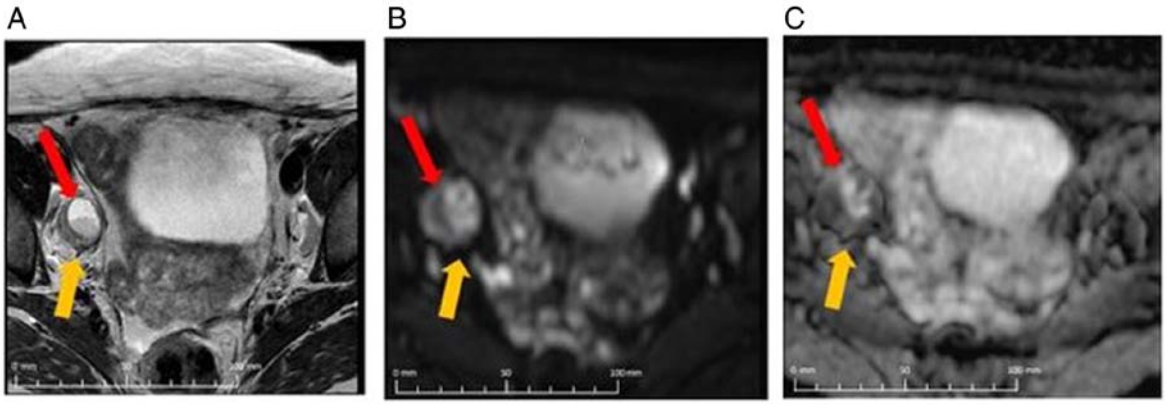

Figure 2. Representative images of a 39-year-old patient with squamous cell cervical cancer, at FIGO stage IA1 and grade II of differentiation. One histological lymph node metastasis was found in the right pelvic chain. MRI images with (A) T2-weighted imaging, (B) diffusion weighted imaging and (C) the apparent diffusion coefficient map are shown. The short-axis diameter was measured 21 mm. Red arrows indicate the location of the right pelvic LN with presence of necrosis associated with liquid level and areas with greater restriction than one would expect for this tissue. In addition, a round morphology and heterogenous appearance was noted. Yellow arrows indicate the location of irregular limits in the posterior edge.

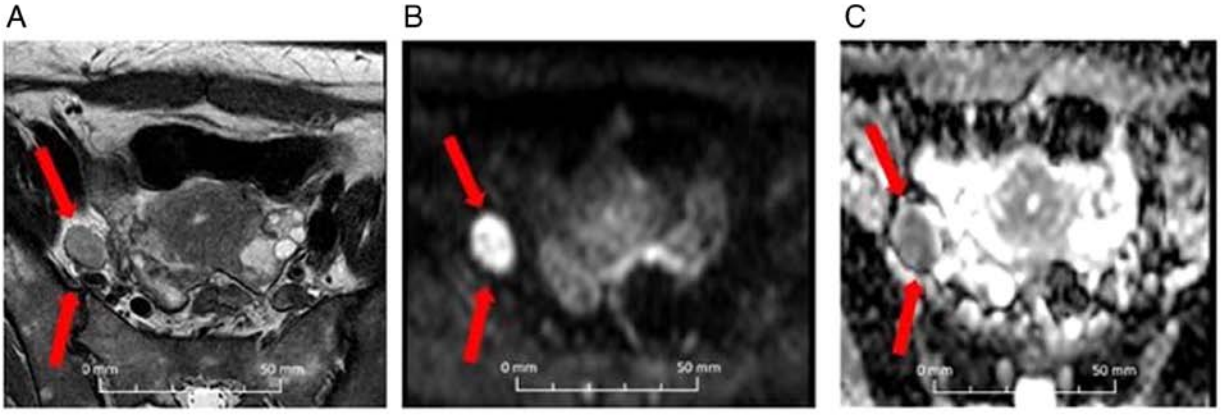

Figure 3. Representative images of a 39-year-old patient with squamous cell carcinoma, at FIGO stage IVA and grade III of differentiation. No lymph nodes metastases were found. MRI images with (A) T2-weighted imaging, (B) diffusion weighted imaging and (C) the apparent diffusion coefficient map are shown. The short-axis diameter measured 14 mm. Red arrows the location of the right pelvic LN with the short axis >10 mm, areas with greater restriction than one would expect for this tissue, a rounded morphology, homogenous appearance with regular limits.

rounded morphology followed by greater restriction than one would expect. It became clear that the combination of these features using MRI can predict suspected LN metastasis with high probability. These findings highlight the benefit of having a protocol to ensure the early and safe diagnosis of metastasis in lymph nodes.

