Staging of Malignant Pleural Mesothelioma: Comparison of CT and MR Imaging

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OBJECTIVE. This article compares the accuracy of CT with that of MR imaging in staging of malignant pleural mesothelioma.

SUBJECTS AND METHODS. Ninety-five patients were enrolled in a prospective staging protocol based on the International Mesothelioma Interest Group staging system. Sixty-five patients underwent CT and MR imaging and a surgical procedure (excluding percutaneous needle biopsy) to stage and resect the tumor. Receiver operating characteristic analyses were performed. CT and MR scans were interpreted independently by observers who were unaware of the results of the other imaging study; these imaging findings were compared with the results of surgery and pathologic examination.

RESULTS. The areas under the receiver operating characteristic curves for eight of 10 features revealed by imaging showed no statistically significant differences between CT and MR imaging. However, MR imaging was superior to CT in revealing invasion of the diaphragm (A_z = .55 for CT versus .82 for MR imaging) and in revealing invasion of endothoracic fascia or solitary resectable foci of chest wall invasion (A_z = .46 for CT; A_z = .69 for MR imaging). Several anatomic regions could not be evaluated because positive findings at surgery were rare.

CONCLUSION. CT and MR imaging are of nearly equivalent diagnostic accuracy in staging malignant pleural mesothelioma. MR imaging is superior to CT in revealing solitary foci of chest wall invasion and endothoracic fascia involvement and in showing diaphragmatic muscle invasion; however, this advantage does not affect surgical treatment. For cost reasons, CT should be considered the standard diagnostic study before therapy.

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Malignant pleural mesothelioma is a highly lethal, although uncommon, tumor with an increasing incidence worldwide that is largely related to the industrial use of asbestos. The rarity of this neoplasm has hampered implementation of clinical trials. In addition, although a number of staging systems have been proposed in the past, many describe only advanced malignant pleural mesothelioma [1–6], further limiting uniformity of approach. None of these staging systems have been universally accepted [7]. More recently, an international TNM staging system for malignant pleural mesothelioma was proposed [8, 9] (Appendix). The intent of this study is to evaluate and compare the accuracy of CT and MR imaging using this new international TNM staging system, with surgical and pathologic staging as the gold standard for imaging comparison.

Subjects and Methods

Ninety-five patients with biopsy-proven primary malignant pleural mesothelioma, who were judged by a surgical oncologist at initial presentation to have clinically resectable disease, were enrolled in this study. Patients with terminal disease or in whom surgical therapy was not a potential option and those with metallic intracranial aneurysm clips, cardiac pacemakers, or severe claustrophobia were excluded. Within this group, 65 patients (54 men and 11 women) underwent complete CT and MR imaging examinations with surgical correlation; they ranged in age from 41 to 79 years (mean, 62 years). The extent of the surgical procedure depended on the extent of tumor shown by imaging and that found at surgical exploration. A complete extrapleural pneumonectomy was planned for all patients but the extent of surgery was subsequently modified by findings at surgery (e.g., extensive chest wall invasion).

Thirty patients were excluded from the study: One was subsequently proven at pathologic reevaluation to have adenocarcinoma of the pleura. Seventeen patients did not undergo surgery (cardiopulmonary disease, n = 6; extensive tumor on imaging, n = 4; distant metastases on imaging, n = 2; other medical reasons, n = 2; refusal of surgery, n = 3). Twelve patients had either no or incomplete CT (n = 3) or MR imaging (n

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= 5) studies or both (n = 4), with the most common reason being claustrophobia (n = 5) and cancellation by patient or physician (n = 3). The remaining 65 patients underwent the following surgical procedures: extrapleural pneumonectomy (n = 34), thoracotomy with partial pleural pleurectomy (n = 13), thoracotomy with biopsies (n = 13), laparoscopy with biopsies (n = 4), and supraclavicular lymph node biopsy (n = 1).

With a single exception, each of the 65 patients in this study underwent CT and MR imaging at our institution; the two imaging studies were performed within 1–3 days of one another. One patient underwent contrast-enhanced CT at an outside facility within 1 week of MR imaging, and the resulting CT scan was judged of high quality. The decision to require that CT be performed at our institution resulted from the different techniques other institutions use to obtain scans and the variable quality of their scans, combined with the fact that most CT scans from other sources had been obtained several weeks to several months before admission to our institution. Such scans were therefore thought to be suboptimal from a comparison and clinical point of view; in addition, their use in this prospective study would have detracted from its value, insofar as the MR images would have been state-of-the-art optimal studies compared with CT scans submitted from outside sources of markedly varying quality and obtained at variable time intervals from presentation.

CT is considered the current standard of care in preoperative staging of malignant pleural mesothelioma at our institution. The cost of MR imaging was defrayed through departmental research funds. Before performing MR imaging, we explained the investigative aspect of the proposed procedure to the patient. The protocol was approved by our institutional review board and patients gave informed consent for both studies.

CT Technique

IV contrast–enhanced dynamic CT of the chest was performed during inspiration from the lung apices to below the adrenals to include the celiac and splenic lymph node chains. One-centimeter contiguous sections were imaged on a Highlight Advantage CT scanner (General Electric Medical Systems, Milwaukee, WI). During the last 18 months of the study, helical scans of the entire chest and upper abdomen with a collimation of 0.7 cm and a pitch of 1.5 were obtained on a HiSpeed helical scanner (General Electric Medical Systems). In cases of suspected or equivocal invasion of the chest wall, diaphragm, or mediastinum, 1.5- or 1.0-mm high-resolution CT scans with high-spatial-frequency reconstruction algorithms were obtained. Technically adequate CT scans of the chest obtained from outside sources were permitted if obtained within 4 weeks of patient enrollment in the study. In practice, few scans were submitted within 4 weeks, and those few scans (with a single exception) were judged to be technically suboptimal. Before introduction of helical scanning, CT scan time was approximately 15 min; after helical CT introduction, scan time was approximately 5 min.

