Review Article

Role of high-resolution magnetic resonance imaging in preoperative tumor-node-metastasis staging evaluation of esophageal cancer: a narrative review

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Background and Objective: Esophageal cancer (EC) is an aggressive disease characterized by high mortality rates and a propensity for locoregional or distant recurrence. The treatment strategies and prognostic estimation for EC depend on accurate pre-treatment tumor-node-metastasis (TNM) staging. The objective of this review was to illustrate the role of various imaging modalities in achieving accurate preoperative TNM staging of EC, with a particular focus on the utilization of advanced high-resolution magnetic resonance imaging (MRI) sequences for T classification, which have shown promise in enhancing the delineation of tumor depth and extent.

Methods: A comprehensive literature search was conducted in PubMed and Web of Science databases. The studies on imaging in preoperative TNM staging of EC published in English from inception of these databases to December 31, 2022 were reviewed.

Key Content and Findings: The review highlights the distinct advantages and inherent limitations of different imaging modalities for the preoperative staging of EC. Endoscopic ultrasound (EUS) provides real-time, high-resolution imaging of the esophageal wall but is operator-dependent. Computed tomography (CT) is widely available and non-invasive, but it may lack sensitivity for early T-stage identification. Positron emission tomography (PET)/CT offers accurate assessment of distant metastasis but has limited value in the evaluation of early-stage tumors. With improved techniques, MRI is particularly useful for visualization of tumor infiltration and the surrounding anatomical structures, gaining prominence in preoperative staging of EC.

Conclusions: Various imaging modalities including EUS, CT, PET/CT, and MRI should be applied as complementary methods for preoperative TNM staging of EC. Notably, high-resolution MRI can overcome motion-related artifacts and provide high-quality images, which may play a more important role in the management of EC in the future.

Keywords: Esophageal cancer (EC); tumor-node-metastasis staging (TNM staging); magnetic resonance imaging (MRI); preoperative assessment

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Introduction

Esophageal cancer (EC) is one of the leading causes of cancer-related mortality globally, with a 5-year survival rate of less than 40% (1,2). Additionally, esophageal squamous cell carcinoma (ESCC) is the most common pathological type in Eastern Europe and Asia, and is reported to have worse prognosis than adenocarcinoma (3). ESCC mainly localizes around the tracheal bifurcation, with a tendency for earlier lymphatic spread (4).

In clinical practice, the current standard treatment for stage I EC is surgery and for stages II/III EC is neoadjuvant chemotherapy or chemoradiotherapy (CRT) followed by surgery, and definitive CRT is recommended for inoperable EC (5,6). In addition, the prognosis of EC mainly depends on T staging and regional lymph node status (7). Therefore, accurate pre-treatment tumor-node-metastasis (TNM) staging of EC is essential for clinical decision-making and improving the prognosis. However, there is a lack of precise preoperative TNM staging guidelines and recommendations (8).

TNM staging requires an evaluation of the extent of local invasion of the primary tumor (T), involvement of regional lymph nodes (N), and presence of distant metastasis (M) (9). In recent years, the accuracy of clinical TNM staging has been greatly improved owing to the development of various imaging modalities, such as computed tomography (CT), positron emission tomography (PET)/CT, and endoscopic ultrasound (EUS). Nevertheless, the clinical stage group compositions and survival profiles still differ from those of the pathological stage groups (10,11). Therefore, it is necessary to find an appropriate method to precisely evaluate the preoperative TNM stage in EC.

The main objective of this review was to illustrate how various imaging modalities can be applied in clinical practice for accurate TNM staging and to evaluate the role of high-resolution magnetic resonance imaging (MRI) in T classification. We present this article in accordance with the Narrative Review reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-24-34/rc).

Methods

The literature search was performed on June 9, 2023 in PubMed and Web of Science databases. The search was conducted using combination of the keywords as follows: "esophageal cancer" and "imaging" and "preoperative TNM staging". Papers published in English between inception of the databases and December 31, 2022 were reviewed. Two reviewers screened the search results independently through titles and abstracts to select the eligible ones. The search strategy summary is shown in *Table 1*.

T staging

The esophagus is an approximately 25 cm long muscular tube with an average diameter of 2 cm, extending from the pharynx to the stomach. It consists of three compartments: cervical, thoracic, and abdominal. The esophageal wall consists of the mucosa (including the epithelium, lamina propria, and muscularis mucosae), submucosa, muscularis propria, and adventitia.

