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Research Paper

Development and Validation of an MRI-Based Radiomics Signature for the Preoperative Prediction of Lymph Node Metastasis in Bladder Cancer

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ABSTRACT

Background: Preoperative lymph node (LN) status is important for the treatment of bladder cancer (BCa). However, a proportion of patients are at high risk for inaccurate clinical nodal staging by current methods. Here, we report an accurate magnetic resonance imaging (MRI)-based radiomics signature for the individual preoperative prediction of LN metastasis in BCa.

Methods: In total, 103 eligible BCa patients were divided into a training set ($n = 69$) and a validation set ($n = 34$). And 718 radiomics features were extracted from the cancerous volumes of interest (VOIs) on T2-weighted MRI images. A radiomics signature was constructed using the least absolute shrinkage and selection operator (LASSO) algorithm in the training set, whose performance was assessed and then validated in the validation set. Stratified analyses were also performed. Based on the multivariable logistic regression analysis, a radiomics nomogram was developed incorporating the radiomics signature and selected clinical predictors. Discrimination, calibration and clinical usefulness of the nomogram were assessed.

Findings: Consisting of 9 selected features, the radiomics signature showed a favorable discriminatory ability in the training set with an AUC of 0.9005, which was confirmed in the validation set with an AUC of 0.8447. Encouragingly, the radiomics signature also showed good discrimination in the MRI-reported LN negative (cN0) subgroup (AUC, 0.8406). The nomogram, consisting of the radiomics signature and the MRI-reported LN status, showed good calibration and discrimination in the training and validation sets (AUC, 0.9118 and 0.8902, respectively). The decision curve analysis indicated that the nomogram was clinically useful.

Interpretation: The MRI-based radiomics nomogram has the potential to be used as a non-invasive tool for individualized preoperative prediction of LN metastasis in BCa. External validation is further required prior to clinical implementation.

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Research in Context

Preoperative lymph node (LN) status is important for the treatment of bladder cancer (BCa). However, a proportion of patients are at high risk for inaccurate clinical nodal staging by current methods. Radiomics, the high-throughput extraction of immense volumes of quantitative image features from standard-of-care medical imaging that can be excavated and applied within disease detection, diagnosis, prognostic evaluation, and prediction of the treatment response, has drawn increased attention in cancer research in recent years. We have reported a radiomics study recently, which developed a CT-based radiomics nomogram with favorable discrimination and calibration for the preoperative prediction of LN metastasis in patients with BCa. Since a proportion of BCa patients are diagnosed clinically via MRI, whether the radiomics features extracted from MRI images can be used for LN metastasis prediction in BCa patients is an interesting problem that warrants investigation. However, there has been no study that has determined whether a radiomics signature extracted from MRI images would be capable to preoperatively predict LN metastasis in BCa to date. In this study, we developed and validated an MRI-based radiomics signature for preoperatively predicting LN metastasis in BCa patients, which showed good discrimination in the training and validation sets. Encouragingly, it also performed well in the MRI-reported LN-negative (cN0) subgroup. Our signature demonstrates that radiomics features extracted from MRI images can be used for LN metastasis prediction in BCa patients. The nomogram, incorporating the radiomics signature and MRI-reported LN status, showed favorable discrimination and calibration, providing a non-invasive preoperative prediction tool to identify BCa patients with a high risk of LN metastasis, which may aid in clinical decision-making.

1. Introduction

Bladder cancer (BCa) is the ninth most common cancer and ranks thirteenth as a cause of cancer-related death worldwide [1]. Lymph nodes (LNs) are a common site of metastatic spread in patients with BCa, as approximately 25–30% of BCa patients who undergo radical cystectomy (RC) and pelvic lymph node dissection (PLND) harbor LN metastases [2–8]. LN metastasis is a negative prognostic factor in BCa patients [9–11]. Thus, accurate prediction of LN metastasis in patients with BCa can improve medical decision-making. Magnetic resonance imaging (MRI) and computed tomography (CT) are recommended for preoperative nodal staging in BCa patients in clinical practice. Both MRI and CT detect malignant LN mainly based on their size. However, normal-sized or minimally enlarged LNs assume a considerable proportion of malignant LNs of BCa patients. Such diagnosis pattern leads to understaging patients with small nodal metastases. Therefore, the sensitivity of CT or MRI for detecting malignant LNs is relatively low (31–45%), which has consequently led to a proportion of patients being understaged [12–15].