TABLE 1 Accuracy of Malignant Pleural Mesothelioma Staging by CT and MR Imaging

T or N Stage	Site	A_z		p
		CT	MR Imaging	
T1b	Scattered foci of visceral pleural involvement	.58	.69	.65
T2	Confluent visceral pleural tumor	.67	.58	.64
T2	Invasion of diaphragm	.55	.82	.01
T2	Invasion of endothoracic fascia (subpleural fat invaded) or solitary resectable focus tumor (or both)	.63	.59	.64
T2	Invasion of lung parenchyma	.46	.69	.05
T3	Mediastinal fat invasion	.80	.70	.39
T3	Nontransmural pericardial involvement	.73	.76	.76
T4	Diffuse or multifocal chest wall invasion (or both)	.65	.52	.44
N1	Ipsilateral hilar lymph nodes	.49	.50	.73
N2	Ipsilateral mediastinal lymph nodes	.49	.51	.85

Note.—A_z = area under the curve; T = size, extent of primary tumor; N = presence of regional lymph node disease.

MR Imaging Technique

Cardiac-gated and respiratory-compensated 10-mm axial sections with T1-weighted (TE = 20 msec) and spin-echo T2-weighted (TE = 80 msec) sequences were performed with a body coil through the chest and upper abdomen to the mid portion of the liver to include celiac and splenic lymph node chains. TR was determined by heart rate: one R-R interval for T1-weighted images and two or three R-R intervals for T2-weighted images. Scans were obtained with two or four signals acquired and 128 or 256 phase-encoding steps. Coronal or sagittal scans of the suspected areas of abnormality in the thoracic or diaphragmatic regions were also obtained. Most patients had both coronal and sagittal T1-weighted scans 5 mm in thickness with a 1-mm interscan gap. MR scan time was 50–60 min. All MR imaging was performed at our institution using a 1.5-T Signa scanner (General Electric Medical Systems).

Scan Interpretation and Surgical Correlation

Scans were interpreted separately and prospectively by board-certified radiologists who have extensive experience in both chest CT and MR imaging. Each interpreting radiologist was unaware of the results of the other cross-sectional scan and of the surgical and pathologic findings. Interpretations were written on data forms and then entered into a computer database. All forms were based on categories proposed in the new staging system (Appendix), the International Mesothelioma Staging Classification, and were designed to permit point-by-point anatomic correspondence for evaluation of the extent of disease.

The interpreting radiologist chose a diagnostic score for each anatomic site from a sliding scale of relative certainty (0 = definitely or almost definitely negative, 1 = probably negative, 2 = indeterminate, 3 = probably positive, 4 = definitely or almost definitely positive) (Table 1). Immediately after thoracotomy, surgeons completed a form similar to that filled out by the radiologists, using identical anatomic sites and staging categories but simpler choices: positive, negative, or not evaluated.

Some categories of the new staging system were not correlated with surgical findings; for example, M1 N3, or contralateral pleural spread of malignant pleural mesothelioma, was typically not evaluated during a thoracic surgical exploration. Thus, the number of evaluations for several staging categories was lower (and for some, e.g., M1, much lower) than the total number of surgical procedures.

Although selective use of surgical exploration can lead to bias in the estimates of diagnostic accuracy, the validity of the statistical comparison of CT and MR imaging was maintained by the paired-sample design [10]. The surgical data form, surgeon's report, and pathology report were used as the gold standard for evaluating the accuracy of the CT and MR imaging interpretations. Individual statistical tests to compare the accuracies of CT and MR imaging at each anatomic site were performed by comparing the areas under the respective receiver operating characteristic (ROC) curves, recognizing the correlated nature of the ratings [11].

Several categories in the new staging system were not evaluated in this study or were incompletely evaluated because of a low number of positive findings at surgery and on imaging. These categories include distant metastatic disease (M stage), direct extension to contralateral pleura (T4), and tumor involvement of the parietal pleura only (T1a).

Results

For a large number of categories, sufficient numbers of patients underwent both imaging and surgery to allow meaningful correlation. Table 1 illustrates these categories. Most of the sites evaluated showed no significant difference between CT and MR imaging in diagnostic accuracy and fairly low diagnostic accuracies for both CT and MR imaging. Significant differences be-

tween CT and MR imaging were seen in only two categories: invasion of the diaphragmatic muscle (A_z = .55 for CT; A_z = .82 for MR imaging; p = .01) and invasion of the endothoracic fascia or a single chest wall focus of involvement (A_z = .46 for CT; A_z = .69 for MR imaging; p = .05).

The areas under the ROC curves for CT and MR imaging reveal somewhat low accuracies. For both imaging techniques, only two of 20 categories had an A_z that was greater than or equal to .80: The A_z value was .82 for MR imaging evaluation of diaphragmatic invasion and .80 for CT evaluation of mediastinal fat invasion. Most areas under the ROC curves were less than .70. The ROC values for N1 and N2 tumor involvement were .49 and .50 for CT and .49 and .51 for MR imaging, respectively. The mediastinum was surgically evaluated for N2 disease in 37 patients: Histologic findings proved tumor involvement of N2 lymph nodes in 21 patients (60%).

