

Visceral Pleural Invasion: Pathologic Criteria and Use of Elastic Stains

Proposal for the 7th Edition of the TNM Classification for Lung Cancer

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on behalf of the International Staging Committee

Objective: To define the anatomic extent of visceral pleural invasion (VPI) and to assess whether elastic stains are useful to determine VPI in lung cancer. The elastic layer of the visceral pleura is not mentioned in the current International Union Against Cancer or American Joint Committee on Cancer staging documents.

Methods: A Pub Med search (www.pubmed.gov) of the National Library of Medicine was made for all articles published between 1970 and 2007 in humans under the search terms lung cancer and pleural invasion. These were reviewed for data regarding the pathologic classification of extent of pleural invasion including the use of elastic stains in this assessment.

Results: Six articles that addressed reported survival data using elastic stains to assess for VPI were reviewed. These articles defined P0 (T1) as lack of pleural invasion beyond the elastic layer, P1 (T2) as invasion beyond the elastic layer, P2 (T2) as invasion to the surface of the visceral pleura and P3 (T3) as invasion of the parietal pleura. In five studies, survival was shown to be significantly worse for VPI defined as P1 or P2 compared with P0.

Conclusions: Based on the currently available data, we propose that the next tumor, node, metastasis (TNM) revision by International Union Against Cancer and American Joint Committee on Cancer define VPI as invasion beyond the elastic layer (PL1) including invasion to the visceral pleural surface (PL2). The abbreviation PL for pleura is recommended rather than P to avoid confusion with the existing use of p (pathologic) TNM in distinction from c (clinical)

TNM. We also recommend that elastic stains be used in cases when the distinction between PL0 and PL1 is not clear based on evaluation of hematoxylin and eosin sections.

Key Words: Visceral pleural invasion, Lung cancer, Stage, Elastic stain, Pathology, Pleura.

(*J Thorac Oncol.* 2008;3: 1384–1390)

The anatomic extent of disease, as expressed by the tumor, node, metastasis (TNM) staging system, is the most important prognostic factor for lung cancer. Visceral pleural invasion (VPI) increases the T staging factor from T1 to T2 and upstages a tumor, even if less than 3 cm in size, from Stage IA to IB according to the TNM staging system for lung cancer by the 6th editions of the International Union Against Cancer (UICC) and American Joint Committee on Cancer (AJCC).^{1,2} This is important because adjuvant chemotherapy is sometimes considered for patients following complete resection for Stage IB non-small cell lung carcinoma (NSCLC) but has not been shown to be of value in Stage IA NSCLC.³ However, a precise definition of VPI is not provided in either the UICC or AJCC publications. In the UICC TNM Supplement, it is stated that “invasion of the visceral pleura (T2) includes not only perforation of the mesothelium, but also invasion of the lamina propria serosae.”⁴ This document does not provide criteria for what is invasion of the “lamina propria serosae” and whether this bears any relationship to the elastic layer of the visceral pleura. The elastic layer of the visceral pleura is not specifically mentioned in either the UICC or AJCC documents. In recent years, the use of elastic stains has been recommended for defining VPI. While this is becoming more accepted, there remains controversy regarding whether tumors that invade beyond the elastic layer but not to the pleural surface should be regarded as T1 or T2.^{5–7}

In 1988, Hammar, suggested a classification of pleural invasion that defined P0 as lack of pleural invasion beyond the elastic layer, P1 as invasion beyond the elastic layer, P2 as invasion to the surface of the visceral pleura and P3 as

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Disclosure: The authors declare no conflicts of interest.

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ISSN: 1556-0864/08/0312-1384

TABLE 1. Survival of NSCLC by Assessment of Visceral Pleural Invasion Using Elastic Stains

