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Original Article

Use of Magnetic Resonance Imaging for N-Staging in Patients with Non-Small Cell Lung Cancer. A Systematic Review

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ABSTRACT

Introduction: The aim of this study is to assess the diagnostic value of the magnetic resonance imaging (MRI) in differentiating metastasic from non-metastatic lymph nodes in NSCLC patients compared with computed tomography (CT) and fluorodeoxyglucose (FDG) - positron emission tomography (PET) or both combined.

Methods: Twenty-three studies (19 studies and 4 meta-analysis) with sample size ranging between 22 and 250 patients were included in this analysis. MRI, regardless of the sequence obtained, where used for the evaluation of N-staging of NSCLC. Histopathology results and clinical or imaging follow-up were used as the reference standard. Studies were excluded if the sample size was less than 20 cases, if less than 10 lymph nodes assessment were presented or studies where standard reference was not used. Papers not reporting sufficient data were also excluded.

Results: As compared to CT and PET, MRI demonstrated a higher sensitivity, specificity and diagnostic accuracy in the diagnosis of metastatic or non-metastatic lymph nodes in N-staging in NSCLC patients. No study considered MRI inferior than conventional techniques (CT, PET or PET/CT). Other outstanding results of this review are fewer false positives with MRI in comparison with PET, their superiority over PET/CT to detect non-resectable lung cancer, to diagnosing infiltration of adjacent structures or brain metastasis and detecting small nodules.

Conclusion: MRI has shown at least similar or better results in diagnostic accuracy to differentiate metastatic from non-metastatic mediastinal lymph nodes. This suggests that MRI could play a significant role in mediastinal NSCLC staging.

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Uso de las imágenes por resonancia magnética para la estadificación ganglionar (N) del cáncer de pulmón de no microcítico. Revisión sistemática

RESUMEN

Introducción: El objetivo de este trabajo es evaluar el potencial diagnóstico de las imágenes por resonancia magnética (RM) para identificar nódulos linfáticos metastásicos frente aquellos no metastásicos en pacientes con cáncer de pulmón no microcítico (CPNM) en comparación con la tomografía computarizada (TC), la tomografía por emisión de positrones con ^{18}F-fluorodesoxiglucosa (PET-FDG) o ambas técnicas combinadas.

Abbreviations: ADC, apparent diffusion coefficient; CT, computed tomography; DW, diffusion weighted; EPI, echo planar imaging; FASE, fast advantage spin-echo; FDG, fluorodeoxyglucose; FN, false negative; FP, false positive; IASLC, International Association for the Study of Lung Cancer; LDCT, low-dose CT; LSR, lymph node saline ratio; MRI, magnetic resonance imaging; NPV, negative predictive value; NSCLC, non-small cell lung cancer; PET, positron emission tomography; SE, spin-echo; SI, signal intensity; STIR, short time inversion recovery; TN, true negative; TP, true positive.

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Métodos: En el análisis se incluyeron 23 estudios (19 estudios y 4 metaanálisis) con tamaños de muestra entre 22 y 250 pacientes. Para la estadificación ganglionar (N) del CPNM se utilizaron imágenes de RM independientemente de la secuencia obtenida. Como estándar de referencia se usaron los resultados histopatológicos y el seguimiento clínico o por imagen. Se excluyeron aquellos estudios con tamaños muestrales menores de 20 casos, aquellos con menos de 10 nódulos linfáticos evaluados o estudios en los que no se usó un estándar de referencia. También se excluyeron los artículos que no presentaron suficientes datos.

Resultados: Se observó que la RM presentaba mayor sensibilidad, especificidad y precisión en la estadificación ganglionar (N) y el diagnóstico de nódulos linfáticos metastásicos o no metastásicos en pacientes con CPNM en comparación con la TC y el PET. Ningún estudio consideró a la RM inferior con respecto a otras técnicas convencionales (TC, PET y PET/TC). Otros resultados destacables de esta revisión son que con la RM se originaron menos falsos positivos en comparación con el PET, y su superioridad respecto al PET/TC en la detección de tumores de pulmón no operables, en el diagnóstico de infiltración en estructuras adyacentes o metástasis cerebrales, así como en la detección de nódulos de pequeño tamaño.