For several categories in the new staging system (T1a, tumor limited to the parietal pleura with no involvement of visceral pleura; T4, transdiaphragmatic extension of tumor to the peritoneum; T4, extension of tumor to one or more mediastinal organs, including the spine; T4, extension to the internal surface of the pericardium with or without effusion or myocardial involvement), the number of true surgical positives was too small to allow a valid analysis of the areas under the ROC curves. Moreover, the nature of the surgical procedure did not permit evaluation of several categories (T4, extension into contralateral pleura; N3, contralateral mediastinal or ipsilateral or contralateral supraclavicular nodal involvement; M1, distant metastatic spread). Findings for a few categories had sufficient numbers for analysis but did not achieve statistical significance; for example, four patients underwent laparoscopy to confirm M1 disease in the abdomen, which was detected by both imaging studies.

Discussion

Previous reports of CT evaluation of malignant pleural mesothelioma have frequently been limited by a low number of patients or the retrospective design of the studies [12–18]. Pathologic correlation of the CT findings has generally been weak. Rusch et al. [19] prospectively examined 20 patients who underwent CT and surgery. CT showed several areas of diagnostic deficiency, notably in evaluating chest wall invasion and in detecting involvement of the diaphragm and underlying peritoneum and involvement of mediastinal lymph nodes. The authors concluded that, despite its limitations, CT is the most accurate diagnostic technique available for the initial evaluation of malignant pleural mesothelioma. Sahin et al. [20] retrospectively reviewed CT scans of 84 patients with proven malignant pleural mesothelioma and described the appearance of these tumors on CT, but because of the lack of surgical or pathologic correlation, they provided relatively little information on verifying the extent of disease. The study by Tammilehto et al. [21] of 88 patients who underwent CT before treatment (debulking surgery, chemotherapy, irradiation) did not provide information about a correlation with surgical or pathologic findings, suggesting that the CT TNM staging may not have been verified in detail. However, these authors make the observation—one that we can confirm on the basis of our findings—that "in clinical practice, it is difficult [with CT] to evaluate separately the tumor (T) and nodal (N) involvement due to the unique plate-like growth pattern of this tumor." Lorigan and Libshitz [22] described the MR findings of three patients with proven malignant pleural mesothelioma. Patz et al. [23] evaluated CT and MR findings of 41 consecutive patients with malignant mesothelioma, focusing on three anatomic regions: the diaphragm, chest wall, and mediastinum. This study showed a high sensitivity (92–100%) but low specificity (25–50%). These authors found a high accuracy of CT and of MR imaging in predicting resectability on the basis of involvement of diaphragm, chest wall, and mediastinum. None of the patients in this series who underwent pneumonectomy had abnormal mediastinal lymph nodes either on imaging or at pathologic examination. None of the reported studies used a mesothelioma staging system, although several systems had been available for more than 15 years [1–3, 5, 6].

Recently, a group of investigators proposed a new staging system for diffuse malignant pleural mesothelioma based on the familiar TNM descriptors to replace previous systems, none of which had been validated or universally used [8, 9]. The group intended to provide an internationally accepted reproducible staging system to be used for staging and clinical trials. The results of our current study are based on this new staging system.

There are inherent difficulties in achieving high accuracies in preoperative local and regional evaluation of malignant pleural mesothelioma, as illustrated by several CT and MR imaging accuracies in the 50–60% range. Accuracy may be suboptimal because malignant pleural mesothelioma spreads locally and regionally in a complex pattern as opposed to, for example, non–small cell lung cancer. Non–small cell lung cancer spreads in a more predictable fashion: A local tumor is followed by local extension, then by involvement of regional nodes, and lastly by the appearance of distant metastases. In addition, progressive involvement of anatomic structures by lung cancer shows some anatomic and temporal separation, allowing easier distinction on cross-sectional imaging. By contrast, malignant pleural mesothelioma spreads along pleural and fissural surfaces to successively involve the visceral pleura, lungs, chest wall, diaphragm (Figs. 1–4), and mediastinum, with involvement of hilar and mediastinal lymph nodes seen in more than 50% of the patients in a recent surgical series [24]. Involvement of thoracic structures by malignant pleural mesothelioma appears to occur simultaneously or asymptomatically (or both) and is present at initial diagnosis. Moreover, many of these structures are contiguous on cross-sectional imaging and consequently are difficult or impossible to visually separate. These findings contrast markedly with those obtained for staging of non–small cell lung cancer in which a discrete primary lesion is frequently visible and is separated from foci of N1 and N2 tumor involvement, thus facilitating visual evaluation on cross-sectional imaging.

With malignant pleural mesothelioma, pleural thickening frequently extends along the mediastinal pleura. Distinguishing irregular pleural thickening from invasion beyond the pleura into mediastinal fat can be difficult (A_z = .80 for CT; A_z = .70 for MR imaging) (Figs. 4B and 4C). Furthermore, visualizing hilar lymph nodes as separate structures from the pleural tumor may not be possible (A_z = .49 for CT; A_z = .50 for MR imaging). In a similar fashion, enlarged ipsilateral mediastinal nodes are often obscured by irregular pleural thickening along the mediastinal pleural surface (A_z = .49 for CT; A_z = .51 for MR imaging). This difficulty probably accounts for the poor accuracy of CT and MR imaging in detecting N2 lymph node involvement (Figs. 1, 3, and 4): Of 36 surgical explorations for N2 disease, positive findings for the lymph nodes were reported in 21 patients at pathology. With CT, observers reported 11 false-negative and eight false-positive interpretations. With MR imaging, observers reported 15 false-negative interpretations and one false-positive interpretation. The low accuracies with which these two techniques reveal this prognostically important feature clearly detracts from their overall

