Awake pulmonary metastasectomy

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Objective: General anesthesia with single-lung ventilation and bimanual lung palpation is considered mandatory in pulmonary metastasectomy. We assessed the safety, feasibility, and early results of awake pulmonary metastasectomy under sole thoracic epidural anesthesia.

Methods: Between December 2003 and December 2005, 14 patients with radiologic evidence of peripheral solitary lung metastases underwent awake thoracoscopic metastasectomy under sole thoracic epidural anesthesia at T4 to T5. To achieve bimanual-like full lung palpation, a modified digital-instrumental palpation method was used. Anesthesia time, operative time, global operating room time, patient satisfaction with the anesthesia, and technical feasibility scored into 4 grades (from 1 = poor to 4 = excellent) were assessed. Preoperative and postoperative data were compared with those of a historical cohort undergoing video-assisted transxiphoid lung metastasectomy through general anesthesia and 1-lung ventilation.

Results: There was neither mortality nor major morbidity. Technical feasibility was excellent in 10 instances and good or satisfactory in 2 instances, whereas anesthesia satisfaction score was excellent to good in 12 patients. Of 18 resected nodules, 15 proved to be metastases. At awake and control group comparisons, significant differences included median operative time (25.5 minutes vs 48.5 minutes, $P < .00001$), global in-operating room time (62.5 minutes vs 147.5 minutes, $P < .00001$), and hospital stay (2.5 days vs 4.0 days, $P = .02$). There was no difference in lung recurrence (2 vs 3, $P = .66$) 3-year actuarial survivals (40% vs 78%, $P = .29$).

Conclusions: Awake pulmonary metastasectomy proved safe and feasible. Global operating room time and hospital stay were significantly shorter than those of the control group who underwent operation with general anesthesia, whereas oncologic results were comparable.

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Surgical metastasectomy has become a standard therapy for select patients with pulmonary metastases.^{1,2} Complete resection remains the most important prognostic factor, and iterative aggressive procedures are frequently performed to pursue this result.² Video-assisted thoracoscopic surgery (VATS) has been proposed as a less-invasive first surgical approach for lung metastasectomy.³ However, because radiologically undetectable lesions can be missed at VATS, its value has been questioned and it is mainly advocated for diagnostic purposes in patients with unilateral nodules.⁴⁻⁶

In 1999 we⁷ proposed the transxiphoid video-assisted approach, which allows complete bimanual palpation of the lungs and is now our technique of choice.^{8,9}

More recently, having started a clinical investigational program of awake thoracic surgery under sole thoracic epidural anesthesia (TEA),^{10,11} we have offered this less-invasive option to a select cohort of patients with radiologic evidence of peripheral solitary pulmonary metastases. To allow bimanual-like full lung palpation without the need for a transxiphoid approach, we used a modified instrumental-digital lung palpation method.

Abbreviations and Acronyms

CT	= computed tomography
PACO ₂	= arterial carbon dioxide tension
PAO ₂ /FIO ₂	= ratio of arterial oxygen tension to fraction of inspired oxygen
TEA	= thoracic epidural anesthesia
VATS	= video-assisted thoracoscopic surgery

In this study we analyzed the feasibility, safety, and early results of this awake surgical modality.

Materials and Methods

Between December 2003 and December 2005, awake pulmonary metastasectomy was performed in 14 patients (8 men and 6 women). The study was designed as a pilot study and approved by the ethics committee of our university. Informed written consent was obtained from all patients once they were informed about the investigational nature of the study, the difference with standard surgical approaches, and the possibility that conversion to general anesthesia and one-lung ventilation may be necessary during the procedure.

Primary outcome measures were technical feasibility and anesthesia satisfaction scored into 4 grades (1 = unsatisfactory; 2 = satisfactory; 3 = good; 4 = excellent).

Secondary outcome measures were anesthesia time, operative time, global in-operating room time, and hospital stay. In addition, the ratio of arterial oxygen tension to fraction of inspired oxygen (PAO₂/FIO₂) and arterial carbon dioxide tension (PACO₂) were assessed intraoperatively at the completion of the surgical procedure and 24 hours after surgery.

Postoperative pain was assessed with the standard Visual Analogue Scale.¹² Visual Analogue Scale assessment was performed 24 hours after the procedure.

The study was conducted following a 2-step plan. The first step included an initial subset of 7 patients who underwent operation. To proceed with the second subset of 7 patients, it was assumed that in the first cohort the procedure was easily performed (technical feasibility > 1) and satisfactorily tolerated (anesthesia satisfaction score > 1) in at least 5 patients with no major side effects, and that the operative time, morbidity rate, and hospital stay did not negatively differ at an interim analysis from those observed in an historical cohort treated with general anesthesia by VATS with transxiphoid bimanual lung palpation.

