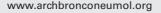


ARCHIVOS DE BRONCONEUMOLOGIA





Original Article

Usefulness of Video-assisted Thoracoscopy for Correctly Staging Tumors as T3 Because of Chest Wall Invasion

Gregorio Gallardo-Valera, Ana Triviño-Ramírez, Miguel Congregado, Rafael Jiménez-Merchán, Francisco Javier Ayarra Jarné, and Jesús Loscertales*

Servicio de Cirugía General y Torácica, Hospital Universitario Virgen Macarena, Sevilla, Spain

ARTICLE INFO

Article history: Received October 28, 2008 Accepted March 18, 2009 Available online May 17, 2009

Keywords: Exploratory video-assisted thoracoscopy Surgical staging T3 lung cancer because of chest wall invasion

Palabras clave: Videotoracoscopia exploradora Estadificación quirúrgica Cáncer de pulmón T3 por invasión parietal

ABSTRACT

Background: Exploratory video-assisted thoracoscopy (EVT) can be used to assess the resectability of lung carcinomas. The aim of this study was to investigate the usefulness of this technique for distinguishing between tumors that invade the chest wall and should be staged as T3 and tumors that have been incorrectly staged as T3 on the basis of imaging studies.

Patients and Methods: From March 1993 through December 2007, we studied 1277 patients, of whom 150 (137 men and 13 women; age range, 28–81 years) presented tumors classified as cT3 because of chest wall invasion on the basis of imaging studies.

Results: After exploratory EVT, 44 pT3 tumors with chest wall invasion were confirmed intraoperatively and by histopathology. Of these, 36 had been correctly classified as cT3 by computed tomography or magnetic resonance imaging. However, tumors had been understaged as cT2 in 6 patients and overstaged as cT4 in 2 patients. The sensitivity, specificity, and positive and negative predictive values obtained were 100%. *Conclusions:* We believe that exploratory EVT is clearly better than computed tomography and/or magnetic

resonance imaging for detecting chest wall invasion. In addition to correctly staging a tumor as T3 because of chest wall invasion, the technique can also help decide the best surgical approach in each case.

© 2008 SEPAR. Published by Elsevier España, S.L. All rights reserved.

Utilidad de la videotoracoscopia para una correcta estadificación de tumores T3 por invasión de pared

RESUMEN

Introducción: La videotoracoscopia exploradora (VTE) es una técnica que permite valorar la resecabilidad del carcinoma de pulmón. El objetivo de este trabajo ha sido comprobar su utilidad para diferenciar los verdaderos tumores T3 por invasión parietal de aquellos que se estadificaron de forma incorrecta por las pruebas de imagen.

Pacientes y métodos: Desde marzo de 1993 hasta diciembre de 2007 se estudió a 1.277 pacientes, de los que 150 (137 varones y 13 mujeres; rango de edad: 28–81 años) presentaron tumores estadificados como cT3 por invasión parietal en las pruebas de imagen.

Resultados: Tras la realización de la VTE, los tumores pT3 por invasión parietal confirmados intraoperatoriamente y mediante estudio anatomopatológico fueron 44. De ellos, 36 se habían clasificado correctamente como cT3 por tomografía computarizada o resonancia magnética. Se observó además que 6 casos habían sido infravalorados como cT2, y otros 2 supravalorados como cT4. La sensibilidad, especificidad y valor predictivo tanto positivo como negativo obtenidos en nuestra serie han sido del 100%. *Conclusiones:* En nuestra opinión, la VTE es una técnica claramente superior a la tomografía computarizada y/o resonancia magnética para detectar infiltración de pared, por lo que, además de estadificar correctamente la situación tumoral T3 por invasión parietal, permite decidir la vía de abordaje adecuada para cada caso.

© 2008 SEPAR. Publicado por Elsevier España, S.L. Todos los derechos reservados

* Corresponding author: *E-mail address:* jloscert@us.es (J. Loscertales).

0300-2896/\$ - see front matter © 2008 SEPAR. Published by Elsevier España, S.L. All rights reserved.