| Author, Year | Resected NSCLC Cases Studied | Frequency of VPI | Definition of VPI | Survival Data | Favor Elastic Stains |
|------------------------------|--------------------------------------|--|--|---|---|
| Bunker ML 1999 ³⁸ | 26 | P0: 12 (46%) P1: 8 (31%) P2: 6 (23%) | Hammar method ⁵ | Significantly worse survival with greater degrees of pleural involvement ($p = 0.0000$) | Yes |
| Manach 2001 ²⁹ | 1281 430 T1: 851 T2 | VPI: $n = 245$ (19%) | Hammar method ⁵ | Significantly worse 5 & 10 yr survival in VPI (35% and 28%) compared to no VPI (52% and 34%), $P = 0.000002$; VPI also independent factor in multivariate analysis | Yes |
| Kang JH 2003 ²⁸ | 439 T2: 234 IB; 95 IIB, 110 IIIA & B | VPI: 114 (26%) | Hammar method ⁵ | VPI assoc higher frequency of N2 or N3 ($p = 0.009$) VPI worse survival: ($p = 0.0006$) even with multivariate analysis | Yes |
| Osaki T 2004 ³⁰ | 474 T1 & T2 | P0: 345 (73%) P1: 110 (23%) P2: 19 (4%) VPI in 129 (27%) | Hammar method ⁵ | Degree of VPI independent prognostic factor by multivariate analysis ($p = 0.033$); P1 & P2 worse than p0, but survival for P1 vs. P2 not different | Yes Recommend P1 and P2 be designated as T2 |
| Shimizu K 2004 ⁷ | 1653 T1, T2 and T3 | P0:1055 (64%) P1: 271 (16%) P2: 81 (5%) T3: 246 (15%) VPI in 352 (21%) | Japanese Lung Cancer Society ⁶ | Survival identical for P1 or P2—significantly worse than for P0 disease for either ≤ 3 cm or >3 cm Worse survival for P1/P2 vs. P0 | Yes Data supports p0 as non-VPI and P1 or P2 as VPI |
| Shimizu K 2005 ³¹ | 1704 T1 and T2 | VPI in 288 (27%) | Japanese Lung Cancer Society ⁶ But used P0* as non-VPI and P1 or P2 as VPI similar to Hammar | 5 & 10 yr survival No VPI: 76 & 53% vs. VPI: 50 and 37% ($p < 0.0001$) VPI also significant by multivariate analysis | Yes VPI significant and independent for prognosis |

VPI, visceral pleural invasion; yr, year; NSCLC, non-small cell lung cancer.

invasion of the parietal pleura and/or chest wall.^{5,8} Hammar also included a category of Px that applied to tumors situated within the lung parenchyma with no relationship to the pleura. According to this scheme, P0 corresponds to T1, P1 or P2 correspond to T2 and P3 corresponds to T3. This approach has been used by several recent studies (Table 1) and the same levels of pleural invasion (except for Px) are recognized by the Japan Lung Cancer Society.⁶ However, according to the Japan Lung Cancer Society, it is required that the tumor invade to the surface of the visceral pleura (P2) to qualify for T2 and tumors that invade beyond the elastic layer but not to the pleural surface (P1) remain T1.⁶ In one study, visceral pleural involvement was defined as tumor extending to within 1 mm of the visceral pleural margin or involving the margin.⁹ So there is need for some clarification of the definition of pleural invasion in the staging of lung cancer.

Many pathologists are not inclined to do elastic stains in assessing the pleura for VPI. In a survey of lung cancer surgical pathology reports from the year 1991 performed by the College of American Pathologists (CAP), Gephardt et al.¹⁰ found that VPI was addressed in only 65% of cases. However, more recently Taube et al.¹¹ surveyed members of the American Association of Directors of Anatomic and

Surgical Pathology who consist of many of the leaders in the field of surgical pathology. Of 49 pathologists who responded, 51% never use elastic stains, 29% use them sometimes, and 20% use them routinely to assess for VPI in lung cancer specimens. Butnor et al.¹² recently used an internet based questionnaire to assess interobserver variability for VPI with a set of photomicrographs of the pleura with elastic stains in lung cancer specimens. The kappa statistic for agreement was “fair” with a value of 0.35. The majority of participants regarded invasion of the elastic layer as necessary for VPI.

In preparation for the Seventh edition of the UICC and AJCC TNM Classification for lung cancer staging, a series of white papers are being published by the International Association for the Study of Lung Cancer staging committee.^{13–18} Extensive statistical analysis of data from 67,725 cases of NSCLC submitted to the project forms the basis for most of the recommendations. As there was no detailed pathologic information regarding VPI submitted to the project the T Factor Committee was unable to perform an analysis of primary data on this subject. Because VPI is becoming established as an important T factor for lung cancer, this article makes recommendations regarding pathologic as-

assessment of the pleura based on analysis of data in the existing literature. The goal is to define pleural invasion in a manner that will allow for accurate collection of data regarding this important T factor for future analysis in a prospective database.