Conclusión: La RM dio lugar a mejores resultados o, al menos comparables, relacionados con la precisión diagnóstica para diferenciar nódulos linfáticos metastásicos de no metastásicos. Esto sugiere que la RM podría jugar un papel importante en la estadificación mediastinal en pacientes con CPNM.

Introduction

Lung cancer is a major health problem worldwide and the most common cause of cancer death in developed countries.[1] In 2017 lung cancer is expected to be the second most frequent tumor in males and women and it will continue being the most frequent cause of cancer death.[2] Tobacco use is the largest preventable cause of cancer.[3] Up to 10-15% of all lung cancers occur in never smokers [4] and radon is the second risk factor of lung cancer in never-smokers.[5]

The TNM classification is the cancer staging system used to describe the anatomical scope of a tumor according to three components. Recently, the International Association for the Study of Lung Cancer (IASLC) has published the 8th edition.[6] Nodal (N) status is important for prognosis and an adequate staging is essential for a subsequent optimal therapeutic approach.

Noninvasive techniques for mediastinal lymph node staging include computed tomography (CT), combined or not with fluorodeoxyglucose (FDG) - positron emission tomography (PET), PET/CT. Since 1980s, the possible role of magnetic resonance imaging (MRI) has been investigated.[7] Traditionally, CT has been the main technique for N staging, but it is limited by a low sensitivity (55-65%) and specificity (65-75%) because it only uses size criteria (an axial short-axis diameter of 1 cm or greater) or abnormal shape or attenuation of the lymph node to suspect metastasic involvement.[8]

PET has been validated as a technique which is superior to CT when differentiating metastatic or non-metastatic lymph nodes as it provides metabolic information based on the glucose consumption from tumor cells. Its sensitivity and specificity are higher than CT but are still greater when both techniques are combined (PET/CT).[9] However, PET has associated diagnostic limitations by confounding malignancy from inflammatory changes resulting in false positives and is limited by spatial resolution,[9] as well as difficulties in detecting certain tumors whose lesions may be PET-negative (adenocarcinoma, carcinoid...), resulting in false negatives.[10]

Recent studies have reported that magnetic resonance imaging (MRI) could be useful for N-staging in non-small cell lung cancer (NSCLC) compared to conventional techniques (CT, PET, PET/CT)[11] by differentiating metastasic from non-metastasic nodes. Those studies have also shown that certain whole-body MRI sequences as short time inversion recovery (STIR) turbo spin-echo (SE) or diffusion weighted (DW) MRI are superior than conventional sequences (T1-weighted MR, T2-weighted MR) or echo planar imaging sequence (EPI-DWI).[12] Once MRI images are obtained, a detailed study of them can be made from the qualitative or quantitative point of view. To determine the qualitative analysis, two radiologists are required to interpret the MR images and evaluate the probability that a lymph node contains metastasis using a five-point visual scoring system. Qualitative analysis depends on the consensus of the radiologists who have analyzed the Images.[12,13] Using the quantitative analysis all signal intensity (SI) of lymph nodes are normalized by comparing them with the signal intensity of the 0,9% saline panthom to produce the lymph node saline ratio (LSR).[13] The rationale for detecting a positive nodule is that malignant tumors have more cellularity and less extracellular space than normal tissue, resulting in higher SI values. DW MRI bases the analysis of the images trough water molecules movement in biological tissues (Brownian movement), taking into account that in malignant tumors and those regions affected by metastasis will have restricted water molecules movement than normal, resulting in a decreased apparent diffusion coefficient (ADC).[14]

The purpose of the present study is to perform a systematic review to assess the overall diagnostic value of MRI to discriminate between metastatic and non-metastatic lymph nodes in primary NSCLC patients in comparison with PET/CT.