Introduction

Lung cancer is currently the leading cause of cancer-related deaths in men, and its incidence continues to increase, particularly in women.¹ Prognosis is very poor in patients with advanced stages of the disease and, to date, the only known treatment with curative intent is surgery. In the TNM staging system, patients with T3 tumors represent a large group with relatively advanced disease who may benefit from surgery.

According to the classification of the American Joint Committee on Cancer, bronchogenic carcinoma is stage T3 when a tumor, regardless of its size, directly invades the chest wall (including tumors of the superior sulcus), diaphragm, mediastinal pleura, or parietal pericardium; when any tumor is located in the main bronchus less than 2 cm from but without invading the tracheal carina; or when the tumor causes atelectasia associated with obstructive pneumonitis of the entire lung with or without pleural effusion.

Diagnosis of T3 tumors requires combinations of different exploratory studies. Computed tomography (CT) is currently the technique of choice for assessing tumor spread and the extent of infiltration/invasion of adjacent structures. It is accepted that both CT and magnetic resonance imaging (MRI) can detect mediastinal invasion (although neither can rule out minimal invasion).^{3,4}

Any peripheral lung tumor can infiltrate the parietal pleura and invade the chest wall. When the chest wall is involved, invasion has a negative impact on the patients' prognosis but is not a contraindication for tumor resection.⁵⁻⁷

CT is useful in preoperative assessment for determining whether or not the chest wall has been infiltrated, with a reported sensitivity between 38% and 87% and a specificity between 40% and 90%.^{8.9} MRI has a similar diagnostic accuracy to CT for detecting wall infiltration (CT, 56%-89%; MRI, 50%-93%).^{3.4}

Chest wall involvement can also be satisfactorily assessed using ultrasonography.⁹ However, the best indicator of infiltration is localized pain,⁶ which is generally present when invasion is evident and particularly if the intercostal nerves are affected. Nevertheless, the staging system still has large gaps, which can be filled with thoracotomy or exploratory video-assisted thoracoscopy (EVT).

One of the problems associated with the resection of tumors classified as T3 because of chest wall invasion is the access route. When such invasion is present, wide posterolateral thoracotomy is needed to facilitate resection of the wall, excision of the lung tumor, and subsequent reconstruction of the chest wall. However, when the invasion is diagnosed on the basis of imaging studies alone and found not to be present during the operation, a Noirclerc lateral amyotonic thoracotomy or even video-assisted thoracic surgery (VATS) would have been sufficient for lung resection.

Thus, some authors, such as Wain,¹⁰ Roviaro et al,¹¹⁻¹³ our group,^{14,15} and Yim¹⁶ suggest that EVT (or "video operative staging" according to the terminology used by Roviaro et al or "last minute staging" according to Yim) would be particularly useful in tumors staged as T3 because of chest wall invasion as the first step in lung resection to provide a final staging before proceeding to thoracotomy. The use of EVT to detect whether invasion is present can, among other things, guide the choice of the most appropriate approach for each patient (lateral and sometimes posterolateral thoracotomy in T3 tumors, and VATS in the remaining cases).

The objective of this study was to confirm the usefulness of EVT in staging T3 tumors that invade the chest wall. The presence of invasion would allow tumors that should actually be staged as T3 to be distinguished from those that appear so in the imaging studies. At the same time, such a distinction would point to the most appropriate approach, that is, an aggressive procedure with substantial muscle incision (wide posterolateral thoracotomy) in cases of correctly staged T3 tumors—involving chest wall resection and subsequent reconstruction with a prosthesis and/or muscle flaps—or a relatively unaggressive amyotonic incision, such as Noirclerc-type lateral thoracotomy or even VATS resection. An appropriate choice of approach would ensure that the patient undergoes as unaggressive surgery as possible, thereby improving the chance of a satisfactory outcome.

Patients and Methods

The present retrospective study was conducted in the General and Thoracic Surgery Department (Prof Loscertales) of the Hospital Universitario Virgen Macarena, Seville, Spain.

From March 1993 through December 2007, 1381 patients underwent surgery for lung cancer. In all cases, EVT was attempted as a first exploratory step. In 104 patients, EVT was not possible due to technical problems (firm adherence, lack of lung collapse), whereas in the remaining 1277 use of the technique managed to determine the exact status of the tumor, lymph nodes, and pleural metastases not associated with clinical suspicion; that is, a final staging was achieved.