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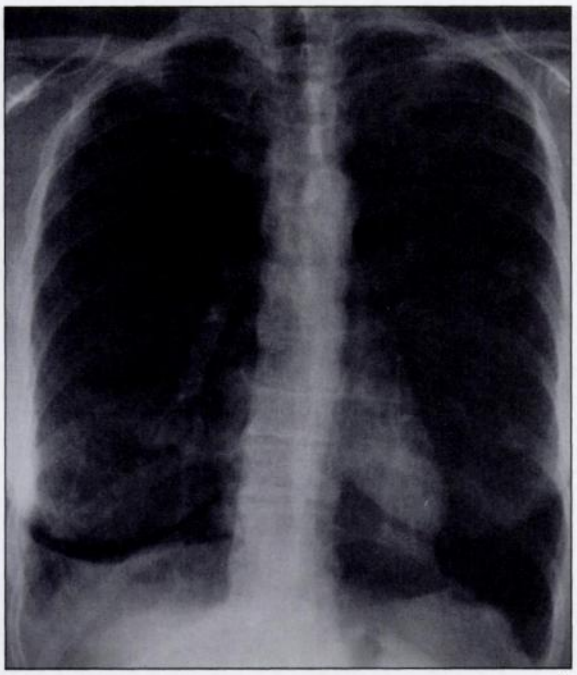

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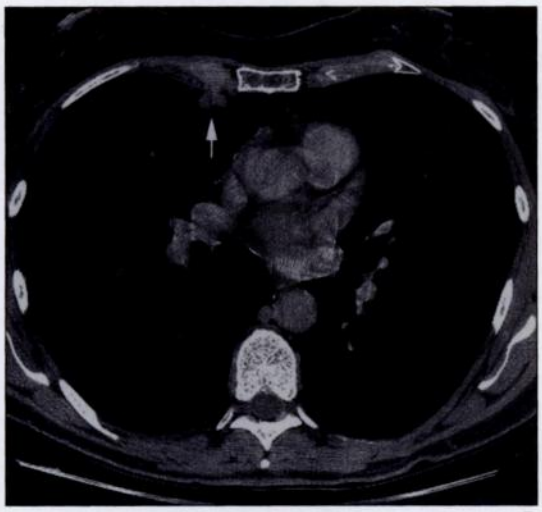

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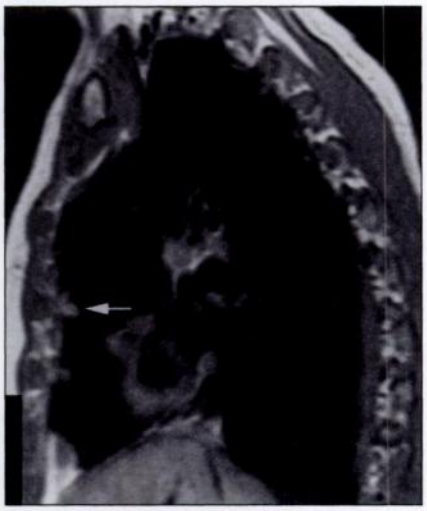

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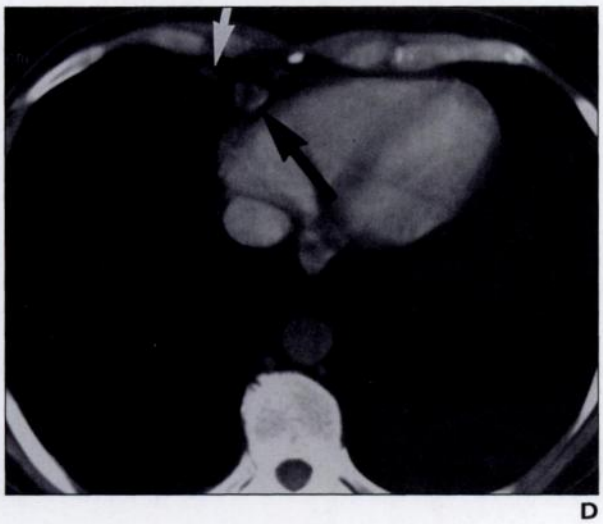

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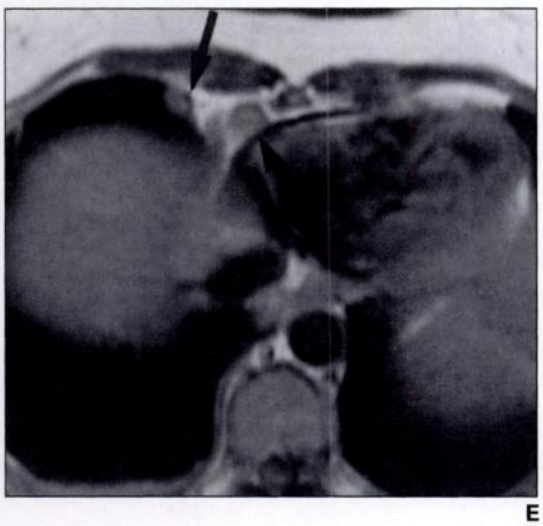