PATIENTS AND METHODS

A Pub Med search (www.pubmed.gov) of the National Library of Medicine was made for all articles published between 1970 and 2007 in humans under the search terms lung cancer and pleural invasion. These were reviewed for data regarding the pathologic classification of extent of pleural invasion including the use of elastic stains in this assessment. Studies with survival data on all NSCLC with at least 25 cases where elastic stains were used to assess for VPI using the criteria of either Hammar⁵ or the Japan Lung Cancer Society⁶ are summarized in Table 1. In addition standard documents such as the UICC TNM 6th Edition¹ including the TNM Supplement,⁴ AJCC Staging documents,² and protocols for the processing of lung cancer specimens from the CAP,^{19,20} Association of Directors of Anatomic and Surgical Pathology,²¹ the AJCC and Department of Health and Human Services Collaborative Staging Manual,²² and Royal College of Pathologists were reviewed.²³ In addition several recent reviews on the topic of pathology reporting of lung cancer specimens and VPI were reviewed.^{24–27}

RESULTS

One hundred ninety nine articles were obtained in the PubMed search. Although there were many articles with data addressing the issue of VPI, of those that met the above criteria, there were six articles that addressed reported survival data with respect to assessment of the visceral pleura using elastic stains for staging of lung cancer. Each of these articles reported data that supports the use of elastic stains in documenting VPI in cases where the status of invasion is indeterminate based on review of hematoxylin and eosin (H&E) stained sections.

In five studies, survival was shown to be significantly worse for VPI defined as P1 or P2 compared with P0 according to the Hammar criteria.^{7,28–31} In only two studies by Shimizu et al.,⁷ and Osaki et al.,³⁰ data were analyzed comparing P1 versus P2 levels of pleural invasion and both showed no difference in survival.

Review of current documents for lung cancer specimen processing from the CAP,^{19,20} Association of Directors of Anatomic and Surgical Pathology,²¹ the AJCC/Department of Health and Human Services Collaborative Staging Manual,²² and the Royal College of Pathologists, revealed that only the Royal College of Pathologists specifically recommends that elastic stains may be helpful in recognition of pleural invasion.²³ An upcoming revised version of the CAP lung cancer guidelines states that VPI should include tumors that penetrate beyond the elastic layer of the visceral pleura and that elastic stains may aid in the assessment of pleural invasion.³² The 2000 Classification of Lung Cancer by the Japanese Lung Cancer Society defines p1 as “invasion beyond the visceral elastic pleura, but limited to the pulmonary pleura”

and p2 as “definite invasion to the surface of the pulmonary pleura”. However, they require p2 for classification of T2 so p1 remains T1.⁶

Several recent reviews of lung cancer pathology specimen evaluation point out the need for more accurate assessment of the pleura with the use of elastic stains to assess for VPI.^{24–27}

DISCUSSION

Proposal for Classification of VPI in TNM Revision

Based on the currently available data, we propose that the next TNM revision by UICC and AJCC define VPI as invasion beyond the elastic layer (Figure 1). We also suggest a slight modification of the Hammar diagram of the pleura with designations of PL for pleura, rather than P, which is also used by TNM for designation of *pathologic* versus *clinical* staging. Therefore PL0 represents either tumor within