In cases of tumors in the esophagus, the T classification represents the extent of primary tumor invasion, which provides details regarding tumor invasion into the different layers of the esophageal wall or even into adjacent structures. The T stage is associated with the risk of nodal and distant metastases and is considered an important prognostic factor in patients with EC (12-15).

Based on the 8th edition of the American Joint Committee on Cancer Staging Manual, the TNM classification for EC was defined as follows: T1 indicates that the tumor is confined to the lamina propria, muscularis mucosae, or submucosa; when the tumor extends to the muscularis propria without breaking through, it is defined as T2; T3 refers to the tumor extending to the adventitia; and T4 indicates that the tumor invades other organs and structures (9). In current studies, patients are stratified into

Table 1 The search strategy summary

Items	Specification
Date of search	June 9, 2023
Databases searched	PubMed and Web of Science
Search terms used	"esophageal cancer" and "imaging" and "preoperative TNM staging"
Timeframe	From inception to December 31, 2022
Inclusion criteria	Papers published in English were included
Selection process	Two reviewers screened the search results independently through titles and abstracts to select the eligible ones

TNM, tumor-node-metastasis.

two groups according to T stages: the early-stage group (T1 and T2) and advanced group (T3 and T4) (8).

EUS

EUS is reported to be the most accurate imaging method for the preoperative T staging of EC, with an accuracy rate of up to 92% depending on the tumor stage and operator experience (16-19). EUS is superior to CT in T classification because it allows for the clear recognition of different layers of the esophageal wall and for the identification of early intramural or regional lesions (7,20).

However, EUS alone is not suitable for determining the resectability of EC because the nodal status and distant metastasis also need to be evaluated (16-19,21). Besides, according to a study by Qu *et al.*, the sensitivity of EUS in T staging ranged from 53.3% to 90.0% for different T stages, with a large number of advanced EC cases being underestimated (22). Additionally, different experience levels among EUS operators can result in evident interobserver variation, and when the endoscope cannot be passed through the lumen due to stenosis, it is difficult to accurately evaluate the entire tumor.

CT

CT is one of the most commonly used imaging modalities for the preoperative evaluation of EC. It is a widely available non-invasive method with quick acquisition of images (23,24). Under normal circumstances, the esophageal wall is <3 mm on CT images, while wall-thickening of >5 mm is considered abnormal. CT also provides information regarding the outside of the esophagus, such as the status of the mediastinal lymph nodes and tumor invasion of other structures.

However, because of poor soft-tissue resolution, early-stage tumors may not be differentiated on CT images (25). Furthermore, T1 lesions are not easily detected on routine CT examination because they usually cause minimal thickening of the esophageal wall. These may explain the relatively low early T-staging accuracy of CT in previous studies (26,27).

PET/CT

PET/CT has limited value in the evaluation of early-stage tumors owing to its low spatial resolution, but it is important for evaluating distant metastasis (5,28). Additionally, esophagitis or gastroesophageal reflux disease may also cause increased fluorodeoxyglucose uptake, resulting in false-positive results (29-31). Furthermore, since distant metastases are rarely seen in early-stage EC, it is not recommended for routine clinical practice (32).

MRI

MRI is a radiation-free, non-invasive imaging method with a high degree of soft-tissue resolution that aids in recognizing the different layers of the esophageal wall and allows for the assessment of both the esophagus and the surrounding structures (20). Therefore, high-resolution MRI would be useful in differentiating tumors abutting surrounding structures (T3) from the direct invasion of the tumor into the surrounding tissues (T4) (33). Guo *et al.* prospectively analyzed 74 patients with EC, and the results showed that MRI outperformed EUS with higher specificity (93% *vs.* 59%, 93% *vs.* 66%) and accuracy (96% *vs.* 81%, 95% *vs.* 85%) (27). Furthermore, the accuracy of MRI was

higher than that of CT (96% *vs.* 82%, 95% *vs.* 80%). Xing *et al.* also found that T2-weighted imaging (T2WI) enabled a more accurate T classification than CT (34). Generally, MRI produced higher specificity and accuracy than EUS and higher accuracy than CT in T staging in both the early and late stages.

