Therapeutic video-assisted thoracoscopic surgical resection of colorectal pulmonary metastases

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Abstract

Objective: Careful patient selection is vital when video-assisted thoracoscopic surgical (VATS) therapeutic pulmonary metastasectomy of colorectal carcinoma is considered. Complete resection of all metastatic disease remains a vital concept. We reviewed our VATS experience for therapeutic metastasectomy of peripheral colorectal pulmonary metastases. Methods: Over 90 months, therapeutic VATS metastasectomy was accomplished upon 80 patients with colorectal metastases. Thin cut computed tomography (CT) was central in identifying lesions. The mean interval from primary carcinoma to VATS resection was 41 months (1–156 months; median, 33). A solitary lesion was resected in 60 patients and multiple (2–7) lesions resected in 20 patients. Statistics were obtained using the Student’s t-test. Results: No operative mortality or major postoperative complications occurred. The hospital stay was 4.5 ± 2.2 days (range, 1–13). All lesions were resected by VATS, with four conversions to thoracotomy to improve the margins. The mean survival of patients with one lesion was 34.8 months compared with 26.5 months for patients with multiple lesions (P = 0.37). The mean survival was 20.5 months when metastases occurred <3 years vs. 28.1 months for >3 years from primary carcinoma resection (P = 0.20). Twenty-five (31%) patients are disease free; with a mean interval of 38.7 (3–84; median, 35) months. Sixty-nine percent (55/80) of patients developed a recurrence: 6/80 (8%) local; 19/80 (24%) regional (same hemithorax away from resection); and 30/80 (38%) distant. The overall survival at 1 year was 81.2%, 48.4% at 3 years and 30.8% at 5 years. Conclusions: Therapeutic VATS resection of colorectal metastases appears efficacious. Preoperative CT can identify peripheral colorectal metastases amenable to VATS. Conversion to thoracotomy is indicated when none of the lesions identified by CT are found or when clear surgical margins are jeopardized. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Pulmonary metastases; Colorectal carcinoma; Lung resection

1. Introduction

The development of isolated pulmonary metastases from colorectal carcinoma is a relatively uncommon occurrence, representing less than 2% of all metastatic circumstances from these malignancies. Complete surgical resection of all demonstrable pulmonary metastases may result in long-term disease free survival. Unfortunately, the reported experiences with therapeutic resection of colorectal metastases are ambiguous with regard to patient selection and the description of pulmonary disease burden among patients undergoing attempted resection.

Due to the fact that alternative systemic chemotherapy has little therapeutic efficacy in the treatment of pulmonary metastases from colorectal cancer, an aggressive surgical resection approach of all demonstrable disease is often considered. Of course, consideration must be given to the individual patient’s physiological reserve and the possible detriment upon this reserve in relation to the surgical intervention. A reasonable approach to the radicality of resection and aggressiveness towards recommending therapeutic metastasectomy must be considered. Surrounding these issues, considerable debate has arisen regarding the most
appropriate operative approach and patient selection for therapeutic colorectal metastasectomy [1–4]. This debate has intensified with the introduction of video-assisted thoracoscopic surgical (VATS) lung resection procedures over the last decade [5–7].

Over the last several years, our multi-institutional group has prospectively evaluated the efficacy of the VATS approach to the therapeutic resection of carefully selected patients with limited peripheral metastatic burden from colorectal carcinoma. Our present indications, patient selection and results of the VATS approach to therapeutic colorectal pulmonary metastasectomy are detailed in this paper.

2. Materials and methods

Over a 90 month period, the VATS approach was utilized to accomplish therapeutic pulmonary metastasectomy of colorectal metastases occurring in 80 patients. The mean age was 63 years (range, 37–87), with a gender distribution of 30 women (38%) and 50 men (62%). Pulmonary metastatic lesions were identified at a median interval of 41 months (range, 1–156) from their primary colorectal cancer resection. Two of the 80 patients were identified with pulmonary nodules at the time of the work-up of their primary colorectal carcinoma. In these patients, VATS resection of the nodule followed recovery of the primary malignancy from the patient’s surgical management. Pulmonary lesions were identified at least 6 months beyond the time of the primary resection colorectal surgery in the remaining 78 patients.

