

What Are the Considerations in the Surgical Approach in Pulmonary Metastectomy?

Tamas F. Molnar,* Cengiz Gebitekin,† and Akif Turna‡

Abstract: There are four matters of uncertainty considered in this working group report, which are distilled into four clinical questions: (1) What is the evidence for the need for palpation of the lung in modern era of imaging? (2) Is there evidence of a difference in outcome for an open versus a closed approach? (3) Is there evidence of a difference in outcome for an initial policy of bilateral versus unilateral exploration? (4) In patients with known bilateral disease, is there a difference in outcome with a simultaneous versus a staged approach?

We searched the literature formally and supplemented this with knowledge from all other sources. We provide evidence tables on the first two questions by relying on a group consensus and frame recommendations for the other two.

There are no randomized trials to guide us but there are comparative studies addressing the need for palpation and the need to and open operation in all cases. The evidence is equivocal, and opinions are divided in the literature.

Palpation of the lung is still seen as necessary in a therapeutic metastasectomy as opposed to a diagnostic procedure when videothoracoscopy is adequate. However, the importance of palpation becomes less clear with advances in imaging. Routine bilateral exploration for unilateral disease was not favored. For bilateral disease, an initial median sternotomy has a place for some cases but sequenced thoracotomy was preferred.

(*J Thorac Oncol.* 2010;5: S140–S144)

Current practice in the surgical approach to lung metastasectomy is highly variable. The choice of approach to resection of pulmonary metastases depends more on surgical schooling, training, and personal conviction than on evidence and probably varies within the same institute or department, not to mention between countries. The European Society of Thoracic Surgeons working group survey of practice that was

undertaken in 2006 showed a wide variation, which reflects to the eclectic and highly individualized nature of the topic addressed.¹ The survey revealed not only variation in practice but also potential inconsistencies between belief and practice. For example, palpation of the lung was regarded as mandatory by 65% of the responding surgeons, but use of videothoracoscopic surgery (without complete palpation) was acceptable to 60%. At first sight, these are incompatible. Does this mean that a third of surgeons have a theoretical desire to palpate the lung but accept a minimally invasive approach with video-assisted thoracoscopic surgery (VATS)? It may reveal something of the lack of cohesions between evidence and practice in this regard.

We have distilled this area of uncertainty into four questions:

1. What is the evidence for the need for palpation of the lung in modern era of imaging?
2. Is there evidence of a difference in outcome for an open versus a closed approach?
3. Is there evidence of a difference in outcome for an initial policy of bilateral versus unilateral exploration?
4. In patients with known bilateral disease, is there a difference in outcome with a simultaneous versus a staged approach?

Methods for Systematic Review

The search conducted by the subgroup was updated by a RefMan search of National Library of Medicine listed publications using the search <metastasectomy> AND <VATS> OR <metastasectomy> AND <thoracotomy>. This returned 97 references. Titles and abstracts were filtered. References were excluded if they were case reports, technical reports containing no data, personal opinions, teaching articles, no comparative data were offered, or the technique surgical approach used was incidental to the main purpose of the report.

We created evidence tables for the first two questions. The process was to a large extent iterative thereafter, that is to say the method was refined or extended depending on what was found. For example, no imaging reports before 2000 were considered sufficiently up to date with technology to be reliable. For the latter two questions, there were insufficient data to populate meaningful tables. Two of the questions (2 and 3) were the subject of recent systematic

*University Medical School of Pecs, Pecs, Hungary; †Department of Thoracic Surgery, Uludag University, School of Medicine Bursa, Turkey; and ‡Süreyyapasa Teaching Hospital for Pulmonary Diseases and Thoracic Surgery, Istanbul, Turkey.

Disclosure: The authors declare no conflicts of interest.

Address for correspondence: Tamas F. Molnar, H-7633 Ifjusag u. 13 Pécs, Pécs, Hungary. E-mail: Tamas.F.Molnar@aok.pte.hu.

Copyright © 2010 by the International Association for the Study of Lung Cancer

ISSN: 1556-0864/10/0506-0140

reviews,^{2,3} so more emphasis was placed on newer evidence in that regard.