Material and methods

Literature research

A literature research was performed in PubMed (Medline), EMBASE and Cochrane databases. To retrieve information the following search strategy was employed in PubMed using a combination of MeSH terms ("Magnetic Resonance Imaging" [Mesh] AND "Lung Neoplasms" [Mesh]); AND "Mediastinal staging" [Mesh] AND "Clinical staging" [Mesh] AND "Non-invasive" [Mesh] AND "NSCLC" [Mesh]. The following limits were used: language (English or Spanish), humans and publications dating from 01/01/2007 to 15/08/2017. The reference lists of identified articles were also manually searched to obtain additional papers. The reports found to be eligible on the basis of their title and, subsequently, from the abstract, were then selected to further determine suitability for inclusion in the present study.

Inclusion and exclusion criteria

Eligible studies were reviewed and included in this systematic review according to the following inclusion criteria: MRI was used for the evaluation of N staging of lung cancer. Sufficient

information regarding true-positive (TP), false-positive (FP), true-negative (TN) and false-negative (FN) values could be identified or calculated from data in the original articles. Studies were excluded if the sample size was less than 20 cases, if less than 10 lymph nodes assessment were presented or studies where standard reference was not used. The only accepted standard reference was histology, excluding those articles that were used as standard reference clinical or imaging follow-up. Histopathology results were determined by percutaneous fine needle aspiration (PCNA), endobronchial ultrasound-guided transbronchial needle aspiration (EBUS), mediastinoscopy or after surgical lymph nodes resection through thoracotomy.

Data extraction and Quality Assessment

Search results were checked by one reviewer and if there were doubts regarding the inclusion or exclusion of a certain paper, this was solved by consensus by all authors. We developed a quality scale to score the quality of the included studies. Similar scales have been used previously by other groups when performing other systematic reviews.[15,16] We considered 6 items to assess the quality of included studies which are shown in Table 1. Each item opted a score between 0 and 1 to 3 points (the higher the score the higher the quality).

Results

The searh resulted in 1,234 studies. Of these 123, were selected for full text reading, and 23 (19 prospective studies and 4 meta-analysis) were finally included. The most frequent exclusion criterion was the study of lung lesions (solitary pulmonary nodule and masses) that did not include lymph nodes. The flowchart of the search is shown in Figure 1. Sample size is ranged between 22 and 250 patients. After careful reading of the studies, we could observe that over the last 10 years different MRI sequences for the study of lymph nodes have been used. We have focused the results in those sequences which have provided the most relevant results (STIR turbo SE and DWI MRI). Only 5 studies used other MRI sequences.[16–20]

Table 1
Quality score to assess the included studies.

Item assessed	Characteristic	Weight
Total sample size	20-50	0
	51-100	1
	≥101	2
Radiologists	1	0
	2	1
	3	2
Type of MR	1,5T	0
	3T	1
Image analysis	Qualitative	0
	Quantitative	1
	Both	2
Use of the standard reference	Not used	0
	Partially nodes confirmed	1
	All nodes confirmed	2
Simultaneity of image tests *	No	0
	Yes	1
TOTAL		10

* Defined as <30 d other than the waiting time for the pathology results after surgery.