Sixty patients had a single site of pulmonary metastasis identified and resected; however, the remaining 20 patients had multiple (2–7) pulmonary nodules removed with a similar therapeutic intent. Fifteen of these latter patients with multiple lesions had unilateral tumor deposits identified preoperatively, and therefore, underwent unilateral VATS resection. Five patients with multiple lesions had bilateral disease managed with simultaneous bilateral VATS resections. Two patients underwent combined simultaneous resection of solitary pulmonary and hepatic metastatic lesions.

2.1. Preoperative evaluation

A full metastatic work-up was undertaken prior to therapeutic VATS resection of colorectal metastases in all patients. Colonoscopic examination was routinely performed, as was computed tomography (CT) scanning of the chest, abdomen and pelvis. Thin cut (0.5–1.0 cm) high resolution CT images were obtained of the entire lung fields. Spiral CT of the chest is now routinely employed to avoid breath to breath errors in CT imaging of the lung parenchyma.

Preoperative carcino-embryonic antigen (CEA) levels were obtained in 40 of the patients immediately before their VATS resection. Physiological assessments, including pulmonary function studies, were undertaken on all 80 patients and all patients were felt to be at a low operative risk for pulmonary resection.

2.2. Patient and lesional selection for therapeutic metastasectomy

As with any other situation in which surgical resection of metastatic disease is contemplated with therapeutic/curative intent, careful patient selection is important. The patient selection criteria for therapeutic colorectal metastasectomy summarized in Table 1 can be generally applied across the entire scope of metastatic resection surgery. Likewise, metastatic lesions amenable to the VATS wedge resection approach are specifically defined in Table 2.

Specific comment regarding the selective application of the VATS approach to pulmonary metastasectomy is warranted. All lesions in question were peripheral in location and amenable to complete VATS resection. If the lesion(s) were not all in a peripheral and a favorable location for VATS resection, the VATS approach was not considered. This necessarily limited the VATS approach to patients with a limited peripheral metastatic disease burden. VATS lobectomy was considered for patients with a deep solitary lesion or multiple lesions within the same lobe. Also, the relative loss of tactile discrimination with the VATS approach compared with open thoracotomy required that a careful review of the preoperative chest roentgenogram and CT scan was performed to determine the best sites of intercostal access needed to accomplish adequate VATS exploration of the lung and pleural cavity and to resect all lesions in question.

2.3. Operative approach

After the induction of general anesthesia, bronchoscopic examination of the airways is undertaken to identify any possible endobronchial metastases [8]. This is performed

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<th>Criteria for ‘therapeutic’ VATS resection of pulmonary metastases</th>
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<td>Primary neoplasm controlled or controllable</td>
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<td>Limited metastatic burden</td>
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<td>Adequate cardiopulmonary reserve to undergo surgery and the extent of pulmonary resection contemplated</td>
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<td>No other effective therapy</td>
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<td>All thoracic metastatic disease potentially resectable by VATS</td>
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<p>| Table 2 |</p>
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<th>Therapeutic VATS metastasectomy</th>
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<td>Wedge resection strategies</td>
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<td>Candidate pulmonary metastatic nodules</td>
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<td>Less than 3 cm in diameter</td>
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<td>Location in the outer 1/3 of the lung</td>
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<td>Absence of endobronchial extension</td>
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<td>Limited overall thoracic disease burden by thin cut CT</td>
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through a single lumen endotracheal tube. In the absence of endobronchial metastases, preparation is made for exploratory thoracoscopy. Conversion to a left sided double lumen endotracheal tube is performed to allow for contralateral single lung ventilation and collapse of the ipsilateral lung. After institution of single lung ventilation, the patient is placed in a full lateral position. The chest is steriley prepared and draped for the VATS intervention and possible conversion to open thoracotomy. The initial VATS access site is usually in the mid-axillary line at the level of the sixth or seventh intercostal space. Subsequent sites of intercostal access are determined by the location of the pulmonary lesion and our desire to maintain bimanual manipulation of thoracoscopic instrumentation about the target pathology [9]. We prefer to use a wide angle, zero degree operative thoracoscope (operating wide angle zero degree Hopkin’s telescope, #26040A, Karl Storz Endoscopic America, Inc., Culver City, CA) for these VATS procedures. The thoracoscope is introduced through a re-useable 12 mm diameter metal trocar (Snowden Pencer, Inc., Tucker, GA). Effective collapse of the lung facilitates identification of the lesions that will become effaced against the atelectatic pulmonary parenchyma. After introduction of instrumentation through two other sites of intercostal access, the lung is examined both visually and by palpation with endoscopic forceps. Once the general pulmonary parenchymal site of the metastasis is located, the surgeon introduces his index finger into the chest through the most accessible intercostal site for direct palpation of the lesion with the aid of customized coaxial endoscopic forceps (‘Mashers’, Starr Medical, Inc., New York, NY).