RESULTS

The searches returned 97 publications. The process of sifting is illustrated in Figure 1 following the principles of QUORUM.⁴ This resulted in 13 articles for inclusion in Tables 1 and 2.

To address the question 1 concerning the need for palpation of the lung as imaging resolution improves progressively, we refer to Table 1. Seven articles were found that examine in various ways whether video surgery, which inherently relies heavily on preoperative imaging, fell short in allowing the surgeon to find and remove as many nodules as can be removed at open surgery.⁵⁻¹¹

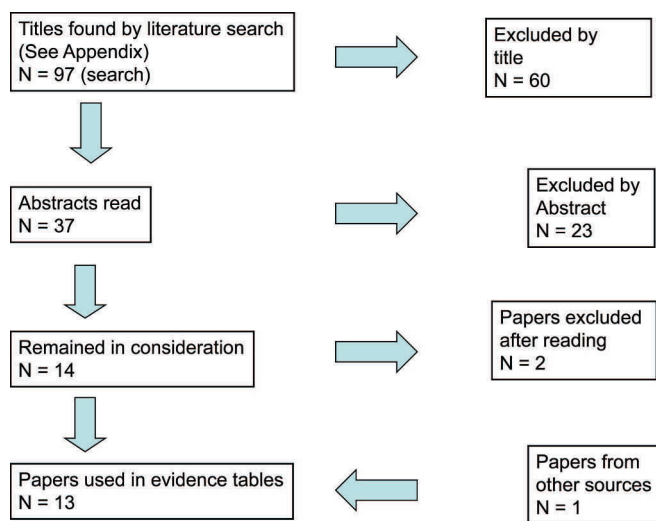


FIGURE 1. Flow diagram of the process of sifting papers for inclusion in the systematic reviews.

Cerfolio et al.⁵ found that of 57 potential VATS patients, 10 had malignant nodules that were found and removed at thoracotomy and these were not revealed by imaging. The conclusion of Mutsaert et al.¹² was similar. In 5 of 17 patients who had VATS followed by thoracotomy, further disease was found. Kayton et al.⁹ found further nodules in 19 of 54 patients, 14 of which were viable sarcomatous metastases.

Nakajima et al.⁸ considered the problem in a different way. Two years after a VATS or open operation, they found significantly more nodules that had not been detected after open surgery compared with VATS, a finding that favors videothoracoscopy. Nakas et al.⁶ found that the potentially missed lesions were few (one in each) and similar whether surgery was open or VATS.

Margaritora et al.¹¹ randomized patients imaged between 1996 and 2000 to either high-resolution computed tomography (CT) scanning or helical CT. They then performed metastectomy by muscle-sparing thoracotomy. Detection was higher with helical CT (82% sensitive versus 75%), but it was still insufficient for them to not to palpate the lung in all cases. It may be that with advancing technology the debate will be resolved. Using 1-mm slice thickness multidetector row CT, Kang et al.⁷ imaged all the nodules that could be found at surgery.

In answer to the second question, seven articles^{6,12-17} provided data on outcome (one article is in both tables). Six of 7 articles showed no difference in survival between a videothoracoscopic and open surgery, but one of them noted significantly more complications with thoracotomy.¹⁰ Nakajima et al.¹⁶ reported significantly lower recurrence-free survival at 5 years in patients having open (21%) rather than videothoracoscopic surgery (34%).

There is a theoretical advantage of VATS: it allows patients to return to their normal life significantly earlier than after an open approach. This effect may be multiplied in a

TABLE 1. Evidence Table: Can Modern Imaging Replace Palpation?