However, the quality of MRI images may be seriously affected by air-containing organs, such as the esophagus and lung, and motion due to respiration, cardiac movement, or arterial pulsation would also add to the challenges involved in obtaining a clear depiction of the structures of the esophagus (35,36).

Significant efforts have been put into overcoming these obstacles; consequently, there have been significant developments, and numerous strategies have been proposed over the last decade. Examples include image acquisition during suspended respiration, navigator-gated schemes for image acquisition, gradient moment nulling, and respiratory-ordered phase encoding (37).

Riddell *et al.* indicated that a high-resolution axial T2WI could provide detailed imaging of tumor invasion into different anatomical layers of the esophageal wall (38). However, according to their study, high-resolution T2WI may result in the overestimation of T1 tumors. Additionally, the sensitivity to motion in T2WI has limited its application in T staging (38-40). Diffusion-weighted imaging can provide information regarding cellular density and tissue structure, and may be useful for identifying the microstructural components of tumors. It reflects water proton mobility via the apparent diffusion coefficient (ADC), which is considered as a promising and novel imaging biomarker for the evaluation of EC (41). Nonetheless, there are still challenges involved in using these sequences to meet the need for high-quality images for the T staging of EC. Hence, technical innovations must be made to overcome the challenges posed by the deep location of the esophagus and the artifacts caused by movement when using MRI for esophageal imaging (38).

In comparison with standard T2WI, the BLADE technique fills the k-space with a set of short echo trains that are radially oriented around the k-space center, which processes the inherent correction of in-plane rotation and translation; therefore, it provides images with fewer motion artifacts compared to standard T2WI, with a comparable image acquisition time. Hence, BLADE may be performed supplemental to initial standard T2WI in patients with obvious motion artifacts (42). In previous studies, BLADE has been shown to greatly improve image quality in T2WI of various organs, such as the liver, kidney, brain, and pelvis (43-47). Studies have also demonstrated that BLADE produces high soft-tissue resolution to accurately delineate the anatomical layers of the esophageal wall with decreased motion artifacts and improved image quality, which could improve the accuracy of T staging of EC (42).

Stack-of-stars volume interpolated breath-hold examination (StarVIBE) is a recently modified sequence that enables free-breathing acquisition. It uses the "stack-of-stars" scheme to acquire k-space data and a conventional sampling strategy in the slice dimension, thereby decreasing motion artifacts and improving imaging quality. Furthermore, this technique enhances the delineation of different anatomical layers of the esophagus, which is important for accurate T staging of EC (48).

In addition to the improved MRI sequences mentioned above, cine MRI is a fast-imaging sequence that enables a dynamic view of esophageal tumors. This technique has proved feasible for analyzing tumor motion and providing guidance for radiotherapy (49). Furthermore, the use of an intracavitary surface coil for examining the esophagus produces an accurate depiction of the three layers of the esophageal wall, and the tumor can be clearly distinguished from surrounding tissues, with an accuracy of up to 86% in assessing the degree of tumor invasion (38). However, this examination is invasive, and there are challenges associated with wide application in routine clinical practice.

Figures 1-4 present MRI and EUS images obtained for T staging in four cases involving different T stages of EC.

N staging

Lymph node metastasis has been reported to correlate with the depth of tumor invasion (50). As the tumor depth increases, the risk of lymph node metastasis increases. Hence, lymph node dissection, which is an integral part of radical esophagectomy, is essential to reduce recurrence and metastasis rates, and it is recommended to remove the regional nodes as much as possible, in cases in which the resultant complications are acceptable (51-56). It has been demonstrated that the number of metastatic nodes is associated with the prognosis (57-59). Therefore, it is necessary to evaluate N stages in detail. *Figure 5* exhibits images obtained from an EC patient with local lymph node metastasis.

According to a previous report, CT exhibited a sensitivity of 35% in evaluating lymph node involvement, while EUS exhibited higher sensitivity than CT (60).