Lesions found on the edge of the lung are resected with an endoscopic stapling device (EndoGIA, United States Surgical Corporation, Norwalk, CT or Endoscopic Linear Cutter, Ethicon Endoscopic, Cincinnati, OH). Occasionally, lesions on the edge of the lung can not be completely resected with the stapler due to the thickness of the pulmonary tissue. For these lesions, resection across the base of the specimen is completed with the Nd:YAG laser (Heraeus Lasersonics, Inc., Milpitas, CA) [10]. After completion of the wedge resection, the specimen is removed from the thoracic cavity in a surgical retrieval bag (Pleatman sac, Cabcott Endoscopic Instruments) to ensure against tumor seeding of the chest wall [9,11,12]. When frozen section analysis reveals metastatic disease and the resection margins are free of tumor, the VATS wedge resection constitutes the definitive therapy. Conversion to an open thoracotomy is performed if none of the lesions identified by preoperative CT scanning were found or if the surgical margins may be compromised.

A single 28 French chest tube is introduced into the chest at the lowest intercostal access sites and guided under direct visualization to the apex of the pleural cavity. The remaining incisional sites are closed with an absorbable suture. Once in the recovery room, we assess the possibility of removing the chest tube early. Tube removal is done if air leak is absent, drainage is minimal, and the chest roentgenogram demonstrates adequate lung expansion [13].

### 2.4. Statistical analyses

The data were analyzed using SAS statistical software on a Macintosh Power PC computer. The survival percentages and mean survival times were estimated using Kaplan–Meier curves. Correlations between CEA levels and survival were accomplished using log rank tests.

### 3. Results

All patients survived their operative intervention and no major postoperative complications occurred. The average postoperative hospital stay was $4.5 \pm 2.2$ days. All metastatic lesions under evaluation were resected by VATS, however, four patients underwent conversion to thoracotomy to improve the surgical margins when the VATS wedge resection margin was close to the tumor. The mean survival of patients with one metastatic lesion was 34.8 months compared with 26.5 months for patients with multiple lesions ($P = 0.37$; Fig. 1). The mean survival was 20.5 ± 4 months when the disease free interval was less than 3 years compared with 28.1 ± 5 months when the disease free interval was greater than 3 years from the primary carcinoma resection ($P = 0.20$).

Twenty-six (33%) patients beyond 1 year of VATS resection were without evidence of disease at a mean interval of 38.7 months. The remaining 54 patients (67%) developed recurrent disease, of which, 41 died from their disease at a mean interval of 21 months. Four patients underwent re-resection (two VATS, two open thoracotomy) of subsequent clinical metastases at a mean interval of 8 months following the initial resection. All of these patients remain alive, one with further clinical metastases found at a follow-up of 5 months.

The patterns of first tumor recurrence seen among these VATS resection patients were local in 6/80 (8%), regional (same hemithorax away from resection) in 19/80 (24%), and systemic in 30/80 (38%). Four of six patients (67%) who developed local recurrence died of systemic disease at a mean interval of 35 months. Eleven of the 19 patients (58%) with regional recurrence died of systemic disease at a mean interval of 26 months, and 21 of the 30 patients

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**Fig. 1. Pulmonary metastasectomy for colorectal cancer. Single vs. multiple metastases survival.**
(70%) with systemic recurrence died at a mean interval of 18 months. The patients alive ‘with’ or ‘without’ recurrent disease at 1, 3 and 5 years from metastasectomy can be seen in Fig. 2. As noted, at 1, 3 and 5 years, 17, 33 and 14% of survivors were alive ‘with disease’ at these time intervals. The overall survival for the entire patient cohort at 1 year was 81.2 and 48.4% at 3 years and 30.8% at 5 years (Fig. 3).