Prospective and retrospective studies' results

The largest prospective study published on N-stage assessment in patients with NSCLC was published by OHNO et al.[21] in 2011 including 250 patients with mediastinal and hilar lymph nodes studied by STIR FASE imaging, DW MR imaging and FDG PET/CT. In both quantitative and qualitative N-stage assessment, STIR turbo SE showed more sensibility and accuracy (82.8% and 86.8%, respectively, in quantitative assessment; 77.4% and 84.4%, respectively, in qualitative assessment) compared to DW MR imaging or FDG PET/CT. The same group carried out the study with the highest quality,[22] which included 140 consecutive patients. The capabilities for TNM classification and the assessment of clinical stage and tumor resectability among whole-body MRI were compared, coregistering PET/MR imaging with or without SI assessment, and FDG PET/CT. It was shown that the capability to assess tumor resectability and accuracy of whole-body MRI and PET/MRI with SI assessment (97.1%) was significantly higher than that of PET/MRI without SI assessment and FDG PET/CT (85%; p< 0.001). In other
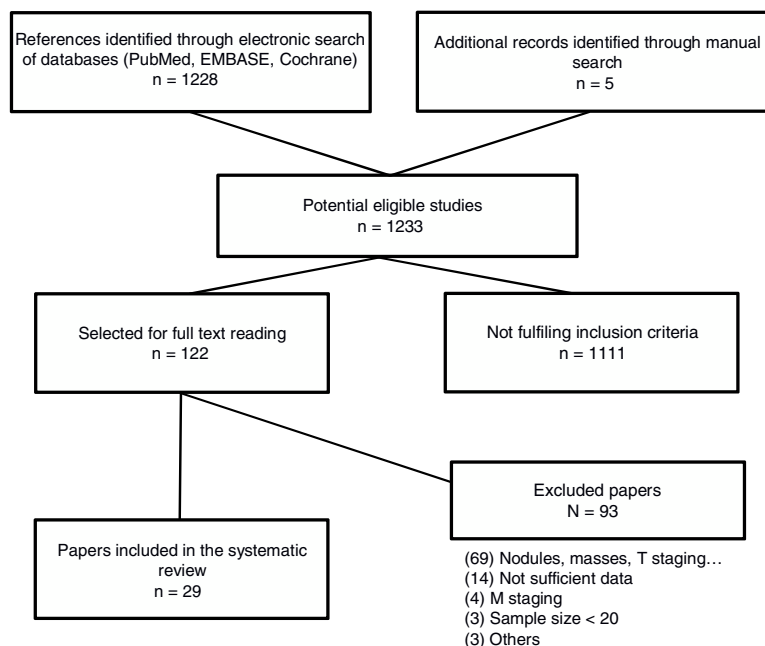

Figure 1. Flowchart of study selection process.

studies by OHNO et al.[12,23] it has been observed that sensitivity and diagnostic accuracy was higher with MRI (STIR turbo SE and fast advantage spin-echo sequence (FASE-DWI)[12]) compared with FDG PET/CT both for quantitative[23] and qualitative[12] analysis.

Other published studies[24–30] comparing MRI sequences (fundamentally DWI-MRI and STIR turbo SE sequences) and FDG PET/CT, showed similar results. Both sensitivity and diagnostic accuracy[25] were higher with MRI sequences than with PET/CT, in addition a high negative predictive value (NPV) of DW-MRI (97%).[27] These studies postulated MRI as a technique that could correctly differentiate metastasic from non-metastasic nodes and showed fewer false-positives than PET in the mediastinum (p = 0.011) and in normal or enlarged lymph nodes. No statistically significant differences were observed between DWI-MRI and STIR turbo SE.[25]

There were three studies[26,28,31] comparing MRI with FDG PET/CT for preoperative -nodal staging in NSCLC (with 93, 52 and 49 patients, respectively). Diagnostic accuracy of MRI was not significantly higher than that of FDG PET/CT, although they concluded that it had fewer false positives, and probably the best option would be to combine both methods for an adequate preoperative staging, even avoiding the use of invasive diagnostic techniques.

One study[32] with 33 patients compared prospectively the diagnostic efficacy of MRI with FDG PET/CT. Results showed that MRI was a feasible technique for the assessment of NSCLC, comparable but not superior to FDG PET/CT in N-staging.

Characteristics of included studies are summarized in Table 2 and Table 3.

Meta-analysis and systematic review results

Four meta-analysis with 12, 10, 18 and 19 studies included, respectively, had been published[11,33–35] comparing the diagnostic value of MRI in N staging of NSCLC which agreed on its high specificity and diagnostic accuracy in detecting metastasic lymph nodes in patients with lung cancer. These studies had restrictive inclusion criteria and were focused in a specific type of MRI. No study reported serious complications.

Study quality

The scoring of the included studies ranged between 0 and 10 points. The highest quality was for three studies with more than 100 patients. The mean scoring of the included studies was 5.6 points. Table 2 presents in detail the quality of each study.