Of these 1277 cases, 346 had been staged as cT3 in imaging studies and, of these, 150 were staged as cT3 because of chest wall invasion (139 by CT and 11 by MRI). These 150 patients were included in the present study. In 7 of these patients who had reported local chest pain, bone scintigraphy was done to rule out distant metastases. Four patients experienced chest pain indicative of chest wall invasion that was not subsequently found in the intervention.

The ages of the patients (137 men [91.33%] and 13 women [8.77%]) ranged from 28 to 81 years (mean, 61 years) for men and from 31 to 78 years (mean, 51 years) for women.

The technique used, which we denote as EVT, involved surgical exploration of the pleural cavity on the affected side in order to assess the tumor and its size, lymph node involvement, possible unsuspected pleural metastases, and the real feasibility of resection. Since 1992, this has been done systematically for all patients attended in our department as the first step in the intervention, prior to thoracotomy or VATS resection. Patients were placed in lateral decubitus and 3 entry incisions were made, the first at the mid axillary line in the seventh or eight intercostal space to introduce the 0° telescope (Karl Storz[®]), another below the scapula, and the third in the third or fourth intercostal space at the anterior axillary line, depending on the anatomy of each patient. These incisions were used to introduce the instruments necessary for an appropriate examination of the entire surgical field, which required not just visualization of the pleural cavity and the tumor, but also-given that this was a surgical exploration-the pulmonary hilum and lymphatic drainage areas (by dissection and sampling for intraoperative analysis). Possible chest wall invasion was also confirmed (Figures 1 and 2) and samples were taken for biopsy if necessary. Biopsies were taken in all cases in which chest wall invasion was confirmed by EVT, with samples of the parietal pleura taken at the point of greatest infiltration.

Although not an objective of the present study, EVT also allows the pericardium to be opened to perform a video-assisted pericardioscopy. This technique, which has been described by our group^{17,18} and modified by other authors,^{19,20} can be used to examine pulmonary vessels when such a study cannot be done outside the pericardium due to tumor invasion. These findings can help the surgeon to decide whether to perform an intrapericardial pneumonectomy.

Results

Of the 1277 patients who underwent EVT, lung resection was not possible in 141 due to tumor invasion or pleural metastases not detected in CT or MRI. In the remaining 1136 patients, surgical

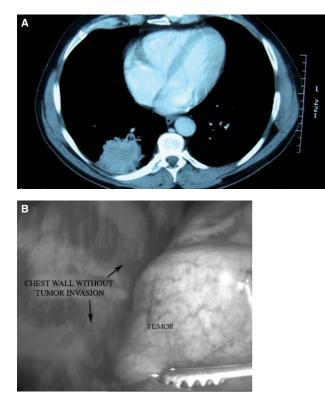


Figure 1. In the computed tomography image the tumor appears to invade the wall (*a*) but the exploratory video-assisted thoracoscopy shows there is no invasion (*b*).

resection was completed satisfactorily (using VATS in 260 cases, lateral thoracotomy in 478, and posterolateral thoracotomy because of large hilar tumors or the large size of the tumor in 398).

Of the 150 cases staged as cT3 because of chest wall invasion (139 by CT and 11 by MRI), only 36 (24%) were pT3 in EVT, that is, there was an error in T staging of these tumors by CT and/or MRI in 76%. In contrast, in thoracotomies performed immediately after EVT for chest wall and lung resection, it was found that all cases had been correctly assessed, and this was confirmed by the pathology report, which showed chest wall invasion. In all cases, the entire wall thickness was involved, including costal bone, even though only 7 patients referred pain in the preoperative period.

We should also highlight that in 8 patients (those with parietal pleural involvement without bone involvement), both clinical overstaging and understaging had occurred as 6 were classified as cT2 and another 2 as cT4 (due to mediastinal involvement). In the EVT, it was found—and confirmed on thoracotomy—that they were actually pT3 because of chest wall invasion. This highlights once again the suitability of EVT—more than CT and/or MRI—for assessing wall invasion by the lung cancer.