Our analysis of the relationship of preoperative CEA levels and survival demonstrated that a preoperative level greater than 10 ng/ml was associated with a significantly poorer prognosis (Fig. 4). A 40% survival at 5 years was seen among patients with CEA levels less than 10 ng/ml, compared with no survivors beyond 2.5 years among patients with preoperative levels above 10 ng/ml ($P = 0.0001$).

4. Discussion

The basic patient selection criteria for therapeutic metastasectomy utilized by many of us today are: local control of the primary malignancy, a long disease free interval from primary tumor resection, no effective alternative therapy, absence of extra thoracic metastases, and the presence of a limited pulmonary metastatic burden that can be ‘completely’ resected [1–5,7]. The validity of these concepts has been further strengthened through the results of the retrospective analysis of therapeutic metastasectomy reported by the International Registry of Lung Metastases [14]. The results of their retrospective investigation demonstrated that the primary determinants of survival after therapeutic metastasectomy were: the complete resection of all clinical disease; a single metastatic lesion resected; and a long disease free interval (greater than 36 months) from the resection of the primary tumor to the development of the pulmonary metastasis.

Although we could not demonstrate a significant difference in survival between patients undergoing resection of one lesion compared with multiple metastatic lesions, this may be a result of the small number of patients in our series and the fact that 13 of the 20 patients undergoing resection of multiple lesions had three or fewer sites of metastases [15].

Candidates for therapeutic resection of colorectal pulmonary metastases represent a very small fraction of those patients with recurrent malignancy. Over 130 000 patients are diagnosed with colorectal carcinoma each year in the United States. Over 50% of these patients will develop recurrent disease. Only 10% of these patients will develop clinically isolated metastases to the lungs. Ten percent of this latter group of patients with limited metastatic burden to the lung (1% of total recurrences) may be candidates for therapeutic metastasectomy. Between 25 and 40% of these colorectal cancer patients undergoing pulmonary metastasectomy may survive 5 years following surgery. It is appreciated that a small number of patients with pulmonary metastases who receive ‘no resectional’ therapy may survive beyond 5 years from the diagnosis of their metastatic disease [16]. The majority of these patients will succumb to their colorectal cancer before the 10 year mark. Aberg has reflected upon this issue of individual tumor biology and has come to the conclusion that the true benefit from resection of pulmonary metastases from colorectal carcinoma should be measured in terms of 10 year survival [15]. The true impact of surgical resection upon the survival of these patients can be better understood at this extended time interval [16].

Unfortunately, following the resection of pulmonary metastases, ‘disease free’ and ‘absolute survival’ are rarely distinguished between in surgical literature. The results of this study warn us further of the limitations of survival analyses based upon crude overall 5 year survival following pulmonary metastasectomy for colorectal carcinoma. In
these circumstances of long-term survival, in spite of disease recurrence, it is hard to believe that the metastasectomy offered a positive influence on patient survival. The individual patient’s tumor biology reigns supreme in these circumstances as the primary determinant of long-term survival. The fact that the patient remains alive for an extended period with disease cannot be considered a surgical triumph, but rather, a demarcation of the indolent nature of the metastatic disease.

A central point of controversy involving the use of VATS for therapeutic metastasectomy regards the inability to identify and remove all metastatic disease which may be discernable through bimanual palpation at open thoracotomy. Indeed, McCormack et al. [6] reported upon a group of patients with colorectal metastases explored first with VATS and then immediately with open thoracotomy at their institution [6]. Of the 18 patients having CT imaging prior to surgery who underwent this two staged surgical intervention, ten patients (56%) were found to have additional metastatic disease within the chest. Four other patients (22%) underwent additional pulmonary resections which identified only benign pathology. These latter processes of unnecessary resection of innocent lung are consistent with those of other individuals advocating radical metastasectomy approaches [17]. From this investigation, they concluded that VATS was an inadequate approach to therapeutic metastasectomy.