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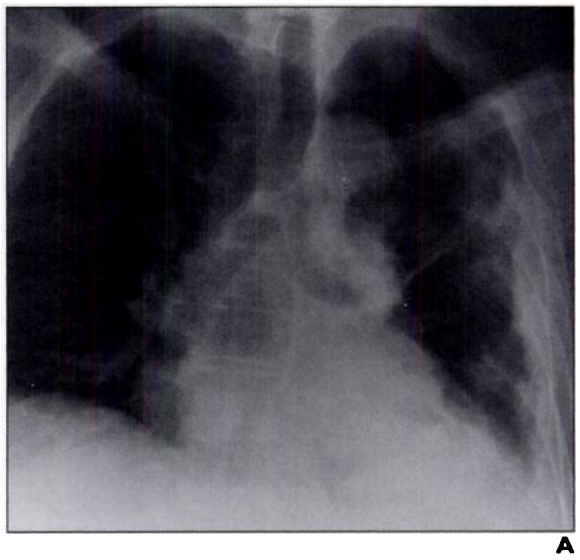
Fig. 1.—53-year-old woman with malignant pleural mesothelioma.
A, Posteroanterior chest radiograph reveals nodular densities along right lower mediastinal surface with pleural fluid or mass at right costophrenic angle. Nodular density overlying right lower lung originates from major fissure.
B and **C**, CT scan (**B**) and T1-weighted sagittal MR scan (**C**) were interpreted as negative for invasion of anterior chest wall (*arrows*); however, at extrapleural pneumonectomy, there was localized extension beyond endothoracic fascia into chest wall.
D and **E**, CT scan (**D**) and T1-weighted axial MR scan (**E**) correctly revealed mediastinal nodal disease along surface of anterior diaphragm (*arrows*). Pathologic stage = T3 N2 M0.



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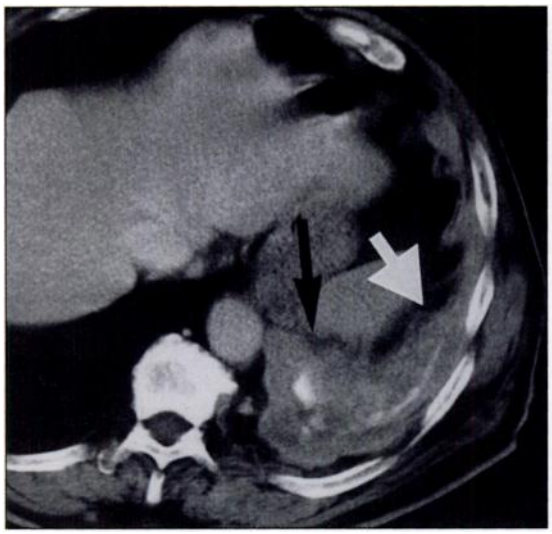

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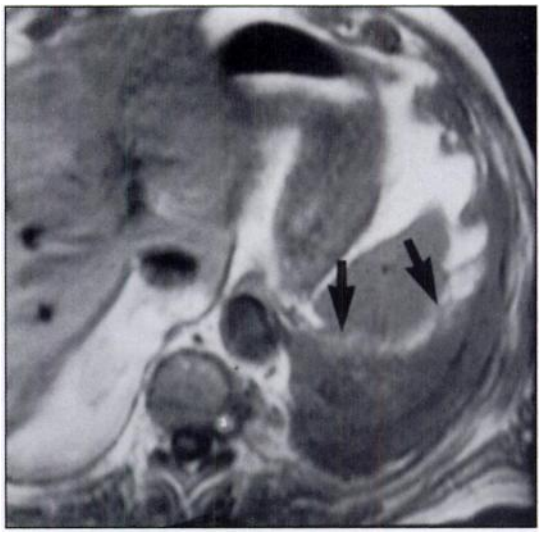

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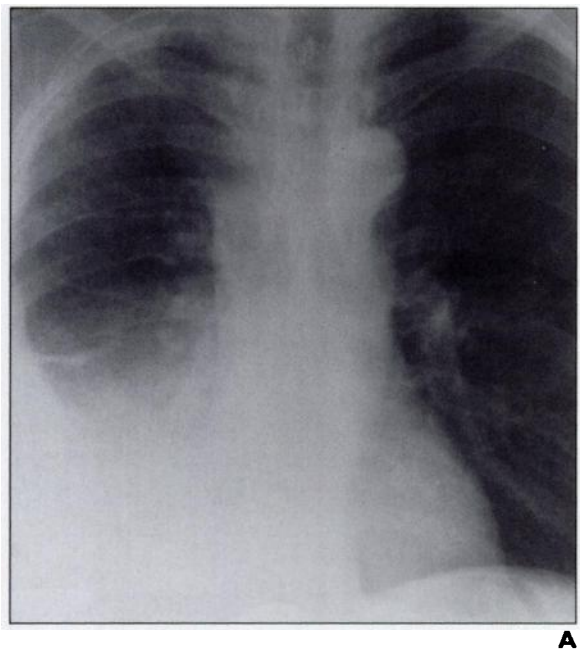
Fig. 2.—70-year-old man with malignant pleural mesothelioma.
A, Posteroanterior chest radiograph reveals extensive thick tumor involvement of almost entire left pleural surface.
B and **C**, CT scan (**B**) and T1-weighted axial MR scan (**C**) were interpreted as showing probable invasion of diaphragm and indeterminate for transdiaphragmatic extension to peritoneal surface (*arrows*). Because of suspicions raised by imaging studies, thoracotomy was cancelled and laparoscopy with biopsy of peritoneal surface of diaphragm was performed, from which positive findings for malignant pleural mesothelioma were obtained. Pathologic stage = T4 NX MX.

value. Recent surgical and pathologic findings indicate a greater than 50% incidence of spread to hilar and mediastinal lymph nodes (including internal mammary nodes and inferior pulmonary ligament nodes), an indicator of poor prognosis [24]. The low accuracies with which CT and MR imaging reveal hilar and mediastinal adenopathy is disappointing but not surprising in view of the aforementioned factors.