Source	Era	Cancers	Population Studied	Comparison Made	Authors' Findings/Conclusions
Cerfolio et al. ⁵	2004–2005	All nodules	57 patients 57 thoracotomies	57 potential VATS candidates had thoracotomy	10 of 57 patients had malignant nodules found by palpation but not imaged
Nakas et al. ⁶	2000–2008	Colorectal	52 patients	25 VATS 27 open (includes 4 conversions)	No difference in missed lesions
Kang et al. ⁷	2005–2006	Mixed	27 patients	Imaging compared with pathological analysis of 101 nodules	High detection rates with 1-mm thick slices of multidetector CT
Nakajima et al. ⁸	1999–2005	Colorectal	102 patients 122 metastasectomies	79 VATS 43 thoracotomies	VATS 34% Thoracotomies 63% Recurrence <2 yr (<i>p</i> = 0.0023) 47 of 250 nodules were not metastases
Kayton et al. ⁹	1996–2004	Sarcoma	28 patients 54 thoracotomies	Surgeons findings and imaged nodules	In 19 of 54, metastases were missed In 14 of 54, viable metastases missed
Margaritora et al. ¹¹	1996–2000	Not stated	166 patients 361 metastases	188 HRCT versus 173 helical CT	75% sensitivity 82% sensitivity Palpation still their choice
Mutsaerts et al. ¹⁹	1992–1996	Not stated	17 patients	17 VATS 17 confirmatory thoracotomy	In 5 of 17, further disease was found

VATS, video-assisted thoracoscopic surgery; HRCT, high-resolution computed tomography.

TABLE 2. Evidence Table: Is There a Difference in Outcome for an Initial Bilateral Versus Unilateral Approach?

Author	Era	Cancers	Population Studied	Comparison Made (None by RCT)	Authors' Findings/Conclusions
Carballo et al. ¹³	1986–2006	Mixed	280 procedures 186 patients	36 VATS 135 thoracotomy Conversion rate 10%	Recurrence free survival not different on noninferiority analysis
Gossot et al. ¹⁴	2000–2007	Sarcoma	113 patients	31 VATS 29 potential VATS 1 or 2 nodules	Survival the same LoS 3.7 vs. 6.2 d ($p < 0.0001$)
Lim et al. ¹⁵	2003–2009	Cervical cancer	23 nodules 21 patients	11 VATS 10 thoracotomy 2 conversions	Approached equivalent in selected patients
Nakas et al. ⁶	2000–2008	Colorectal	52 patients	25 VATS 27 open (includes 4 conversions)	Survival and recurrence data not different
Nakajima et al. ¹⁶	1987–2005	Colorectal	143 patients	72 VATS 71 open thoracotomy	34% 21% Recurrence-free survival ($p = 0.047$)
Mutsaerts et al. ¹²		Not stated	35 patients with solitary peripheral <3 cm nodule	16 VATS 19 open	Similar numbers of recurrence and survival More complications with thoracotomy ($p = 0.049$)
Watanabe et al. ¹⁷		Not stated	46 patients	23 VATS 23 thoracotomy	Similar survivals

VATS, video-assisted thoracoscopic surgery; RCT, randomized controlled trial.

TABLE 3. Preferences Expressed With Regard to the Surgical Responders to the European Society of Thoracic Surgeons.¹

“Which is your preferred approach for clinical unilateral disease?”	
Anterolateral thoracotomy	53 (36.3)
Thoracoscopy (VATS)	42 (28.8)
Posterior muscle sparing thoracotomy	38 (26)
Posterolateral thoracotomy	33 (22.6)
Horizontal axillary thoracotomy	15 (10.3)
Vertical axillary thoracotomy	10 (6.9)
Sternotomy	2 (1.4)
Other	7 (4.8)
“Which is your preferred approach for clinical bilateral disease?”	
Bilateral staged thoracotomy	96 (66.2)
Sternotomy (one stage)	39 (26.9)
Bilateral sequential thoracotomy (one stage)	28 (19.3)
Bilateral staged thoracoscopy	18 (12.4)
Bilateral thoracoscopy (one stage)	11 (7.6)
Clamshell (one stage)	11 (7.6)
Other	3 (2.1)

VATS, video-assisted thoracoscopic surgery.

patient who requires multiple resections. However, a redo operation is not always possible via VATS due to adhesions as a consequence of previous operations.

One aspect of videothoracoscopic surgery that has caused concern is whether it increases the potential for pleural or port-site dissemination.^{18–20} Clearly, it occurs but the data do not support the contention that it is a new problem

unique to VATS: appropriate precautions are now used routinely in practice.