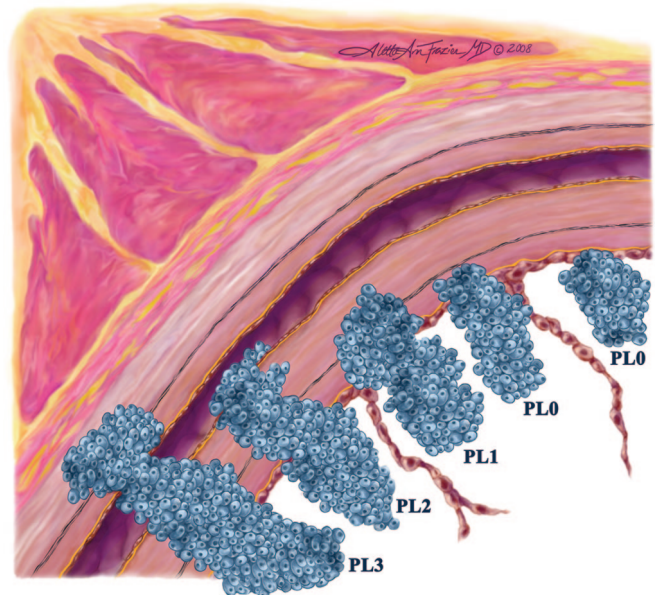


FIGURE 1. Modified Hammar Classification⁴⁸ of visceral pleural invasion (VPI) for lung cancer. The different clusters of blue cells represent tumors with varying levels of VPI. PL0 represents either tumor within the subpleural lung parenchyma or invading superficially into the pleural connective tissue beneath the elastic layer. If a tumor invades beyond the elastic layer it is PL1. Tumors that invade to the pleural surface are PL2 and those that invade into any component of the parietal pleura are PL3. PL0 is not regarded as a T descriptor and the T category should be assigned on other features. PL1 or PL2 indicate VPI and are a T2 descriptor. PL3 indicates invasion of the parietal pleura and is a T3 descriptor. Reprinted with permission from Aletta Ann Frazier, MD.

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the subpleural lung parenchyma or invading superficially into the pleural connective tissue beneath the elastic layer. If a tumor invades beyond the elastic layer it is PL1. Tumors that invade to the pleural surface are PL2 and those that invade into any component of the parietal pleura are PL3. PL0 is not regarded as a T descriptor and the T category should be assigned on other features. PL1 or PL2 indicate VPI and are a T2 descriptor. PL3 indicates invasion of the parietal pleura and is a T3 descriptor. In addition, we recommend that the Px category proposed by Hammar, be discontinued in this context, and if used at all, be reserved for use as the “x” category is used elsewhere in the TNM classification, i.e., where the PL category is unknown (PLx).

If a tumor achieves T2 status based on VPI, and it is 5 cm or less in size it is classified as T2a. If such a tumor is greater than 5 cm but 7 cm or less in size it is T2b. If it is larger than 7 cm it becomes T3.

We also recommend that elastic stains be used in cases where it is difficult to distinguish PL0 from PL1 status on review of H&E stains for VPI. It is the thick elastic layer within the visceral pleura that should be invaded. The location of this thick elastic layer is variable sometimes being situated close to the alveolar parenchyma and in other cases being closer to the middle of the visceral pleural connective tissue. The tumor needs to cross beyond this thick elastic layer for PL1 classification. In some cases there is a perceptible connective tissue layer between the lung parenchyma and the thick elastic layer; invasion of this connective tissue that falls short of traversing the elastic layer is regarded as PL0. A tumor remains classified as PL0 if tumor cells intermingle with elastic fibers without penetration beyond the elastic layer. In some cases the elastic fibers can be visualized on H&E by lowering the microscope condenser. However, the elastic layer is often completely imperceptible on H&E and only visualized with elastic stains; these cases are regarded as “indeterminate for VPI” on H&E alone. In difficult cases where the visceral pleura elastic layer is not clearly discernible or there is prominent reduplication of the elastic fibers, one has to apply General Rule 4 of the TNM classification and assign the lower category in such circumstances.³³

Histologic assessment of the pleura with elastic stains should be performed on the histologic section(s) where there is the greatest concern for VPI. Histologic sampling of the pleura in the lung cancer resection specimen should be obtained in the area where there is the greatest concern for invasion by gross examination.

Rationale for Assessment of VPI

There are multiple studies demonstrating the prognostic significance of VPI in NSCLC,^{7,28–31,34} especially those that use the Hammar method for evaluating lung cancer specimens for VPI.^{7,28–31} The studies by Kang et al., Manac’h et al., Osaki et al., and Shimizu et al. reported that VPI correlated with worse survival even in multivariate analysis.^{28–31} Kang et al. also demonstrated that VPI was an adverse prognostic factor in T2 NSCLC and it correlated with more extensive mediastinal lymph node involvement.²⁸ Shimizu et al. showed that VPI was a significant independent adverse