The earliest stage of malignant pleural mesothelioma (T1a, tumor limited to parietal pleura and no involvement of visceral pleura) was not evaluated in this study because there were no true-positive findings at surgery. In North America, where most patients are referred for evaluation when they have a more locally advanced disease, stage T1a is an unusual presentation of malignant pleural mesothelioma. Detection of T1b malignant pleural mesothelioma (scattered foci with both parietal and visceral tumor involvement) had low accuracies for CT (A_z = .58) and MR imaging (A_z = .69); usually CT scans of patients with T1b malignant pleural mesothelioma show significant pleural effusion, a nonadherent pleural space, and minimal pleural thickening or irregularity. Diagnosis of confluent visceral pleural tumor (T2) had similar suboptimal accuracies (A_z = .67 for CT; A_z = .58 for MR imaging), as did evaluation for invasion of lung parenchyma (T2) (A_z = .63 for CT; A_z = .59 for MR imaging). These accuracies reflect the impossibility of distinguishing anatomically adjacent thin layers of tissue (parietal pleura, visceral pleura, adjacent lung parenchyma) with current cross-sectional imaging techniques in evaluating a tumor that grows on and then destroys these anatomic structures.

The new staging system attempts to organize the preoperative examination of patients with malignant pleural mesothelioma in several ways: to identify that small cohort of patients with early disease (T1a and T1b) and a potentially better prognosis; to distinguish patients who may potentially benefit from surgery, but not necessarily be cured (T2 and T3), from patients for whom surgery may have no benefit because of short survival and extensive local tumor spread (T4); and to diagnose extensive locoregional (T4 N3) disease or distant spread (M1) for patients in whom surgery is not an option. In addition, the new staging system is intended to provide a common basis to compare the results of different treatment regimens and thus to determine if a specific treatment, such as surgical resection, has an impact on survival [24].



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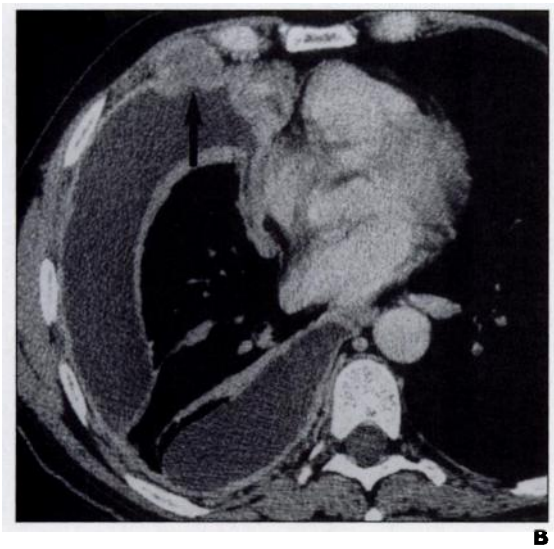

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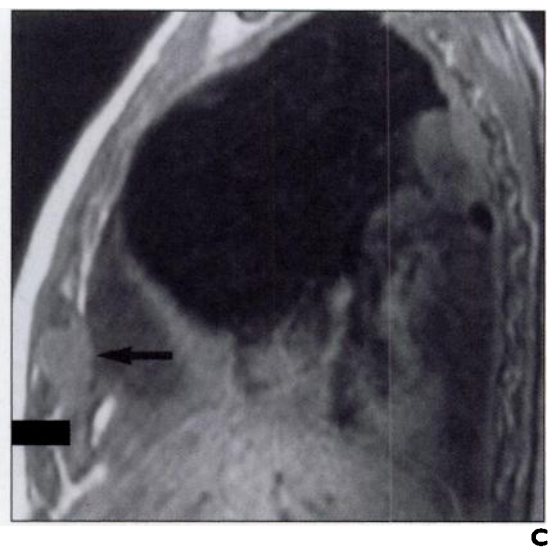

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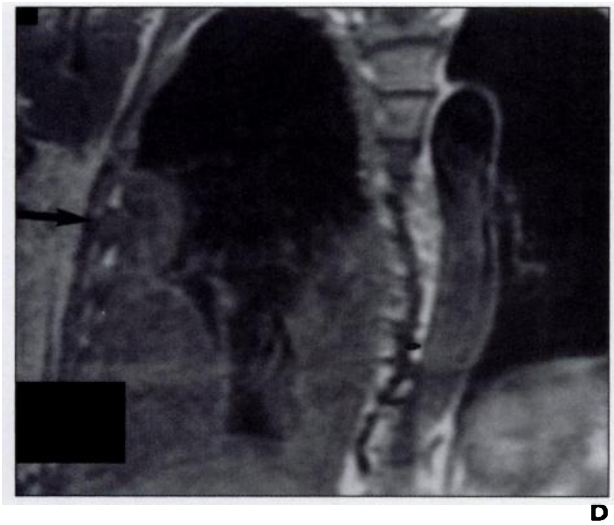

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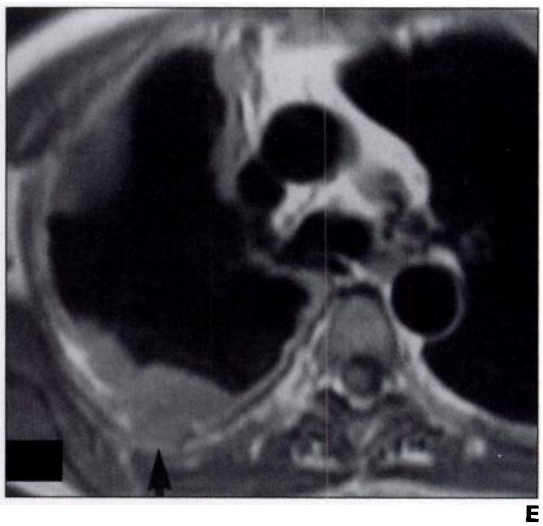