Discussion

The results of this systematic review point out that MRI, especially in some sequences such as STIR turbo SE and DW-MRI, has a high diagnostic accuracy to diagnose metastasic or non-metastasic lymph nodes in N-staging in non-small cell lung cancer patients. These studies specially highlighted its high sensitivity, specifity and diagnostic accuracy. In comparison with conventional techniques such as combined FDG PET/CT or both techniques separately, some studies considered MRI sequences superior for N-staging, and some other studies considered MRI sequences comparable but not superior to conventional techniques. No study considered MRI inferior than conventional techniques. Even in those studies where MRI was comparable but not superior to FDG PET/CT, MRI had fewer false positives.

Knowing that MRI has a useful role in the preoperative mediastinal and hiliar nodal staging, the next step is where this imaging test may fit in clinical practice. Some authors speculate that MRI sequences are superior to FDG PET/CT and can be used in place of it as an alternative in the clinical practice.[17,27] Other study [32,34,24]

support that MRI and FDG PET/CT, would provide complementary information, so using them together without eliminating or replacing any test as part of the usual protocol would improve significantly diagnostic capability for N-staging[28] and making it less necessary to use invasive diagnostic techniques.[31] Finally, the remaining studies, regardless of whether they conclude that MRI is superior or similar than FDG PET/CT, do not make recommendations on the ideal time to perform the MRI in the preoperative staging, whether it should replace some conventional test, or if otherwise, it would be better to combine them.

Some advantages of MRI should be highlighted: 1) there is no radiation exposure; 2) patients do not have to fast before examination; 3) less test time (30 minutes for DWI or STIR vs. 90 minutes for PET/CT); 4) less test cost;[24] 5) administration of contrast medium is not necessary;[27] 6) easier accessibility to MRI because not all hospitals have PET/CT.[14] MRI is a simple technique available in most hospitals that allows performing between 5-20 sequences, each of which provides a type of information about tissues (anatomical or functional). In some of them, as in case of STIR sequence that is performed with cardiac synchronization, the use of some software that usually comes integrated in the resonance device itself may be required. It should also be noted that there are also disadvantages: presence of motion artifacts (breathing, cardiac movement, pulsations...) or other artifacts as metallic bodies, tatoos, prostheses, surgical clips, etc. They might negatively affect the quality of lung image. Claustrophobia is the main inconvenient of this technique.[36]

Methodological shortcomings of the available literature

Different methodological problems continue to hinder MRI use in clinical practice. Radiologists and nuclear medicine physicians have more experience and availability with FDG PET/CT images than MRI[37] probably because their use has not been sufficiently encouraged or protocols have not been developed. It would be convenient to investigate which sequence of MRIs are more useful for mediastinal staging with multicenter comparative studies and establish an optimal acquisition protocol that has not been defined currently. It is also necessary to develop a standard acquisition protocol as a routine clinical application.[33] The methods that have been used until now to differentiate metastatic from non-metastatic lesions have been the quantitative (ADC value) and qualitative (visual score) methods. Although no significant differences have been demonstrated between them, the sensitivity and accuracy of quantitative methods has been found to be slightly higher compared to the qualitative method (93% and 87% vs. 88% and 86%, respectively).[13] Tumor lesions are known to have a decreased ADC value; however, cut off values have not been established to clearly differentiate between metastatic and non-metastatic lymph nodes to date.[13] It is important to keep in mind that specifically lesions (necrotic lesions, mucinous carcinoma or small nodules) could not be diagnosed by MRI. For example, ADC value for necrotic lesions could be lower than lesions without necrosis. Mucinous carcinoma, with its hypointense nature, could incurr in false negative because it behaves with high ADC values.[38] Nodules smaller than 3 mm cannot be detected by MRI[38] and between 4-6 mm[23,25,29] could go unnoticed even if they have micrometastatic foci.