Among the supporters of the open approach, various forms of thoracotomy are used for resection of disease, which is apparently unilateral on the basis of preoperative investigations; sternotomy is not popular (Table 3). For bilateral disease, two out of three surgeons favor bilateral staged thoracotomy, thus accepting that the intervention will require major operations. Two thoractomies at the same operating session is the approach preferred by one in five surgeons; fewer than 1 in 10 operate through a “clamshell” incision. For most surgeons (>80%), the surgical approach varies depending on performance status and lung function, type of tumor and its location, and the number of metastases.

As for as the fourth question, concerning an initial bilateral approach, in the 1980s, median sternotomy was evaluated as an approach to bilateral metastasectomy. Roth et al.²¹ studied a series of 65 patients who underwent 78 median sternotomies between 1981 and 1984 for resection of pulmonary metastases for soft tissue sarcoma. In a comparison with thoracotomy in two groups of 42 patients who had complete resection, the authors concluded that it avoided the need for a second operation and allowed discovery of unsuspected contralateral metastases. In an institutional review of 131 patients, Regal et al.²² concluded that median sternotomy reduced morbidity and allowed sooner resumption of systemic therapy. On the basis of experience in 53 operations in 46 patients (40 of 46 had sarcoma), Johnston²³ regarded median sternotomy as the incision of choice, reducing morbidity, finding undetected lesions on the contralateral side, and sparing patients with known bilateral disease a second thoracotomy.

Bilateral staging and finding of occult metastases, complete surgical clearance in a one-stage procedure, and lower morbidity are the reasons for van der Ween et al.²⁴ to suggest that median sternotomy is the procedure of choice for resection of pulmonary metastases. The utility of a bilateral approach to discover unsuspected disease may progressively diminish in importance as imaging advances.

The Working Group's Approach and Deliberations

The working group found no randomized controlled trials nor meta-analysis. The original working group followed the approach of the Swiss team of Kuester et al.²⁵ They differentiated between five levels of consensus: perfect, very good, good, some, and no consensus. Every surgeon has his/her own protocol, which is based partly on his/her theoretical knowledge from teaching material and partly on personal experiences. The final result is a mixture of these elements with a wide range of proportion of the different ingredients. Data are filtered through and adjusted (sometimes biased) by personal judgment. These are well recognized as traditional and appropriate in surgery, and they have served us well.^{26,27} Are there good grounds to leave this to the "common sense" of the individual? There is such evident variation that depends on the particular needs of the patient and the preference of the surgeon that it might well be a situation in which it is a decision for individual craftsmen to do what works best in their hands.²⁸

It should be said that individual members of the panel did not necessarily put the same value on the sources cited or agreed unanimously on many topics. The authors have tried to reflect the balance of opinion.

Vertical axillary or horizontal axillary thoracotomies are equally preferred. Staged thoracotomy was recommended in cases that are not suitable for median sternotomy, such as posteriorly placed metastases and repeat metastasectomy. Full or partial clamshell incision is not among the favored approaches for metastasectomy although promulgated as an improved approach.²⁹ The discussion of the article by Margaritora et al.¹¹ indicates the strength of feeling for and against bilateral thoracotomy in the same operative session.

If a planned two-stage resection is undertaken then the side with the greater number of metastases is opened first. The same consideration would apply if difference in tumor mass was considered. In terms of time frame, a minimum of 2- to 3-week interval is accepted but 4 to 6 weeks on average is preferred. This is approximately the time course of uncomplicated postoperative course. One justification for staged surgery is that it allows a time window for detecting intercurrent appearance of metastatic foci that were previously below the threshold of detectability. Performing re-CT before the second stage offers a check on a possible significant progression.

The question we have not addressed is whether lymphadenectomy should be a routine part of pulmonary metastasectomy. That is the subject of another article in this supplement.

What we lack is an evidence-based approach to inform this practice. There are three main problems to be solved in this attempt using an evidence-based approach:

1. The lack of properly controlled evidence.
2. An overgrowth of audit-like independent reports mimicking an objective approach.
3. The "fog of war."

The third is a borrowed expression ascribed to the Prussian military analyst, Carl von Clausewitz. Almost as soon as battle began, the gunpowder smoke drifted across the battlefield making it extremely difficult to get an accurate assessment of who was winning and who was losing. In clinical practice, there are many extraneous factors that obscure our view as we try to determine what exactly is having an effect.