prognostic factor in NSCLC with or without lymph node metastases.³¹

Several older studies suggest there is no impact of VPI on survival in small, early stage NSCLC.^{35,36} However, neither the Padilla nor Martini studies used either the detailed Hammar approach to pathologic assessment or elastic stains to evaluate the specimens for VPI.^{35,36} Furthermore, the Padilla study only had 158 patients³⁵ and the Martini study of 598 Stage I NSCLC found VPI had a *p* value of 0.06 which is close to being significant for overall survival.³⁶ In a recent paper, Ou et al.³⁷ report data from the California Cancer Registry that suggest that VPI carries an increased risk of mortality and that it may vary depending on tumor size. However, in this study the Surveillance, Epidemiology, and End Results code EOD40 does not distinguish between VPI, hilar atelectasis or obstructive pneumonitis, so VPI could not be specifically analyzed.³⁷ In addition, there are limited data regarding the question whether there is a difference in the significance of VPI as an adverse prognostic factor according to tumor size with a greater significance to VPI in larger (>3 cm) compared with smaller (\leq 3 cm) tumors.^{7,36} While Martini et al.³⁶ did not find VPI to be a significant adverse prognostic factor in Stage I NSCLC overall, in tumors over 3 cm in size it was significant. Shimizu et al. suggested that VPI in a tumor larger than 3 cm should be classified as T3 rather than T2 as recommended by the previous Sixth Editions of the UICC and AJCC staging systems and the revision proposal by the International Association for the Study of Lung Cancer (IASLC) staging committee.^{1,2,7,13,16} However, Shimizu et al.⁷ found that VPI significantly correlated with worse outcome in tumors smaller than 3 cm. The IASLC Staging committee choose to give equal weight to the nonsize T2 factors of (1) VPI, (2) involving the main bronchus 2 cm or more distal to the carina and atelectasis or (3) obstructive pneumonitis that extends to the hilar region but does not involve the entire lung.^{13,16} The question of the effect of tumor size on the impact of VPI remains to be determined in studies of larger numbers of cases such as the prospective IASLC database.

Usefulness of Elastic Stains

In most cases an elastic stain is not needed to assess the pleura for invasion. Only in cases where the distinction between PL0 and PL1 is unclear on H&E sections, is an elastic stain needed. Elastic stains may also be helpful in cases where the visceral and parietal pleura are adherent, making it difficult to know where is the visceral pleural surface and the parietal pleura. The usefulness of elastic stains for VPI has been emphasized recently by Taube et al.¹¹ who in a series of 100 NSCLC smaller than 3 cm in size, demonstrated that VPI could be identified in 19% of cases where no VPI was seen on H&E stains only. Therefore these tumors were changed from Stage IA to Stage IB. They also found VPI occurred in all histologic types of NSCLC except for bronchioloalveolar carcinoma.¹¹ Bunker et al.³⁸ found in a series of 26 cases that the use of elastic stains changed the pathologic stage in 1 case or 4% of lung cancers overall. They also found penetration of the elastic layer in 8/20 cases (40%) that were indeterminate for pleural invasion and were missed

on examination of routine H&E sections. However, because of other T factors, this only increased the stage from T1 to T2 in 1/20 cases (5%).³⁸ In 1/20 cases (5%), the use of elastic van Gieson stains helped to exclude VPI that had been overcalled on H&E, so it decreased the stage from T2 to T1.³⁸ In summary, among the 20 cases indeterminate for VPI on H&E examination, Bunker et al.³⁸ found that elastic stains for VPI changed the overall assessment of VPI in 9/20 (45%) of cases (8 cases T1 to T2, 1 case T2 to T1), however, because of other T factor status, the actual T stage for the patient changed in only 2/20 (10%) cases.

Several types of elastic stains can be used including Verhoeff's elastic van Gieson stain, Elastin hematoxylin and eosin, Weigert's elastic stain, and the Movat or pentachrome stain.³⁹ The decision on which stain to use is largely a factor of which one the histology staff and pathologists are the most comfortable performing and interpreting, respectively.