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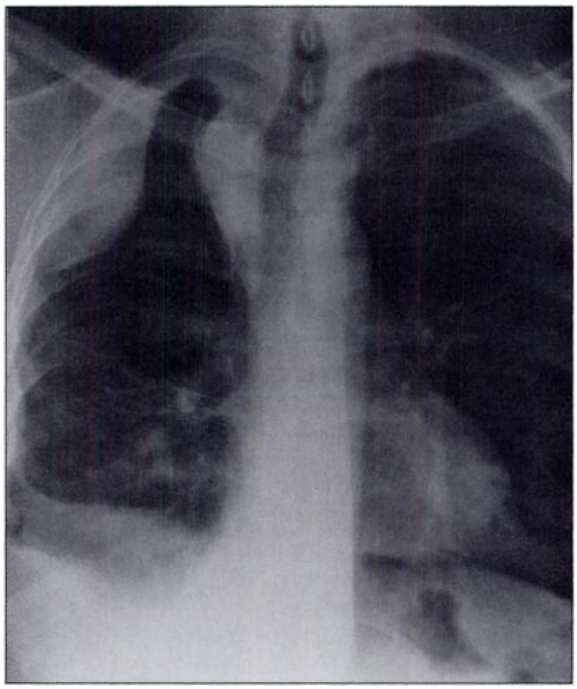
Fig. 3.—53-year-old man with malignant pleural mesothelioma.
A, Posteroanterior chest radiograph reveals extensive confluent right pleural density. Configuration of pleural density at right base suggests fluid component.
B, CT scan revealed definite local anterior chest wall invasion with probable multiple other foci of chest wall invasion.
C, T1-weighted sagittal MR scan also revealed positive findings for chest wall invasion in same location.
D and **E**, T1-weighted coronal MR scan (**D**) and T1-weighted axial MR scan (**E**) revealed lateral (**D**) and posterior (**E**) chest wall invasion. Surgical examination revealed only anterior local chest wall invasion (*arrows*, **B** and **C**), which was resected; findings were negative for other areas of chest wall that were suggestive on imaging of extension beyond endothoracic fascia (*arrows*, **D** and **E**). At surgery, multiple lymph nodes were removed and described as grossly normal. False-negative interpretations based on CT and MR imaging were reported for lymph node involvement: Pathologic examination revealed microscopic tumor involvement of hilar node and partial replacement by tumor of paraesophageal and diaphragmatic lymph nodes and a single internal mammary lymph node. Pathologic stage = T3 N2 M0.

Fig. 4.—50-year-old man with malignant pleural mesothelioma.
A, Posteroanterior chest radiograph reveals smooth contoured masses in upper thorax abutting chest wall and mediastinum. Indistinct pleural density is present in right lower thorax, particularly in region of right cardiophrenic angle.
B and **C**, CT scan (**B**) and T2-weighted axial MR scan (**C**) allowed correct identification of superficial resectable involvement of pericardium without tumor involvement of pericardial cavity (*arrows*).
D and **E**, CT scan (**D**) and T1-weighted axial MR scan (**E**) were incorrect in diagnosing local chest wall invasion. CT scan (**D**) was interpreted as showing probably positive solitary focus of local invasion of lateral upper chest wall (*arrow*); MR scan (**E**) was interpreted as showing positive solitary focus in lateral lower chest wall (*arrow*): Both of these regions were negative for local chest wall invasion at surgery. Hilar and mediastinal nodes removed during surgery were described as normal in surgical report. However, at pathologic examination of resected mediastinal lymph nodes, tumor was found in two nodes at level 7 (subcarinal) that was not revealed by either CT or MR imaging. Pathologic stage = T3 N2 M0.



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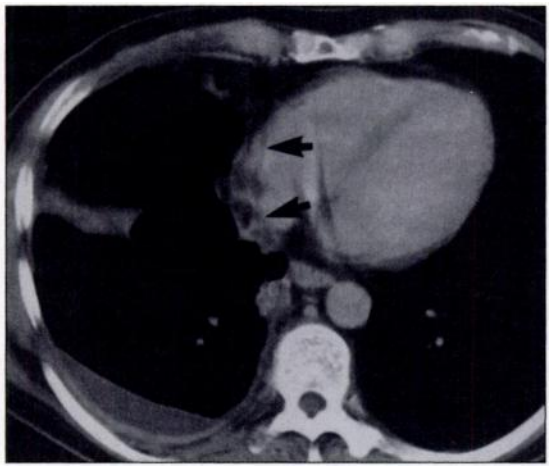

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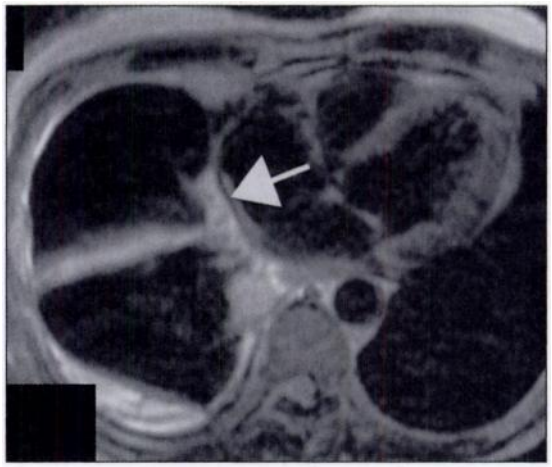