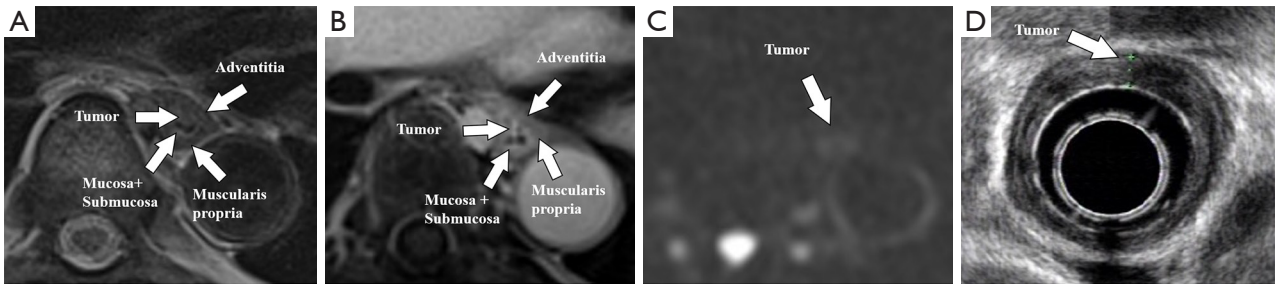

Figure 1 A 49-year-old male patient with T1 esophageal cancer: (A) T2WI BLADE, (B) enhanced T1WI StarVIBE, (C) DWI (b =800), and (D) EUS. The tumor is located in the mucosa and submucosa and protrudes into the lumen without muscularis propria invasion. T2WI, T2-weighted imaging; T1WI, T1-weighted imaging; StarVIBE, stack-of-stars volume interpolated breath-hold examination; DWI, diffusion-weighted imaging; EUS, endoscopic ultrasound.

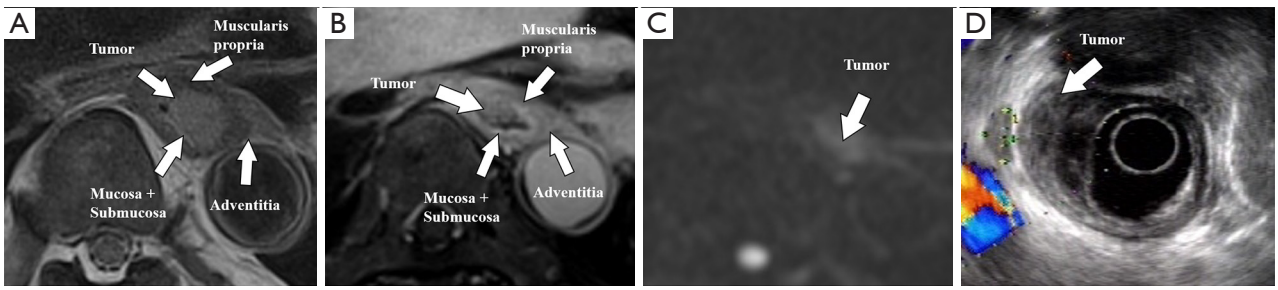

Figure 2 A 68-year-old male patient with T2 esophageal cancer: (A) T2WI BLADE, (B) enhanced T1WI StarVIBE, (C) DWI (b =800), and (D) EUS. The tumor breaks through the submucosa and is limited to the muscularis propria. T2WI, T2-weighted imaging; T1WI, T1-weighted imaging; StarVIBE, stack-of-stars volume interpolated breath-hold examination; DWI, diffusion-weighted imaging; EUS, endoscopic ultrasound.

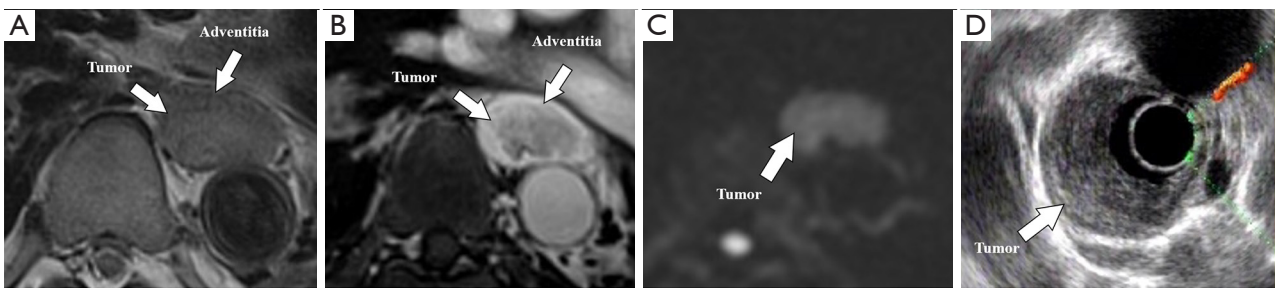

Figure 3 A 70-year-old male patient with T3 esophageal cancer: (A) T2WI BLADE, (B) enhanced T1WI StarVIBE, (C) DWI (b =800), and (D) EUS. The tumor is confined to the adventitia. T2WI, T2-weighted imaging; T1WI, T1-weighted imaging; StarVIBE, stack-of-stars volume interpolated breath-hold examination; DWI, diffusion-weighted imaging; EUS, endoscopic ultrasound.