Other published reviews

The published meta-analyses did not offer a global view of MRI and this was the reason for performing the present review. SHEN et al.[34] included in their meta-analysis 18 studies but they only studied DW-MRI sequence. CHEN et al.[33] only studied DW-MRI sequence too. The conventional method of usual clinical practice with which MRI was compared was PET or CT separately and, in few studies with PET/CT (both combined). WU et al.[35] included 19

Table 2
Characteristics of included studies (19 prospective studies; does not include meta-analysis).

AUTHOR/YEAR	COUNTRY	DESIGN	N	NODES	AGE	SEX (M/W)	NODES LOCATION	TUMOR	MR	SEQUENCES	STANDARD REFERENCE	CONCLUSION	STUDYŚ QUALITY
Nomori, 2016 [30]	Japan	P	157	1033	70	95/62	Hilar and mediastinal	124 ADC, 24 SQC, 3 ADSC, 4 LCC, 2 OTH	1.5T	T1-weighted T2-weighted DWI-MR	Histology *TCT	Superior to PET; correct identification of false positives	6 points
Huellner, 2016 [16]	Switzerland	P	42	ND	65	29/13	Hilar and mediastinal	ND	3T	T1-weighted T1-inversion T2-weighted	Histology *TCT	Comparable to PET/CT (not superior)	6 points
Ohno, 2015 [12]	Japan	P	95	78	72	56/39	Hilar and mediastinal	71 ADC, 10 ADCis, 8 SQC, 4 ADSC, 2 LCC	3T	STIR-FASE FASE-DWI EPI-DWI	Histology *TCT	STIR-FASE and FASE-DWI superior to PET/CT and EPI-DWI (sensibility and accurate)	7 points
Ohno, 2015 [22]	Japan	P	140	ND	72	75/65	Hilar and mediastinal	103 ADC, 20 ADCis, 13 SQC, 1 LCC	3T	T1 field echo T1-weighted STIR-FASE	Histology *TCT	Superior to PET/CT	8 points
Schaarschmidt, 2014[17]	USA	P	38	146	60.1	24/14	ND	16 ADC, 6 SQC, 16 OT	3T	T1 FLASH TIRM T2 BLADE TSE T2 HASTE T2 TrueFISP	Histology *EBUS *TCT	Superior to PET/CT	5 points
Heusch, 2014 [18]	Germany	P	22		65	12/10	Hilar and mediastinal	ND	3T	VIBE sequence T1-weighted T2-weighted T1 FLASH	Histology *EBUS *TCT	Comparable to PET/CT (not superior)	7 points
Xu, 2013 [29]	China	P	42	119	55	27/15	Mediastinal	ND	1.5T	DWI-MR	Histology *TCT	Clinically useful to detect malignancy	4 points
Usuda, 2013 [38]	Japan	P	158	ND	68	94/64	Hilar and mediastinal	114 ADC, 36 SQC, 10 OT	1.5T	T1-weighted T2-weighted DWI-MR	Histology *TCT	DWI-MR superior to PET/CT	4 points
Sommer, 2012 [32]	Switzerland	P	33	ND	63.9	24/9	Hilar and mediastinal	16 ADC, 8 SQC, 2 LCC, 1 ADSC, 1 NET, 6 OT	1.5T	T1-weighted T2-weighted DWIBS	Histology (no data) or citology	DWIBS comparable to PET/CT (not superior)	4points
Kim, 2012 [31]	Korea	P	49	ND	62	29/20	Hilar and mediastinal	32 ADC, 14 SQC, 2 LCC, 1 PDN	1.5T	T2-weighted DWI-MR	Histology *PCNA *EBUS *MDT *TCT	Combined MRI and PET/TC improve the sensitivity	5 points
Ohno, 2011 [21]	Japan	P	250	1122	72	136/114	Hilar and mediastinal	218 ADC, 23 SQC, 6 LCC, 3 ADSC	1.5T	STIR-FASE DWI-MR	Histology *MDT *TCT	STIR-FASE superior to PET/CT and DWI-MR (sensibility and accurate)	6 points
Nakayama, 2010 [25]	Japan	P	70	441	68	38/32	Hilar and mediastinal	52 ADC, 18 SQC	1.5T	T1-weighted T2-weighted DWI-MR STIR-MR	Histology *TCT	DWI-MR useful differentiating malignancy	4 points