We question the significance of the result from this small study. We wonder as to the quality of the CT imaging obtained preoperatively, and also, of the analysis of these studies prior to surgery. Quality CT imaging is crucial to success when considering the VATS approach to pulmonary metastasectomy. We also believe that analysis of the CT imaging by the radiology staff and surgeons is crucial in limiting resection to the peripheral lesions identified roentgenographically when the VATS approach is considered. All suspicious lesions identified by CT are sought out during the VATS intervention. Resection is aimed at the target pathology.

The second point of contention regarding this study relates to the pathological analysis and potentially to the extent of resection utilized. An unfavorable prognosis is understandable when gross unresectable disease is left within the operated hemithorax. Such patients have a more obvious, and frequently, more significant tumor burden than those with small roentgenographically occult lesions within the pulmonary parenchyma. The question to be asked is, ‘how does the discovery and resection of additional, otherwise occult, lesions at the time of pulmonary metastasectomy improve the survival of these patients?’ Gundry has reported a high incidence of unrecognized microscopic metastases on close inspection of pulmonary metastasectomy specimens from sarcomatous lesions. An unfavorable prognosis was the rule when such findings were present [18]. It is also recognized that post-resectional recurrence following metastasectomy is common (greater than 50%), even when open thoracotomy is used as the operative approach [14]. We believe that the findings of such occult disease in the setting of visceral malignancy metastatic to the lung has an equivalently ominous prognosis. Although the patients involved in this Memorial study are limited [6], it may be valuable to examine the pattern of recurrence among those patients in which VATS identified all lesions accurately (44%) and compare this recurrence pattern (and survival) to that of patients who had additional lesions removed at the subsequent thoracotomy. Although unrecognized by the authors, this parameter could have been the crucial end point of their study that may now be unobtainable due to the premature termination of their investigation.

Until this issue is settled, we must rely upon the recognition of Gundry and others [18–20], who have retrospectively surmised that, when multiple metastases are identified at thoracic exploration, the prognosis is significantly affected in a negative way. Although some exceptions exist, the identification of numerous other pulmonary lesions (reseactable or not) at thoracic exploration is a harbinger of poor prognosis. When this is the case, we believe that the surgical intervention primarily evolves into a ‘diagnostic’ maneuver. The patient survival in these circumstances, as seen in this report and echoed in the literature, leads us to conclude that the biology of the individual patient’s tumor is the primary determinant of long-term survival when several metastatic lesions are identified.

This does not mean to say that resection is an unreasonable option for some patients with more than one metastatic lesion to the lung. However, circumstances surrounding the nature and natural history of pulmonary metastases from visceral primary malignancies (such as colorectal, renal, melanoma and breast) suggest that the number of pulmonary metastases encountered and resected is important in estimating the patient’s prognosis [15,21]. This concept is also supported by the results of the International Registry of Pulmonary Metastasectomy, mentioned earlier [14].

As demonstrated in our limited experience, re-resection of pulmonary metastases is possible by VATS or by open thoracotomy following an initial VATS metastasectomy. This concept is in accordance with the experiences of other thoracic surgeons using VATS resection. The survival benefit of repeat resection has been demonstrated to be minimally affected when limited recurrent disease is addressed. Accordingly, we believe that no bridges are burnt by utilizing the VATS resection for colorectal metastases.

The initial use of the VATS approach to resection of peripheral colorectal metastases may avoid the morbidity of a thoracotomy and the loss of functional lung parenchyma for the majority of patients who will unfortunately develop systemic recurrence following their initial metastasectomy [22]. Salvage surgical resection done open or through VATS interventions directed towards roentgenographically demonstrable recurrent disease can be accomplished with
a reasonable chance of prolonged survival. The survival following re-resection may be a further reflection of an indolent biology of the pathological condition [23,24]; however, compromise of the patient’s overall course does not appear to be affected by the subsequent identification and removal of subclinical resectable disease.