Anatomy of the Pleura

To best assess VPI in lung cancer specimens, it is helpful to consider the microscopic anatomy of the visceral pleura. For the purpose of evaluating the visceral pleura for VPI, if a tumor invades past the elastic layer that is closer to the alveolar lung parenchyma then it is classified as PL1 (T2); if it does not penetrate this elastic layer, it is PL0 (T1). The visceral pleural anatomy has previously been described to have five layers that are best appreciated with elastic stains.^{5,38,40} However, there is some variation in the number and composition of tissue layers in the visceral pleura and most commonly there are only four layers that can reliably be identified. In general, moving from the visceral pleural surface to the lung parenchyma, the visceral pleura consists of: (1) a single layer of mesothelial cells resting on a basement membrane, (2) a submesothelial connective tissue layer, (3) elastic fibers that usually form a single prominent layer, but may also form a second discontinuous layer (the fifth layer sometimes described) with varying amounts of fibrous connective tissue between the 2 elastic layers, (4) a connective tissue layer of varying thickness that separates the elastic layer from the lung parenchyma which is demarcated by a layer of pneumocytes resting on a thin basement membrane (Figure 1). So the number of layers in the visceral pleura may vary from four to six. The thick elastic fiber layer is regarded as the demarcation between PL0 and PL1. So if a tumor invades the connective tissue of the pleura below the thick elastic layer without penetrating it, the tumor is classified as PL0. The articles cited in Table 1 that report data supporting the use of elastic stains for assessment of VPI do not refer to more than one elastic layer, so their results are consistent with our recommendation of using the thick elastic layer as the limit between PL0 and PL1, regardless of whether it is closer to the lung or the visceral pleural surface. If there happens to be two thick elastic layers, if the one nearest the lung parenchyma is penetrated, this would qualify as PL1.

The anatomy of the parietal pleura is more variable than the visceral pleura. In general it is covered by a mesothelial layer that rests upon a basement membrane and a thin layer of loose connective tissue. This is followed by a discontinuous elastic layer, then another layer of loose connective tissue.

Below this lies a dense collagenous layer or endothoracic fascia that may have varying amounts of fat on both sides and after this are the skeletal muscle fibers of the chest wall. A tumor is classified as PL3 (T3) if it invades any of the anatomic structures of the parietal pleura. There is no data evaluating lung cancer survival according to different levels of invasion of the parietal pleura. Given the variability of the parietal pleural anatomy, this may be difficult to achieve.

Problems in Interpretation of Elastic Stains

Elastic stains are very helpful in distinguishing some cases of PL0 from PL1 VPI, but they do not solve all difficult problems. There are a number of problematic issues that need to be considered in evaluating the visceral pleura for invasion. The normal visceral pleura anatomy shows some degree of variation; however, significant anatomic alterations occur when the pleura is affected by inflammation and fibrosis. These changes are frequent in the setting of lung cancer where the tumor is situated beneath the pleura or if it invades the pleura. Pleural puckering is a common finding in subpleural tumors, particularly adenocarcinomas. Gallagher et al.⁴¹ pointed out that the visceral pleural elastic layer could be invaded in 3 patterns: (1) without eliciting any secondary changes, (2) with prominent elastic reduplication and inflammatory infiltrate, and (3) with thick fibroblastic proliferation. It may be very difficult to assess for pleural invasion when there is reduplication of elastic layer leading to many layers of elastic fibers. When there is pleural puckering sometimes VPI occurs in an area where the pleura invaginates into the lung along an interlobular septa. Elastic stains can also help to define VPI in cases where there are dense fibrous adhesions between the visceral and parietal pleura causing fusion and obliteration of the pleural space.

Invasion of the parietal pleura often is highlighted by tumor growing into fat. Since fat can be present within the connective tissue of the visceral pleura, especially when there is underlying pulmonary fibrosis, the presence of tumor cells within fat should not be assumed to represent parietal pleural invasion unless the surgical specimen includes parietal pleura in the area being examined.

Problems with the Interlobar Fissure

According to the current TNM "a tumor with local invasion of another ipsilateral lobe without tumor on the visceral pleural surface should be classified as T2."⁴ In contrast, according to the 2000 Classification of Lung Cancer by the Japanese Lung Cancer Society, "invasion of the adjacent lobes where the interlobar borderline should be in case with incomplete lobe formation should be recorded as P0," which is classified as T1.⁶ Unfortunately the data on this point are not definitive as the few studies that address this problem have small numbers of patients.⁴²⁻⁴⁴ Miura et al.⁴³ report 18 patients including 8 that were N0M0, 6 N1M0 and 4 N2M0. They found the 5-year survival of 34% for these patients was significantly better ($p < 0.001$) than the 14% for patients with parietal pleural invasion (PL3) and no different from those with only VPI. Pneumonectomy was performed in 4, bilobectomy in 4, and lobectomy with parietal resection with a "sufficient safety margin" was performed in 10 cases.