These 44 patients underwent chest wall resection and the appropriate type of lung resection. The site was on the right side in 33 patients (75%) (26 in the upper lobe, 1 in the middle lobe, and 6 in the lower lobe) and on the left side in 11 (25%) (9 in the upper lobe and 2 in the lower lobe).

In the 114 patients with cT3 tumors in the imaging studies that turned out to be false positives in EVT (76%), the staging obviously changed. The stage decreased in 77 patients—5 to pT1 (3.3%) and 72 to pT2 (48%)—but increased in 37 to pT4 (24.7%) (in 30 cases because of large vessel involvement, 4 because of cardiac infiltration confirmed by video-assisted pericardioscopy, and 3 because of esophageal invasion).

It is important to highlight that the approach in the 44 patients with correctly staged T3 tumors confirmed in EVT who underwent

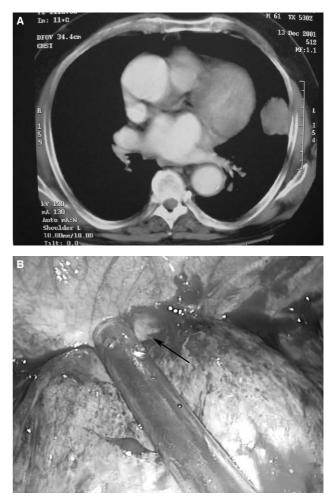


Figure 2. *a*) Computed tomographic image (mediastinal window) in which the tumor appears to invade the wall, and *b*) detail of the wall invasion during video-assisted thoracoscopy (arrow), proven with intraoperative biopsy: stage pT3 after exploratory video-assisted thoracoscopy.

chest wall and lung resection was posterolateral thoracotomy. In contrast, in the remaining patients with tumors classified as cT3 because of chest wall invasion (n=114), which were not confirmed by EVT, the approach was posterolateral thoracotomy in 24 patients, lateral thoracotomy in 72, and VATS in 18.

Thus, thanks to EVT before thoracotomy, 90 posterolateral thoracotomies—the most aggressive approach and the one with most sequelae—were avoided.

Histology of correctly staged T3 tumors demonstrated by EVT and confirmed during the intervention was as follows: 27 squamous cell carcinomas (61.36%), 16 adenocarcinomas (36.36%), and 1 oat cell carcinoma (2.27%).

The specificity and sensitivity of EVT in our series were both 100% compared to CT and/or MRI, which had values of 89.3% and 81.8%, respectively. We should likewise highlight that both the positive and negative predictive values were also 100%, much better than the results obtained with the imaging studies (positive predictive value of 23.6% and negative predictive value of 99.18%).

Discussion

TNM staging of lung carcinoma is the cornerstone of the therapeutic approach and prognosis in these patients. In recent years, video-assisted thoracoscopy has undergone a notable growth both in indications for staging and in the treatment of such patients.

Its utility and efficacy were demonstrated initially by Wain¹⁰ and Roviaro et al,¹¹⁻¹³ and subsequently by our group,^{14,15} Yim,¹⁶ Sihoe and Yim,²¹ Hoffmann,²² and Sebastián-Quetglas et al,²³ all of whom confirmed the validity of the technique for staging lung cancer. Hoffmann²² and Thomas et al²⁴ affirmed that it is an important complement to the usual diagnostic techniques, and some authors, such as our group,^{14,15} even maintain that it is superior to other techniques such as CT and MRI for diagnosis of T4 tumors due to intrapericardial vascular invasion.^{17,18}

With regard to the objective of our study, the assessment of a tumor staged as T3 because of chest wall invasion, not only could EVT detect tumors erroneously staged as T3 in the imaging studies (in our series, 114 out of 150 cT3 cases) but it could also demonstrate that some tumors staged clinically as T2 (n=6) or T4 (n=2) were actually T3 tumors due to chest wall invasion. This could only be achieved by EVT although, logically, thoracotomy would also have correctly staged these tumors. With EVT, it is therefore possible to accurately stage the tumor in terms of chest wall invasion (the objective of our study) with a specificity, sensitivity, and positive and negative predictive value of 100%; that is, there were no T3 tumors (whether suspected or not in the imaging studies) mistakenly staged according to subsequent chest wall and lung resection and histological study of the piece, which in all cases confirmed wall invasion by the lung tumor. These findings are consistent with results published by other authors.25,26