The authors offer these steps as their recommendations:

In the debate concerning thoracotomy versus sternotomy for bilateral lesions, a thoracotomy approach seems to be preferred over sternotomy. Some place emphasis on the need to provide access to the lymph nodes for proper staging.³⁰ Sequential thoracotomies for bilateral diseases with an interval of 3 to 6 weeks are recommended with an in-between CT check.

As for VATS, there is a lack of convincing evidence for its superiority as regards pain, discomfort, and length of staying compared with muscle-sparing thoracotomy. VATS is usually compared with the antero- or posterolateral thoracotomy, neglecting the muscle-sparing axillary thoracotomy and not to mention the hand-assisted combined methods.³¹⁻³⁴

It seems to be fair to declare that there is an obvious consensus in the general acceptance of VATS in diagnostic procedures. VATS as an alternative therapeutic modality in metastasis surgery is still not accepted as a rule. Preoperative diagnostic accuracy and imaging remain to be a crucial limiting factor. At the present time, the group concluded that there was no alternative to palpation.

REFERENCES

1. Internullo E, Cassivi SD, Van Raemdonck D, et al. Pulmonary metastasectomy: a survey of current practice amongst members of the European Society of Thoracic Surgeons. *J Thorac Oncol* 2008;3:1257-1266.
2. Naunheim K. Thoracoscopy versus the open approach for resection of solitary pulmonary metastases. In M Ferguson. *Difficult Decisions in Thoracic Surgery: An Evidence Based Approach*. London: Springer-Verlag, 2007. Pp. 151-157.
3. Patel A, de Camp M. Unilateral or bilateral approach for unilateral pulmonary metastatic disease. In M Ferguson. *Difficult Decisions in Thoracic Surgery: An Evidence Based Approach*. London: Springer-Verlag, 2007. Pp. 158-164.
4. Moher D, Cook DJ, Eastwood S, et al. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of Reporting of Meta-analyses. *Lancet* 1999;354:1896-1900.
5. Cerfolio RJ, McCarty T, Bryant AS. Non-imaged pulmonary nodules discovered during thoracotomy for metastasectomy by lung palpation. *Eur J Cardiothorac Surg* 2009;35:786-791.
6. Nakas A, Klimatsidas MN, Entwisle J, et al. Video-assisted versus open pulmonary metastasectomy: the surgeon's finger or the radiologist's eye? *Eur J Cardiothorac Surg* 2009;36:469-474.
7. Kang MC, Kang CH, Lee HJ, et al. Accuracy of 16-channel multi-