Based on these data they recommended that invasion beyond the interlobar pleura should be classified as T2. Two other studies favored classification as T3. Demir et al.⁴² reported 60 of 351 NSCLC cases that had minimal invasion of the adjacent lobe including 40 treated with pneumonectomy, 10 with bilobectomy, and 10 with lobectomy plus partial adjacent lobe resection. There were 23 N0, 29 N1, and 8 N2 patients in this group. Five year survival for the adjacent lobe invasion group was 36% which was significantly poorer than survival for T2 patients in multivariate analysis ($p = 0.049$), but not significantly different from survival of patients with T3 patients. Therefore these authors recommended that invasion beyond the interlobar pleura be classified as T3.⁴² Okada et al.⁴⁴ reported 19 patients including 6 N0M0, 7 N1M0, and 6 N2M0 cases that showed a 5-year survival of 37%. Because this was similar to the 40% and 38% 5-year survival for their patients with invasion of the parietal pleura and chest wall, they recommended interlobar pleural invasion be classified as T3.⁴⁴

These studies have not completely resolved this question. Interestingly the 5-year survival is virtually identical in each study (34–37%), but one study favors classification of interlobar invasion as T2 and 2 studies favor T3. This is complicated by the fact that in some cases with no fissure, invasion of the adjacent lobe can occur across the lung parenchyma without involvement of the visceral pleura. More data from larger studies will be required to resolve whether the T2 classification by the 6th edition of the UICC/AJCC staging system^{1,2} or the T1 classification by the Japanese Lung Cancer Society proposal (T1) are appropriate.⁶

Anatomic variation of the interlobar fissure can potentially impact clinical and pathologic assessment of lung cancers for involvement of adjacent lobe(s). This includes an incomplete interlobar fissure⁴⁵ or fusion of the adjacent lobes.⁴⁶ Craig et al.⁴⁷ proposed a classification of pulmonary fissures ranging from Grade 1 with a complete fissure with entirely separate lobes, Grade 2 with complete visceral cleft but parenchymal fusion at the base of the fissure, Grade 3 with a visceral cleft for part of the fissure and Grade 4 with complete fusion of the lobes with no apparent fissural line. Kamiyoshihara et al.⁴⁵ found incomplete interlobar fissures in 74 (31%) of 239 NSCLC but there was no difference in survival or recurrence compared with patients with complete fissures. Nomori et al.⁴⁶ addressed this problem from the point of view of surgical technique when attempting video assisted thoracoscopic surgical lobectomy and found this approach to be satisfactory in most patients with largely fused fissures. Determination of the appropriate T factor designation for invasion of adjacent lobes of lung cancers will require careful attention by surgeons and pathologists to the status of completeness or incompleteness of the interlobar fissures.

CONCLUSION

In the 7th edition TNM proposal we recommend the use of a modified Hammar Classification for pathologic assessment of VPI. VPI is defined as invasion beyond the elastic layer (PL1) including invasion to the visceral pleural surface (PL2). We also recommend the use of elastic stains when the

distinction between PL0 and PL1 is not clear based on evaluation of H&E sections. Because of the impact of T1 versus T2 status on survival and the consequent discussions regarding adjuvant chemotherapy after complete resection for Stage IA versus IB NSCLC patients, the use of elastic stains may be clinically important. Hopefully this recommendation will result in more careful attention to pathologic assessment of the visceral pleura in the evaluation of lung cancer specimens. Study of larger numbers of cases with careful documentation of VPI will hopefully provide an answer to the question whether size has any impact on the significance of this T factor. Until sufficient data is available to address this issue, our recommendation is to maintain the current TNM recommendation that “a tumor with local invasion of another ipsilateral lobe without tumor on the visceral pleural surface should be classified as T2.”⁴ Hopefully these issues will be resolved in the prospective IASLC lung cancer staging project.

ACKNOWLEDGMENTS

Eli Lilly and Company provided funding to support the International Association for the Study of Lung Cancer (IASLC) Staging Committee's work to suggest revisions to the 6th edition of the TNM classification for Lung Cancer (staging) through a restricted grant. Lilly had no input into the Committee's suggestions for revisions to the staging system. The project was also supported by the AJCC grant "Improving AJCC/UICC TNM Cancer Staging." The authors gratefully acknowledge input and suggestions from Drs. Kelly Butnor, Douglas B. Flieder, Samuel P. Hammar, Alberto Marchevsky, Victor Roggli, Dori Giroux, and Gabriel Sicca.

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