In addition to the accuracy of T3 staging because of chest wall invasion, EVT has a further advantage in that it can help decide the most appropriate surgical approach in each case because, inevitably, in correctly staged T3 tumors, posterolateral thoracotomy is unavoidable for en bloc removal of the lung (in its entirety or 1 or 2 lobes) with the corresponding wall. This was the case in 44 patients in our series. By contrast, different approaches may be used to manage the tumors shown by EVT to have been incorrectly staged as T3 in the imaging studies. Thus, an amyotonic lateral thoracotomy was performed in 72 patients, VATS in 18 patients, and posterolateral thoracotomy in 24 due to the size and/or site of the tumor.

In short, EVT is, in our opinion, the examination that best defines T3 tumors because of chest wall invasion, given that with CT—as indicated by Gdeedo et al²⁷—agreement is only 35% between imaging data and surgical findings. T staging is therefore only correct in 54% of the patients, and 27% are assigned a higher and 18.9% a lower stage. These data are similar to those obtained by us for the relationship between CT and EVT.

We should point out the importance of EVT for staging the process and for assessing the therapeutic indications of patients in whom imaging studies reflected an incorrect staging, particularly in the case of cT3 because, as we have seen, the T stage changes in 76% after EVT, with 51.3% moving to a lower stage (pT2 or pT2) and 24.7% to a higher stage (pT4).

In conclusion, EVT is a very useful technique for refining the staging in tumors staged as T3 because of chest wall invasion. EVT can correct understaging when T3 tumors have been staged as T2 on the basis of imaging studies It is also useful in identifying tumors that have been incorrectly staged by CT as T4 and that are actually stage T3. It is also a beneficial technique when chest wall involvement might affect the preferred access to the thorax. The technique is therefore appropriate for confirming or ruling out T3 staging with greatest clinical certainty, and, thanks to EVT, posterolateral thoracotomy—an excessively aggressive access for tumors that are

not really stage T3 and involve no chest wall invasion-can be avoided.