Preoperative CEA levels do appear to be a significant predictor of survival following resection of pulmonary metastases [25]. Among our patients undergoing VATS resection, CEA levels correlated with recurrence and resection in overall patient survival. Further insight into the relationship between this tumor marker and the considerations for surgical resection of otherwise limited intrathoracic metastatic colorectal carcinoma is warranted.

Although these intermediate term results with VATS metastasectomy are encouraging, longer term follow-up and a larger patient base of experience will be necessary to determine subtle differences in this VATS approach to the therapeutic resection of peripheral colorectal metastases compared with ‘open’ thoracic resection of patients with similar metastatic disease burdens. Conversion to thoracotomy is indicated when all lesions identified by CT are not found or when clear surgical margins are jeopardized.

References


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Appendix A. Conference discussion

Dr S. Barnard (Bradford, UK): Firstly, do you feel that this is increasing; i.e. the requests by colorectal surgeons to operate on their patients, because in Leeds, we have operated on 10 of these patients so far this year, and our feeling is that it is going to be a more frequent operation that we do?

And secondly, are they coming via the liver surgeons, having had hepatic secondaries taken out as well?

Dr Landreneau: We are finding that the colorectal surgeons and the medical oncologists are more favorably influenced with the minimally invasive approach for selected patients with minimal peripheral disease burden, so I agree with you that our experience is increasing recently. Two of the patients did have concomitant resection of isolated metastases to the liver at the same time as their pulmonary resections.

Dr Barnard: But they hadn’t had a liver resection before?

Dr Landreneau: No, it was not before, but it was concomitant resection, and survival is not really mature enough to say anything about it.
Dr J. Nakajima (Tokyo, Japan): Did you perform lymph node dissection or lymph node biopsy during the procedure?

Dr Landreneau: No.

Dr Nakajima: I also have the experience of more than 50 cases of metastatic cancer through thoracoscopy, but the lymph node metastasis was a very important predictor of survival. So, I think that we should do a lymph node biopsy at least.

Dr Landreneau: Well, we explore the hilum, but in these cases that I am describing, where there was a therapeutic intent, we didn’t really identify significant adenopathy, and I am familiar with your work and Vogt-Moykopf’s work also describing the importance of metastatic nodal involvement in this setting.

Dr P. Van Schil (Antwerp, Belgium): First, regarding the value of CT scan. As you know, some years ago there was a report from Memorial Sloan, New York where they used a regular or classical CT scan. During thoracotomy, they found additional malignant nodules which were not seen on CT scan in more than 50% of patients. Could you comment on the way you did the CT scan, was it a spiral CT? Did you look at sensitivity and specificity? Did you have many false-positives or did you pick up some nodules that were not seen on CT scan?

Dr Landreneau: We didn’t analyze that. Specifically, these were 0.5–1 cm cuts. Over the last 3 years, it has been primarily spiral CTs, but I don’t have the number with me. The false-positive rate, meaning the resection of scar or granulomatous tissue or benign lymph node diseases, was not included here, but it represents about 15–20% of patients that we encounter.

I am not sure what to say about that Memorial study, because we would expect that in any circumstance, regional or systemic recurrence with involvement elsewhere in the lung with this metastatic process to be about 50–55%. I think theirs was 56% in the 18 patients that they studied. My biggest problem with that study is it was prematurely ended. I think we could have learned a lot by going to the full cohort of patients that they wanted to study to see if it made a survival difference, whether they found those occult lesions or not.

Dr Van Schil: Did you have a standardized follow-up protocol by CT or PET scan?

Dr Landreneau: No, just the usual protocol that our radiologists use. 0.5–1 cm cuts were used at various institutions.

Dr V. Ambrogi (Rome, Italy): As you have shown and said, CT can miss some metastases. What is your opinion about digital palpation? Can you perform it by VATS or do you exclude this?

Dr Landreneau: Say that again.

Dr Ambrogi: Do you always exclude one finger digital palpation? Do you normally perform a VATS without palpation?

Dr Landreneau: No, we usually palpate the lung.

Dr Ambrogi: With one finger?

Dr Landreneau: With a finger introduced not through a thoracotomy, through one of the access sites. We try to palpate all lobes. It is obviously not as good as by manual palpation.