M staging

PET/CT has been reported to exhibit high sensitivity and specificity for the detection of distant lymph node and organ metastases (28,51,61,62). In patients with advanced EC, PET/CT is usually used to detect suspected metastases and evaluate treatment response (61,63,64). *Figure 6* shows MRI and PET/CT images of an EC patient with liver metastases.

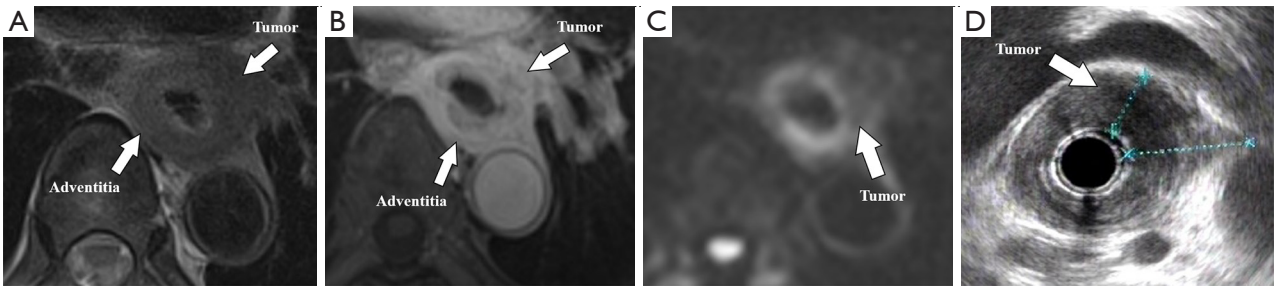

Figure 4 A 61-year-old male patient with T4 esophageal cancer: (A) T2WI BLADE, (B) enhanced T1WI StarVIBE, (C) DWI (b =800), and (D) EUS. The tumor invades the pleura. T2WI, T2-weighted imaging; T1WI, T1-weighted imaging; StarVIBE, stack-of-stars volume interpolated breath-hold examination; DWI, diffusion-weighted imaging; EUS, endoscopic ultrasound.

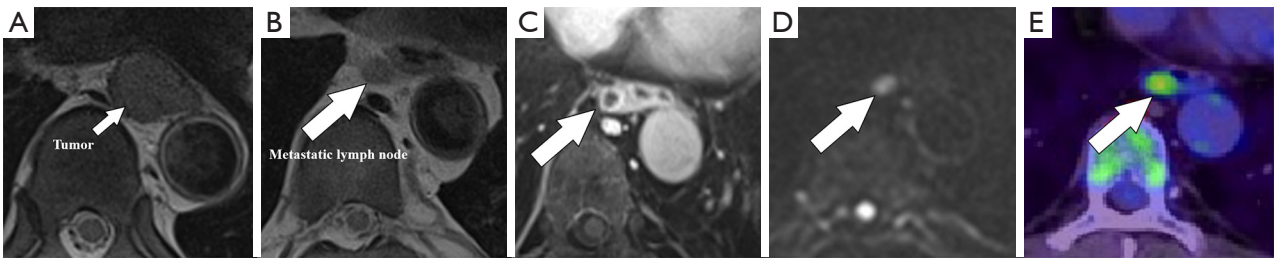

Figure 5 A 55-year-old male esophageal cancer patient with local lymph node metastasis: (A,B) T2WI BLADE, (C) enhanced T1WI StarVIBE, (D) DWI (b =800), and (E) PET/CT. Metastatic lymph node with ring enhancement (white arrow in C), restricted diffusion in DWI (b =800) (white arrow in D) and high ^{18}F-FDG uptake (white arrow in E). T2WI, T2-weighted imaging; T1WI, T1-weighted imaging; StarVIBE, stack-of-stars volume interpolated breath-hold examination; DWI, diffusion-weighted imaging; PET/CT, positron emission tomography/computed tomography; ^{18}F-FDG, ^{18}F-fluorodeoxyglucose.