References

- 1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, et al. Cancer statistics. 2008 CA. Cancer J Clin. 2008;58:71-96.
- Mountain CF. Revisions in the International System for Staging Lung Cancer. Chest. 1997;111:1710-7.
- Godelman A, Haramati LB. MR imaging in diagnosis and staging of pulmonary carcinoma. Magn Reson Imaging Clin N Am. 2008;16:309-17.
- Plathow C, Aschoff P, Lichy MP, Eschmann S, Hehr T, Brink I, et al. Positron emission tomography/computed tomography and whole-body magnetic resonance imaging in staging of advanced non-small cell lung cancer – initial results. Invest Radiol. 2008;43:290–7.
- Lin YT, Hsu PK, Hsu HS, Huang CS, Wang LS, Huang BS, et al. En bloc resection for lung cancer with chest wall invasion. J Chin Med Assoc. 2006;69:157-61.
- Voltolini L, Rapicetta C, Luzzi L, Ghiribelli C, Ligabue T, Paladini P, et al. Lung cancer with chest wall involvement: predictive factors of long-term survival after surgical resection. Lung Cancer. 2006;52:359-64.
- 7. Doddoli C, D'Journo B, Le Pimpec-Barthes F, Dujon A, Foucault C, Thomas P, et al. Lung cancer invading the chest wall: a plea for en-bloc resection but the need for new treatment strategies. Ann Thorac Surg. 2005;80:2032-40.
- 8. Coche E. Screening for lung cancer with low-dose CT. JBR-BTR. 2008;91:1-5.
- Bandi V, Lunn W, Ernst A, Eberhardt R, Hoffmann H, Herth FJ. Ultrasound vs. CT in detecting chest wall invasion by tumor: a prospective study. Chest. 2008;133:881-6.
- 10. Wain JC. Video-assisted thoracoscopy and the staging of lung cancer. Ann Thorac Surg. 1993;56:776-8.
- Roviaro GC, Varoli F, Rebuffat C, Vergani C, Maciocco M, Acalambra SM, et al. Videothoracoscopic staging and treatment of lung cancer. Ann Thorac Surg. 1995;59:971-4.
- 12. Roviaro GC, Varoli F, Rebuffat C, Sonnino D, Vergani C, Maciocco M, et al. Videothoracoscopic operative staging for lung cancer. Int Surg. 1996;81:252-4.
- Roviaro GC, Varoli F, Vergani C, Maciocco M. State of the art in thoracoscopic surgery: a personal experience of 2000 videothoracoscopic procedures and an overview of the literature. Surg Endosc. 2002;16:881-92.
- Loscertales J, García Díaz F, Jiménez Merchán R, Girón Arjona JC, Arenas Linares CJ. Valoración de la resecabilidad del cáncer de pulmón mediante videotoracoscopia exploradora. Arch Bronconeumol. 1996;32:275-9.
- Loscertales J, Jiménez-Merchán R, Arenas Linares C, Girón-Arjona JC, Congregado-Loscertales M. The use of videoassisted thoracic surgery in lung cancer: evaluation of resectability in 296 patients and 71 pulmonary exeresis with radical lymphadenectomy. Eur J Cardiothorac Surg. 1997;12:892-7.
- Yim APC. Routine video-assisted thoracoscopy prior to thoracotomy. Chest. 1996;109:1099-100.
- Jiménez Merchán R, Congregado Loscertales M, Girón Arjona JC, Arenas Linares JC, Ayarra Jarne J, Loscertales J. Videopericardioscopia: una nueva exploración para valorar la resecabilidad de los cánceres de pulmón cT4 por invasión vascular. Arch Bronconeumol. 2000;36:612-9.
- Loscertales J, Jiménez-Merchán R, Congregado-Loscertales M, Arenas-Linares C, Girón-Arjona JC, Tristán AA, et al. Usefulness of videothoracoscopic intrapericardial examination of pulmonary vessels to identify respectable clinical T4 lung cancer. Ann Thorac Surg. 2002;73:1563-6.
- Ohno K, Utsumi T, Sasaki Y, Suzuki Y. Videopericardioscopy using endothoracic sonography for lung cancer staging. Ann Thorac Surg. 2005;79:1780-2.
- Pompeo E, Tacconi F, Mineo TC. Flexible videopericardioscopy in cT4 nonsmallcell lung cancer with radiologic evidence of proximal vascular invasión. Ann Thorac Surg. 2007;83:402-8.
- 21. Sihoe AD, Yim AP. Lung cancer staging. J Surg Res. 2004;117:92-106.
- Hoffmann H. Invasive staging of lung cancer by mediastinoscopy and videoassisted thoracoscopy. Lung Cancer. 2004;45:125.
- Sebastián-Quetglas F, Molins L, Baldo X, Buitrago J, Vidal G. Clinical value of videoassisted thoracoscopy for preoperative staging of non-small cell lung cancer. A prospective study of 105 patients. Lung Cancer. 2003;42:297-301.
- Thomas P, Massard G, Giudicelli R, Reynaud-Gaubert M, Wihlm JM, Fuentes P. Role of video-thoracoscopy in the pre-treatment evaluation of lung carcinoma. Rev Med Interne. 1999;20:1093-8.
- Santambrogio L, Nosotti M, Bellaviti N, Pavón G, Volterrani F. Videothoracoscopy in the spreading evaluation of bronchogenic cancers. Cancer Radiother. 1997;1:178-80.
- 26. Menconi GF, Ambrogi MC, Melfi FM, Dini P, Davini F, Goletti O, et al. Endothoracic sonography with color Doppler availability during video assisted thoracic surgery (videothoracoscopic operative staging with ultrasound color Doppler) for lung cancer staging. Surg Endosc. 1998;12:816-9.
- Gdeedo A, van Schil P, Corthouts B, van Mieghem F, van Meerbeeck J, van Marck E. Comparison of imaging TNM [(i)TNM] and pathological TNM [pTNM] in staging of bronchogenic carcinoma. Eur J Cardiothorac Surg. 1997;12:224-7.