Exner *et al* (4) hypothesized that the most important predictor for the probability of malignancy is the size of the LN. By contrast, Hawnaur *et al* (27) demonstrated a LN to be malignant when the short-axis was calculated to be >10 mm. However, other authors claimed that size alone is not a sufficiently adequate prognostic indicator whilst highlighting the necessity for including morphological data into the analysis, including limits, morphology and the presence of necrosis (11,12,28); all of which were included in the present study in addition to functional aspects (DWI). Indeed, diagnostic accuracy can be improved by combining morphological and functional data found using MRI, especially short axis >10 mm, T2 hypointensity, rounded morphology and greater restriction than one would expect. However, when patients are exposed to radiation and/or chemotherapy, morphology and diffusion can alter the tumor tissue, increasing the difficulty in obtaining parameters of the tissue itself without any interference. Liyanage *et al* (29) previously confirmed that when the specificity and sensitivity for the standard criteria as aforementioned is low (29-86%), the difficulty in detecting micro-metastases in normal sized LNs increases.

The importance of using PET-CT for pre-operative examinations of potential LN metastases to detect anatomical and metabolic deviations from healthy LNs should also be recognized (30). Lin *et al* (31) evaluated the use of PET-CT in pre-operative assessments of patients with squamous cervical cancer associated with positive pelvic LN metastasis, which showed the sensitivity, specificity, PPV and NPV to be 44, 99, 95 and 78%, respectively. A meta-analysis performed by Yu *et al* (32) investigated sensitivity and specificity for patients with cervical cancer and positive for para-aortic LN, which were found to be 71 and 95%, respectively. The present study yielded the sensitivity, specificity, PPV and NPV for using MRI obtained for diagnosing pelvic and para-aortic LN metastasis to be similar to those obtained from PET-CT

analysis in previous studies: 85.7, 83.9, 70.6, 92.9 and 84.4%, respectively. Therefore, focusing on short axis >10 mm, T2 hypointensity, rounded morphology and greater restriction than one would expect using MRI can increase the accuracy of early diagnosis. Some of these aspects were mentioned in previous studies with PET-CT (30) and the present study demonstrated that these same aspects can also be applied in MRI examinations without compromising accuracy.

The strength of the present study was that the morphological features of the LN metastases obtained using MRI were evaluated in several categories, which were then analyzed in association with DWI and histopathological results. The limitation of the present study is the low sample number of patients. However, the patients included in this study required nodal commitment and were admitted to receive systematic lymphadenectomy. In addition, it should be recognized that MRI alone is insufficient for providing correct evaluations of metastasis in the paraaortic chain. Novel studies to confirm the results obtained from the present study is strongly encouraged. However, since the results performed in the present study were concordant with the current literature, it can serve as an template that can be replicated in a subsequent study involving larger cohorts of patients.

In conclusion, to the best of the authors' knowledge, the present study was the first to evaluate LN metastasis by using a number of morphological and functional categories. It was found that the most important features found in LN metastases using MRI are short axis >10 mm, T2 hypointensity, rounded morphology and greater restriction than one would expect. If these four categories are combined in MRI, the likelihood of the LN in question harboring a metastatic tumor by subsequent histological examination is high. This can potentially guide the decision-making process in the types of surgery or even types of therapeutic intervention required. If PET-CT is not available, the use of DWI to obtain morphological data in defining LN metastasis is recommended for pre-operative examinations.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are available in the [Figshare] repository (https://figshare.com/s/878e54ea121d972aa408).

Authors' contributions

TD reviewed and collected patient data from patient charts, participated in statistical analyses and was the main writer. RRR and MDS reviewed and analyzed the MRI images, and participated in paper construction and provided final approval of the version to be published. CEMDCA, RS and MAV collected data from patients, participated in paper construction and final approval of the version to be published. MAL performed statistical analyses and participated in paper construction. DAPDA contributed to the discussion of results and participated in paper construction and final approval of the version to be published. RDR collected data from patients in consults in our hospital, reviewed and oriented all steps in the study, including reviewing the paper in all phases, participated in paper construction and designed the study. All authors read and approved the final version of this manuscript.

Ethics approval and consent to participate

Approval for the present study was obtained from The Ethical Committee of Barretos Cancer Hospital (approval no. 1150/2016; Barretos, Brazil). All patients consented to the use of their medical records in the current study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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