- detector row chest computed tomography with thin sections in the detection of metastatic pulmonary nodules. *Eur J Cardiothorac Surg* 2008;33:473–479.
8. Nakajima J, Murakawa T, Fukami T, et al. Is finger palpation at operation indispensable for pulmonary metastasectomy in colorectal cancer? *Ann Thorac Surg* 2007;84:1680–1684.
 9. Kayton ML, Huvos AG, Casher J, et al. Computed tomographic scan of the chest underestimates the number of metastatic lesions in osteosarcoma. *J Pediatr Surg* 2006;41:200–206.
 10. Mutsaerts EL, Zoetmulder FA, Meijer S, et al. Outcome of thoracoscopic pulmonary metastasectomy evaluated by confirmatory thoracotomy. *Ann Thorac Surg* 2001;72:230–233.
 11. Margaritora S, Porziella V, D'Andrilli A, et al. Pulmonary metastases: can accurate radiological evaluation avoid thoracotomy approach? *Eur J Cardiothorac Surg* 2002;21:1111–1114.
 12. Mutsaerts EL, Zoetmulder FA, Meijer S, et al. Long term survival of thoracoscopic metastasectomy vs metastasectomy by thoracotomy in patients with a solitary pulmonary lesion. *Eur J Surg Oncol* 2002;28:864–868.
 13. Carballo M, Maish MS, Jaroszewski DE, et al. Video-assisted thoracic surgery (VATS) as a safe alternative for the resection of pulmonary metastases: a retrospective cohort study. *J Cardiothorac Surg* 2009;4:13.
 14. Gossot D, Radu C, Girard P, et al. Resection of pulmonary metastases from sarcoma: can some patients benefit from a less invasive approach? *Ann Thorac Surg* 2009;87:238–243.
 15. Lim MC, Lee HS, Seo SS, et al. Pathologic diagnosis and resection of suspicious thoracic metastases in patients with cervical cancer through thoracotomy or video-assisted thoracic surgery. *Gynecol Oncol* 2010;116:478–482.
 16. Nakajima J, Murakawa T, Fukami T, et al. Is thoracoscopic surgery justified to treat pulmonary metastasis from colorectal cancer? *Interact Cardiovasc Thorac Surg* 2008;7:212–216.
 17. Watanabe A, Yamauchi A, Ichinomiya Y, et al. [A therapeutic metastasectomy of pulmonary metastases by VATS]. *Kyobu Geka* 2000;53:30–33.
 18. Downey RJ, McCormack P, LoCicero J III. Dissemination of malignant tumors after video-assisted thoracic surgery: a report of twenty-one cases. The Video-Assisted Thoracic Surgery Study Group. *J Thorac Cardiovasc Surg* 1996;111:954–960.
 19. Mutsaerts EL, Zoetmulder FA, Rutgers EJ. Port site metastasis as a complication of thoracoscopic metastasectomy. *Eur J Surg Oncol* 2001;27:327–328.
 20. Ang KL, Tan C, Hsin M, et al. Intrapleural tumor dissemination after video-assisted thoracoscopic surgery metastasectomy. *Ann Thorac Surg* 2003;75:1643–1645.
 21. Roth JA, Pass HI, Wesley MN, et al. Comparison of median sternotomy and thoracotomy for resection of pulmonary metastases in patients with adult soft-tissue sarcomas. *Ann Thorac Surg* 1986;42:134–138.
 22. Regal AM, Reese P, Antkowiak J, et al. Median sternotomy for metastatic lung lesions in 131 patients. *Cancer* 1985;55:1334–1339.
 23. Johnston MR. Median sternotomy for resection of pulmonary metastases. *J Thorac Cardiovasc Surg* 1983;85:516–522.
 24. van der Veen A, van Geel AN, Hop WC, et al. Median sternotomy: the preferred incision for resection of lung metastases. *Eur J Surg* 1998;164:507–512.
 25. Kuester JR, Frese S, Stein RM, et al. Treatment of primary spontaneous pneumothorax in Switzerland: results of a survey. *Interact Cardiovasc Thorac Surg* 2006;5:139–144.
 26. Treasure T. The evidence on which to base practice: different tools for different times. *Eur J Cardiothorac Surg* 2006;30:819–824.
 27. Treasure T. Are randomised trials needed in the era of rapidly evolving technologies? *Eur J Cardiothorac Surg* 2009;35:474–478.
 28. Treasure T. Do whatever works in your hands. *Lancet* 1996;347:559–560.
 29. Bains MS, Ginsberg RJ, Jones WG, et al. The clamshell incision: an improved approach to bilateral pulmonary and mediastinal tumor. *Ann Thorac Surg* 1994;58:30–32.
 30. Pfannschmidt J, Klode J, Muley T, et al. Nodal involvement at the time of pulmonary metastasectomy: experiences in 245 patients. *Ann Thorac Surg* 2006;81:448–454.
 31. Ambrogi V, Paci M, Pompeo E, et al. Transxiphoid video-assisted pulmonary metastasectomy: relevance of helical computed tomography occult lesions. *Ann Thorac Surg* 2000;70:1847–1852.
 32. Mineo TC, Ambrogi V, Paci M, et al. Transxiphoid bilateral palpation in video-assisted thoracoscopic lung metastasectomy. *Arch Surg* 2001;136:783–788.
 33. Detterbeck FC, Egan TM. Thoracoscopy using a substernal handport for palpation. *Ann Thorac Surg* 2004;78:1031–1036.
 34. Taniguchi Y, Suzuki Y, Suda T, et al. Video-assisted thoracoscopic bilateral lung metastasectomy with a subxiphoid access port. *J Thorac Cardiovasc Surg* 2005;130:916–917.