Table 2 (*Continued*)

AUTHOR/YEAR	COUNTRY	DESIGN	N	NODES	AGE	SEX (M/W)	NODES LOCATION	TUMOR	MR	SEQUENCES	STANDARD REFERENCE	CONCLUSION	STUDYŚ QUALITY
Moriwaka, 2008[28]	Japan	P	93	137	66.1	76/17	Hilar and mediastinal	39 ADC, 28 SQC, 12 OTH, 14 BNG	1.5T	STIR-FASE	Histology *EBUS *MDT *TCT	STIR-FASE not superior to PET/CT. Better combine them.	5 points
Hasewaga, 2008[27]	USA	P	42	ND	66	30/12	Mediastinal nodes	ND	1.5T	DWI-MR	Histology *TCT	Useful (high negative predictive value)	2 points
Yi, 2008 [19]	Korea	P	135	712	61	125/40	Hilar and mediastinal	86 ADC, 59 SQC, 9 PDN, 3 PLC, 3 ADSC, 3 SRC, 2 LCC	3T	T1-weighted T2-weighted	Histology *PCNA *TCT	Comparable to PET/CT (not superior)	8 points
Plathow, 2008 [26]	Germany	P	52	ND	62	36/16	ND	ND	1.5T	WB-MRI	Histology *MDT *TCT	Combined WB-MRI and PET/TC has positive effects for TNM staging	6 points
Nomori, 2008 [24]	Japan	P	88	734	70	47/41	Mediastinal nodes	67 ADC, 18 SQC, 3 ADSC	1.5T	DWI-MR	Histology *TCT	Superior to PET/CT (less false positives)	4 points
Ohno, 2007 [23]	Japan	P	115	ND	68	59/56	Hilar and mediastinal	96 ADC, 13 SQC, 6 LCC	1.5T	STIR-Turbo SE	Histology *MDT *TCT	STIR-Turbo SE superior to PET/CT (sensibility and accurate)	7 points
Kim, 2007 [20]	Korea	P	113	570	61	91/22	Hilar and mediastinal	58 ADC, 41 SQC, 3 LCC, 3 ADSC, 3 PLC, 2 SRC, 2 PDN, 1 CND	3T	T1-weighted T2-weighted	Histology *MDT *TCT	Useful detecting malignancy	9 points

ADC: adenocarcinoma. ADCis: adenocarcinoma in situ. ADSC: adenosquamous. BLADE: proprietary name for periodically rotated overlapping parallel lines with enhanced reconstruction [PROPELLER] in MR systems. BNG: benign. CND: carcinoid. DWI-MR: diffusion weighted imaging magnetic resonance. DWIBS: single shot echo planar imaging. EBUS: endobronchial ultrasound-guided transbronchial needle aspiration. FLASH: fast low angle shot gradient echo sequence. HASTE: half fourier acquired single short turbo spin echo sequence. LCC: large cell carcinoma. M: male. MDT: mediastinoscopy. MEC: mucoepidermoid carcinoma. MR: magnetic resonance. MX: mixed small cell carcinoma and adenocarcinoma. NET: neuroendocrine tumor. NSCLC: non-small cell lung cancer. OTH: others. P: prospective. PCNA: percutaneous fine needle aspiration. PDN: poorly differentiated non-small cell lung cancer. PLC: pleomorphic carcinoma. R: retrospective. SCC: small cell carcinoma. SQC: squamous cell carcinoma. SRC: sarcomatoid carcinoma. TCT: thoracotomy.

Table 3
Comparison of diagnostic performance for lymph node metastasis by all methods.

