MR study of N2 disease in lung cancer: contrast-enhanced method using gadolinium–DTPA

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Received 14 November 1995; revised 9 May 1996; accepted 1 July 1996

Abstract

Objective: In several previous studies, including one of our own, CT and MRI provided similar information on N2 detection in the staging of lung cancer. Both imaging techniques can be considered effective in detecting enlarged mediastinal lymph nodes but the results are often inaccurate when confronted with pathological findings. The purpose of this study was to assess the diagnostic accuracy of gadolinium–DTPA enhanced MRI in the detection of mediastinal lymph nodes in lung cancer.

Methods: A prospective study to compare standard unenhanced MRI and Gd–DTPA enhanced MRI was carried out in patients with diagnosed lung cancer. The study focused on the status of mediastinal lymph nodes. Gd–DTPA was administered at a dosage of 0.2 mmol/kg before T1 weighted sequences. Qualitative visual analyses of both standard and contrast enhanced MRI images were performed on each patient by 2 independent radiologists. The imaging results were then compared to pathological findings obtained after surgical operation.

Results: In the identification of mediastinal lymph node metastases standard MRI was 62% sensitive, 100% specific and 74% accurate whereas Gd–DTPA enhanced MRI was 100% sensitive, 91% specific and 97% accurate.

Conclusions: Gd–DTPA enhanced MRI was more accurate than standard MRI in the detection of metastatic lymph nodes in patients with lung cancer. These initial results can be considered encouraging especially with regards to the reduction of false negative findings although further confirmation is, understandably, required. © 1997 Elsevier Science B.V.

Keywords: Lung cancer; MRI imaging

1. Introduction

The extended utilization of more accurate and technologically advanced diagnostic methods in recent years has significantly reduced incorrect evaluations in the preoperative staging of lung cancer, reducing as a consequence the incidence of explorative thoracotomies. Nevertheless in the assessment of cTNM, the main problem is still represented by evaluation of mediastinal lymph nodes, whose metastatic involvement is remarkable in conditioning both the operability and the prognosis.

Computed tomography (CT) and magnetic resonance (MRI) currently represent the best available non-invasive procedures in this sector of staging [5,6,9,10]. Both of these imaging techniques have been shown to provide comparable information about the presence of enlarged mediastinal lymph nodes but they have shown poor accuracy when their results are compared with the pathological findings. These limitations are not totally unexpected since the criterion used for diagnosing metastatic lymphadenopathy is only the node size.

Our study group was already interested in this problem during the past years [1], and in the present paper we would like to assess in particular the diagnostic effectiveness of gadolinium–DTPA (GD) enhanced MRI in the detection of mediastinal lymph nodes involvement from lung cancer [4]. This prospective evalu-
ation has been carried out by both standard and GD enhanced MRI examination whose data were finally compared with the surgical pathological findings.

2. Materials and methods

In the period between January 1 and December 31 1994, 20 patients were included in this study protocol, which was carried out by cooperation between the Chair of Thoracic Surgery and the Chair of Radiology of the University of L’Aquila.

There were 18 men and 2 women with an age range between 54 and 71 years, in whom a biotic diagnosis of non small cell bronchogenic cancer had just been established. All the patients exhibited positive oncologic criteria and functional respiratory conditions for resectability, established on the basis of the Mountain classification. Within a 10 day period before undergoing surgery, the patients underwent MRI evaluation of the chest and mediastinum.

MRI images were obtained by means of a superconducting imager operating at 0.5 T. First acquisition of T1 weighted sequences was performed in the same MRI structure in two consecutive moments: the first examination was carried out in basal conditions and a second one soon after the i.v. administration of GD at a dosage of 0.2 mmol/kg. GD [11] is a paramagnetic contrast agent which determines signal enhancement in the accumulation sites in T1 weighted sequences. The characteristics of GD let us expect enhancing areas in metastatic lymph nodes (N2) [2,3,7,8]. Therefore, the aim of the present study was to assess whether GD can assume a reliable role as N2 indicator, helping differentiate between N2 and non-metastatic enlarged nodes and allowing MRI to overcome the merely dimensional criteria. Conventional MRI images and contrast enhanced MRI images were evaluated by two independent observers. The analysis of the images was performed taking into account the following interpretation criteria:

(1) dimension of the nodes expressed in cm and measured along the short axis diameter;
(2) topographic location of mediastinal lymph nodes classified according to the nomenclature of Naruke’s mapping;
(3) qualitative analysis of the signal intensity in T1 weighted sequences after GD administration.

In the course of surgical operation, always carried out by the same surgical team, a systematic and accurate exploration of all the mediastinal nodal group areas potentially involved with metastases was always performed. Surgical exploration allowed us to verify the size enlargement and the site of the lymph nodes. Furthermore, their dissection allowed the acquisition of specimens for pathological examination which is crucial to assess the real presence of metastases and to evaluate the correlation with the MRI imaging data. Seven pneumonectomy and thirteen lobectomy were performed.

3. Results

In the 20 patients enrolled in this study protocol the analysis of the images achieved with both of the MRI methods has allowed us to detect the presence of 35 mediastinal lymph nodes, considering all the nodes larger than 0.5 cm in diameter. Among these, 20 had a short axis diameter of less than 1.5 cm and 15 equal to or more than 1.5 cm.