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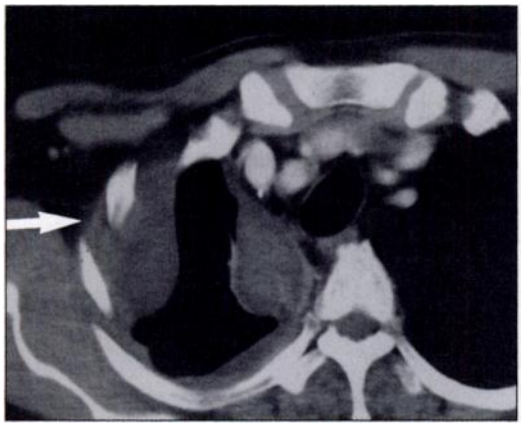
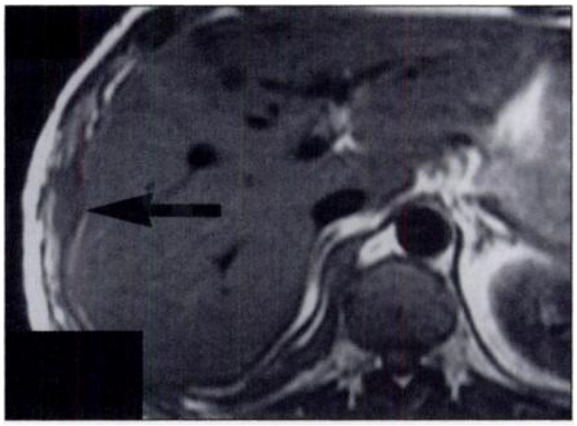


D



E

The system was designed to provide clinical and prognostic information, but the limitations of cross-sectional imaging were not considered; many staging categories in the system cannot be distinguished reliably by CT or MR imaging.

CT has been the standard imaging method in this patient group and has been evaluated by other investigators. The availability of coronal and sagittal images on MR imaging potentially allows improved evaluation of mediastinal, chest wall, and diaphragmatic invasion. However, various thoracic motion artifacts on MR imaging are only partially avoided by cardiac gating and respiratory compensation.

No significant difference was found in the areas under the ROC curves for most findings. In comparing CT and MR imaging in the two findings in which MR imaging showed significant superiority, the difference between the two techniques is diminished because therapy is not changed on the basis of these findings. In addition, most patients (43/49) examined for diaphragmatic invasion had such invasion, indicating that this finding represents a common occurrence and that the surgeon should be prepared to resect the diaphragm and, in cases of larger areas of diaphragm resection, secure the defect with a surgical supporting mesh patch.

For most categories described in the new International Mesothelioma Staging Classification System, CT and MR imaging achieved similar accuracies. MR imaging showed superiority in revealing involvement of endothoracic fascia, a solitary focus of chest wall involvement, and involvement of diaphragmatic muscle, although the improved demonstration of involvement of these structures would not affect a decision at our institution about surgery. Because CT costs less, is more widely available, and takes less time, CT should remain the standard preoperative cross-sectional technique for staging malignant pleural mesothelioma. MR imaging should be reserved for problem solving in specific cases, such as for a patient with an allergy to IV contrast material or to confirm or support suspicion of involvement of anatomic structures revealed by CT.

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APPENDIX: International Staging System for Diffuse Malignant Pleural Mesothelioma

T: Size, extent of the primary tumor
T1a: Tumor limited to the ipsilateral parietal pleura, including mediastinal and diaphragmatic pleura
• No involvement of the visceral pleura
T1b: Tumor involving the ipsilateral parietal pleura, including mediastinal and diaphragmatic pleura
• Scattered foci of tumor also involving the visceral pleura
T2: Tumor involving each of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least one of the following features:
• Involvement of diaphragmatic muscle
• Confluent visceral pleural tumor (including the fissures) or extension of tumor from visceral pleura into the underlying pulmonary parenchyma
T3: Locally advanced but potentially resectable tumor that involves all the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least one of the following features:
• Involvement of the endothoracic fascia
• Extension into the mediastinal fat
• Solitary, completely resectable focus of tumor extending into the soft tissues of the chest wall
• Nontransmural involvement of the pericardium
T4: Locally advanced technically unresectable tumor that involves all the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral) with at least one of the following features:
• Diffuse extension or multifocal masses of tumor in the chest wall, with or without associated rib destruction
• Direct transdiaphragmatic extension of tumor to the peritoneum
• Direct extension of tumor to the contralateral pleura
• Direct extension of tumor to one or more mediastinal organs
• Direct extension of tumor into the spine
• Tumor extending through to the internal surface of the pericardium with or without a pericardial effusion or involving the myocardium
N: Presence of regional lymph node disease
NX: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastases
N1: Metastases in the ipsilateral bronchopulmonary or hilar lymph nodes
N2: Metastases in the subcarinal or the ipsilateral mediastinal lymph nodes, including the ipsilateral internal mammary nodes
N3: Metastases in the contralateral mediastinal, contralateral internal mammary, ipsilateral, or contralateral supraclavicular lymph nodes
M: Presence of distant metastases
MX: Presence of distant metastases cannot be assessed
M0: No distant metastases
M1: Distant metastases present

Descriptions of stages of malignant pleural mesothelioma
Stage I
Ia: T1a N0 M0
Ib: T1b N0 M0
Stage II
T2 N0 M0
Stage III
Any T3 M0
Any N1 M0
Any N2 M0
Stage IV
Any T4
Any N3
Any M1

Source: The International Mesothelioma Interest Group [8, 9].