STUDY	MRI					PET/CT or CT[*]				
	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Nomori, 2016 [30]	79	92	75	75.2	57.5	58	90	67	ND	ND
Huellner, 2016 [16]	ND	ND	77	ND	ND	ND	ND	86	ND	ND
Ohno, 2015 [12]	82.1	98.7	90.4	98.5	84.6	57.7	97.4	77.6	95.7	69.8
Ohno, 2015 [22]	100	92.9	98.6	98.2	100	93.8	85.7	92.1	96.3	77.4
Schaarschmidt, 2015 [17]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Heusch, 2014 [18]	88	93	91	88	93	75	86	82	75	86
Xu, 2013 [29]	85.2	100	87.8	100	60	ND	ND	ND	ND	ND
Usuda, 2013 [38]	63.9	98.4	90.6	75.9	93.1	36.1	96.8	83.1	68.4	85.1
Sommer, 2012 [32]	44	93	85	61	89	47	96	88	71	90
Kim, 2012[#] [31]	69	93	89	71	93	46	96	87	75	88
Ohno, 2011 [21]	82.8	89.2	86.8	81.9	89.7	72.4	94.2	85.6	85.2	85.8
STIR (top)										
DWI (lower)										
	74.2	904	84.4	82.1	85.5					
Nakayama, 2010 [25]	50	98.1	87.1	88.9	86.9	ND	ND	ND	ND	ND
STIR (top)										
DWI (lower)										
	56.3	100	90	100	88.5					
Moriwaka, 2008 [28]	96.3	67.3	84.7	81.4	92.5	90.2	60.5	80.3	79.6	81.8
Hasewaga, 2008 [27]	80	97	95	80	97	92	100	ND	ND	ND
Yi, 2008 [19]	52	94	86	75	88	48	96	86	75	88
Plathow, 2008 [26]	88.5	96.1	ND	ND	ND	92.3	100	ND	ND	ND
Nomori, 2008[#] [24]	67	99	ND	95.6	97.1	67	97	ND	92.3	0
Ohno, 2007 [23]	89	99	98.2	89	99	83.2	96.2	95.1	65.9	98.3
Kim, 2007 [20]	53	91	86	ND	ND	ND	ND	ND	ND	ND

[*] depending on the study; [#]Kiḿs study: MRI results are combined with PET/CT, not MRI alone.
PPV: positive predictive value; NPV: negative predictive value.

studies where they compared DW-MRI with FDG PET/CT but only in 3 of the 19 studies patients underwent DW-MRI, in the remaining 16, they only underwent FDG PET/CT. Finally, PEERLINGS et al.[11] included only 12 studies with very strict selection criteria. For this reason, we considered to carry out this systematic review to offer a larger number of studies, with a broader view and considering all MRI sequences for the mediastinal lymph nodes study.

Recently, the first screening of lung cancer using low-dose CT (LDCT) compared to MRI has been published, and suitable results have been obtained in favor of MRI with an excellent sensitivity and specificity for the detection of nodules compared to LDCT. These results seem to reaffirm the promising use of resonance in the study of this type of neoplasms.[39]

Conclusion

With the studies available, it can be concluded than MRI, and specially DWI sequence, seems to play a relevant role in the N-staging of patients with NSCLC, compared to conventional methods (CT, PET, separately and both combined). MRI has shown at least similar or better results in diagnostic accuracy to differentiate metastatic from non-metastatic lymph nodes. Conversely, it cannot be established with the current evidence which would be the best time to do it, if it could replace any of the usual imaging tests or if it could be combined with them.

It would be convenient to validate a resonance protocol, as well as the standardization of ADC values to differentiate between malignant and benign lesions. In the near future, additional prospective and multicenter studies are warranted to confirm the clinical role of MRI in the staging of lung cancer.

Authors contribution

Tara Pereiro. Conception of the work. Data collection. Data analysis and interpretation. Drafting the article. Critical revision of the article. Final approval of the version to be published.

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José Martín Carreira. Critical revision of the article. Final approval of the version to be published.

Antonio Golpe. Critical revision of the article. Final approval of the version to be published.

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Luis Valdés. Conception of the work. Drafting the article. Critical revision of the article. Final approval of the version to be published.

Conflicto de intereses

Los autores declaran no tener ningún conflicto de intereses.

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