With regard to the aims of this study, the different signals shown by these 35 lymph nodes in T1 weighted sequences after GD administration has to be especially underlined (Table 1). Among the 20 nodes with a diameter of less than 1.5 cm and considered N0 according to the dimensional criteria adopted in conventional MRI, 10 showed GD enhancement and therefore they were reclassified as N2, while 10 did not show enhancement and were classified as N0 also after the contrast enhanced method. Conversely, all the 15 nodes presenting a short axis diameter equal to or more than 1.5 cm (thus N2 by conventional MRI) showed a contrast enhancement in T1 sequences so that they were confirmed as N2.

The 35 lymph nodes detected in their dimensions and location by MRI were surgically located and excised for pathological examination. The postoperative pathological examination of the 35 excised nodes revealed that 24 of them presented a massive or partial metastatic involvement (N2). More precisely, all the 15 lymph nodes with a short axis diameter equal to or more than 1.5 cm and 9 of the 20 lymph nodes with a diameter of less than 1.5 cm proved to be metastatic.

By comparing pathological data with GD enhanced MRI data we can show (Table 2) 9 of the 10 nodes of less than 1.5 cm dimensioned and showing a contrast enhancement were metastatic as well as all the nodes of more than 1.5 cm dimensioned. Furthermore, all the 10 lymph nodes of less than 1.5 cm dimensioned and not showing a GD enhancement proved to be metastases free at surgery.

Table 1

<table>
<thead>
<tr>
<th>Lymph nodes</th>
<th>MRI</th>
<th>MRI-GDpos</th>
<th>MRI-GDneg</th>
</tr>
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<tbody>
<tr>
<td>&lt; 1.5 cm</td>
<td>20</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>≥ 1.5 cm</td>
<td>15</td>
<td>15</td>
<td>0</td>
</tr>
</tbody>
</table>
Evaluating, on the basis of these data, the diagnostic patterns of both the MRI imaging methods we can confirm the results obtained in our previous study of conventional MRI, with a sensitivity of 62%, a specificity of 100% and an accuracy of 74%; conversely, GD enhanced MRI shows a sensitivity of 100%, a specificity of 91% and an accuracy of 97%.

4. Comment

In this prospective study we demonstrated that GD-DTPA enhanced MRI is more accurate than standard unenhanced MRI in detecting the involvement of mediastinal lymph nodes in patients with diagnosed lung cancer.

Several reports have shown that the technological progress in imaging techniques has not been matched by a similar improvement in detecting metastatic lymphadenopathy, with great variability in the reported accuracies. In one of our previous studies concerning 50 case of lung cancer, CT and standard MRI compared well in evidencing enlarged mediastinal nodes. However the diagnostic accuracy was only about 60% for both techniques when results were compared with the pathological findings. The parameter taken into consideration with regards to a possible metastatic involvement, in all cases, was node size. A lymph node with a short axis diameter equal to or greater than 1.5 cm, was considered metastatic. However, not all enlarged nodes are metastatic (previous inflammatory processes, aspecific adenopathies, etc.) and conversely metastases can be discovered in smaller nodes. Nevertheless MRI is surely the most suitable means of studying mediastinal structure as it permits a better visualization of sub-carinal and aorto-pulmonary window lymph nodes in sagittal and coronal images. In standard MRI dimension is currently the only parameter suitable for diagnosis of metastatic lymphadenopathy as, unfortunately, characterization of nodes on the basis of signal as node size is the only criteria adopted, thus no significant improvement in performance can be expected from MRI in the detection of metastatic mediastinal lymph nodes.

To overcome this limitation we performed an MRI study of mediastinum after GD i.v. administration to assess if the expected tissue characterization could help in reducing false negative results and/or false positive findings. Of remarkable interest in the detection of cancer in normal sized nodes was the demonstration that 10 out of 20 normal sized nodes showed a GD uptake and 9 of these resulted in involvement with the tumour. This reduction in the false negative rate is the main reason that GD enhanced MRI was more accurate than standard MRI in our series. However uptake of GD-DTPA is not indeed completely specific to tumours; indeed in our series all enlarged nodes showed a contrast enhancement associated with cancer whilst one normal sized node believed to be metastatic proved to be a false positive. A better assessment of the specificity of the method might be achieved by evaluating the relationship between node size and pattern of GD uptake. One reason for this being that modest GD enhancement by a large node may not have the same prediction value as intense uptake by a normal sized node. More data of GD accumulation times may be of more use than our qualitative method.

Nevertheless when considering the overall data obtained from contrast enhanced MRI, in 24 out of 25 cases enhancement was correlated to the actual presence of metastases (N2) with a diagnostic accuracy of 97%. Clearly, the method requires more extensive prospective evaluation but our initial data leads us to conclude that GD enhanced MRI may be an effective approach for non-invasive staging of mediastinal lymph nodes in patients with lung cancer.

References

[6] Martini N, Heelan R, Wescott J, Zaman M. Comparative merits of conventional, computed tomographic and magnetic resonance imaging in assessing mediastinal involvement in surgically confi-