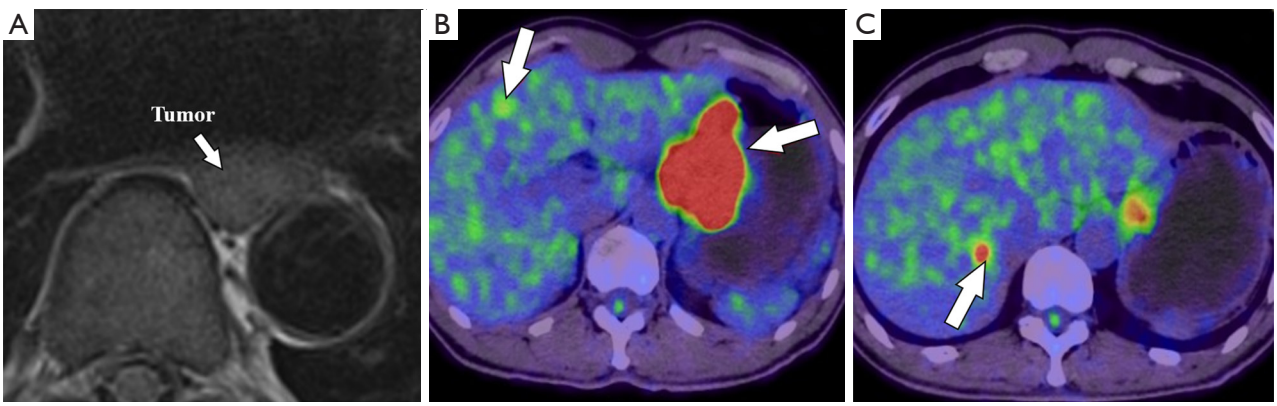

Figure 6 A 62-year-old male esophageal cancer patient with liver metastases: (A) T2WI BLADE and (B,C) PET/CT. The liver metastases exhibit high metabolism (white arrows in B and C). T2WI, T2-weighted imaging; PET/CT, positron emission tomography/computed tomography.

Discussion

The treatment of EC depends on TNM staging, which assesses the extent of tumor invasion into different layers of the esophageal wall, status of lymph nodes, and presence of distant metastasis. Accurate preoperative staging of EC allows for appropriate treatment plan and improves patient outcomes. High-resolution MRI is a valuable imaging modality for preoperative TNM staging of EC. It provides

excellent soft-tissue resolution, allowing for accurate visualization of the esophageal wall layers and adjacent structures. Multiplanar MRI can reveal the extent of tumor invasion, lymph node involvement, and potential invasion into adjacent structures, such as the trachea, aorta, or other organs, which facilitates individualized decision-making. Additionally, MRI can be used to monitor tumor response to neoadjuvant therapy, which is often administered to patients with locally advanced EC to shrink the tumor and improve resectability, and predict the likelihood of successful resection.

Optimized MRI techniques make it possible to obtain better EC images for T staging. However, there are some limitations. The relatively long acquisition time in StarVIBE makes it difficult to scan the entire esophagus, resulting in the inability to evaluate lymph nodes along with the esophagus using this sequence. Post-neoadjuvant TNM staging is used for patients with EC receiving neoadjuvant therapy (65,66). Although preoperative assessment of residual tumor on MRI after neoadjuvant therapy for EC is feasible, the high sensitivity and low specificity may result in overstaging of complete responders and, consequently, overtreatment (67). With improved techniques, there have been promising quantitative imaging biomarkers obtained from MRI, such as ADC and T2 star relaxation time, which play important roles in the evaluation of pre-treatment stage, treatment response and prognosis of EC (41,68-70). Moreover, the integration of MRI biomarkers with clinical, genomic and pathological data, combined with the application of artificial intelligence, may further improve the management of EC (41).

Conclusions

An optimal and repeatable imaging method is required for the diagnosis, treatment decision, follow-up evaluation, and prognosis prediction in EC. Based on an understanding of various imaging modalities, EUS, CT, PET/CT and MRI should be applied as complementary imaging methods for preoperative TNM staging of EC. Moreover, high-resolution MRI can overcome motion-related artifacts and provide high-quality images, which may play a more important role in the management of EC in the future.

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Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-24-34/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-34/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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