Radiomics, the high-throughput extraction of immense volumes of quantitative image features from standard-of-care medical imaging that can be excavated and applied within disease detection, diagnosis, prognostic evaluation, and prediction of the treatment response, has drawn increased attention in cancer research in recent years [16, 17]. Radiomics-based signatures have been developed for precision diagnosis and treatment, which may serve as a novel and powerful tool in modern precision medicine [16]. An MRI-based radiomics study has demonstrated that radiomics features extracted from MRI images can be used to distinguish tumor grade in BCa [18]. However, to our knowledge, there has been no study that has determined whether a radiomics signature extracted from MRI images would be capable to preoperatively predict LN metastasis in BCa to date. Recently, we reported a CT-based radiomics study, which developed a radiomics nomogram with favorable discrimination and calibration for the preoperative prediction of LN metastasis in patients with BCa [19]. Since a proportion of BCa patients are diagnosed clinically via MRI, whether the radiomics features extracted from MRI images can be used for LN metastasis prediction in BCa patients is an interesting problem that warrants investigation.

Therefore, the aim of this study was to construct and validate an MRI-based radiomics signature for the preoperative prediction of LN metastasis in patients with BCa. Moreover, we developed an inclusive nomogram that incorporated the radiomics signature and clinical risk factors for providing an individual, preoperative assessment of the risk of LN metastasis in BCa patients.

2. Materials and Methods

2.1. Patients

Ethical approval was obtained from the institutional review board for this retrospective analysis. A total of 103 consecutive BCa patients treated between August 2010 and April 2018 were enrolled in this study according to the specified inclusion and exclusion criteria. Inclusion criteria consisted of the following: (a) BCa patients with pathologically confirmed urothelial carcinoma; (b) laparoscopic RC and extended PLND performed; and (c) standard pelvic MRI performed <20 days before surgery. Exclusion criteria included the following: (a) neoadjuvant chemotherapy or preoperative radiotherapy performed; (b) other tumor diseases occurring at the same period; and (c) have imaging artifacts in the MRI images. The patient recruitment pathway is presented in Supplementary Fig. S1. All enrolled patients were divided into two independent data sets: 69 patients treated between August 2010 and July 2016 were assigned to the training set, whereas 34 patients treated between August 2016 and April 2018 were assigned to the validation set.

Baseline clinical data (age and sex) and pathologic N stage were derived from the medical records. MRI data, including the size of the largest tumor, the number of tumors, T stage and LN status, were recorded by two radiologists with 15 (Yong Li) and 10 years (Zhuo Wu) of experience in pelvic MRI interpretation after reviewing all of the MRI scans. Any disagreement was resolved by a consultation. Note that those patients with pelvic LN > 8 mm or abdominal LN > 10 mm in the maximal short-axis diameter on MRI scans were regarded as clinically LN-positive (cN1-3) [20]. Tumor pathologic staging was performed on the basis of the UICC 7th edition TNM staging system [21].

2.2. Imaging Acquisition, Volumes-of-Interest Segmentation and Radiomic Feature Extraction

Fig. 1 shows the radiomics workflow. All patients underwent pelvic MRI with a 3.0 T MR scanner (Intera Achieva, Philips Medical Systems, Best, the Netherlands). On T2-weighted (T2-w) MR images, urine has a high signal intensity, which allows the bladder tumor margins to be delineated more accurately. Thus, axial T2-w Digital Imaging and Communications in Medicine (DICOM) images were retrieved for radiomics feature extraction. The T2-w image acquisition parameters were as follows: repetition/echo time, 3500-4200/100–120 msec; slice thickness, 4 mm; and spacing, 0.5 mm. Regions of interest (ROIs) of bladder tumors were segmented slice-by-slice using the publicly available 3D Slicer software version 4.7.0. Then, the corresponding ROIs were stacked up to construct volumes of interest (VOIs) of the bladder tumor. More information about the segmentation procedure is shown in the Supplementary Methods. A large set of quantitative radiomics features were extracted using the *PyRadiomics* platform implanted in the 3D Slicer software [22]. The features could be divided into four categories:

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