In all patients the diagnosis of lung metastases was presumed because of recently developed lung nodules with radiologic characteristics compatible with a metastatic lesion discovered at chest roentgenogram or computed tomography (CT) during the oncologic follow-up. After the discovery of the lung lesion, all patients underwent further examination to exclude primary or extrapulmonary recurrence. The lung lesions were also restaged immediately before planned surgery by means of a helical chest CT scan. The mean interval between the helical CT scan and the surgical exploration was 12 ± 5 days. The scanning protocol included a tube voltage of 120 kVp, tube current of 250 mA, slice thickness of 5 mm, and table increment of 5 mm per rotation. No intravenous

contrast medium was administered. Reconstruction was performed at 5-mm intervals, and images were printed at a window center of -530 H and a window width of 1,500 H.

Eligibility criteria included the complete control of the primary tumor, the absence of extrapulmonary metastases, and a newly discovered solitary pulmonary nodule localized in the peripheral one third of the lung and measuring not more than 3 cm on CT. Exclusion criteria included the presence of multiple metastases, lesions located more than 2 cm from the visceral pleura or measuring more than 3 cm in maximal size, radiologic evidence of pleural scarring, or a history of thoracic surgery on the side targeted for metastasectomy.

Contraindications for TEA included unfavorable anatomy, previous surgery of the cervical or upper thoracic spine, compromised coagulation (thromboplastin time < 80%, prothrombin time > 40 seconds, or platelets < 100/nL), or bleeding disorder.

Criteria for discharge were standardized and were the same in both the awake and control groups. In particular, discharge was decided when complete lung reexpansion was demonstrated by chest roentgenogram, pleural drainage was less than 150 mL/day, and there was no air leak for 24 hours. No patient was discharged with a Heimlich valve.

Anesthesia

The objective of TEA was to achieve somatosensory and motor block at the T1 to T8 level. The maximum permissible block level was C6, which was monitored by the development of Horner's syndrome. One of the major objectives was to achieve motor block of the intercostal muscles while preserving diaphragmatic respiration. The thoracic epidural catheter was inserted at the T4 level; after that, patients were premedicated orally with 7.5 mg of midazolam. In the operating room, patients received a continuous infusion of ropivacaine 0.5% and sufentanil 1.66 µg/mL into the epidural space. Sensory block was achieved between the neck and the abdomen, including the arms.

During the procedure patients breathed O₂ through a ventimask as required to keep oxygen saturation greater than 90%. Whenever somatosensory block was judged unsatisfactory by the patient, additive anesthesia was provided by local injection of a 50% mixture of ropivacaine (7.5%) and bupivacaine (2%). Whenever anxiety or a panic attack occurred perioperatively, sedation was slightly increased by the continuous infusion of propofol (0.5 mg/kg) while maintaining spontaneous breathing. During wound closure, the TEA anesthetic regimen was changed to ropivacaine 0.16% and sufentanil 1 µg/mL at 2 to 5 mL per hour to provide postoperative analgesia. All patients received lactated Ringer's solution at 12 mL/kg⁻¹/h⁻¹. The epidural catheter was removed 24 hours after surgery.

Transxiphoid VATS resection was performed under general anesthesia with single-lung ventilation and thoracic epidural catheterization on T5 and T8. General anesthesia was induced with intravenous propofol (1.5-2 mg/kg), fentanyl (0.1 mg), and vecuronium (0.1 mg/kg), and maintained with a continuous infusion of propofol (4-8 mg/kg), fentanyl, and vecuronium. A left-sided double-lumen tube was placed under fiberoptic control. In both groups, usual monitoring was performed. Continuous infusion of ropivacaine started during surgery and was continued for the first postoperative 24 hours to ensure postoperative analgesia.

Figure 1. Schematic drawing (A) and intraoperative thoracoscopic view (B) of full lung palpation performed by a modified digital-instrumental method entailing forefinger palpating targeted lung tissue through the open ring (R1) and against the flat filled-in ring (R2) of the modified ring forceps showed in cartouche. In this way, fine bimanual-like lung palpation is likely to be performed as we previously performed through the transxiphoid VATS approach.

In the awake group, liquid infusion was stopped immediately postoperatively, and drinking, meal intake, and ambulation were started on the same day of surgery.

Surgical Technique

All of the procedures were performed with the patient placed in a full lateral decubitus position and through a 3-flexible-thoracoscopic-trocars access. To permit fine full-lung palpation, a modified digital-instrumental palpation method, which we believe allows bimanual-like lung palpation, was used. With this method, the entire lung tissue is carefully palpated between the forefinger and the flat side of the modified ring forceps, starting from the apex and proceeding toward the basal segments (Figure 1). Identification of lung nodules was also facilitated by the partially deflated lung status induced by the open pneumothorax, which reduced lung tissue density, thus facilitating identification of millimetric nodules.

Excision of the nodules was performed by staple wedge resection or precise lung excision. During the procedure the surgeon talked to the patient to test his or her overall wellness and the effectiveness of the analgesia. The surgeon periodically reassured the patient and informed him or her about the ongoing operation. Low-volume classic music was also usually played in the operating room throughout the procedure. It was also important to inform the patient about the possibility that induction of the open pneumothorax might reflect temporary fatigue and to encourage the patient to continue to breathe at a normal rate. The vital parameters' monitor was positioned so the patient could directly visualize his or her status, including arterial oxygen saturation. Some patients asked to follow the operation on the operating video. Dependent pleural drainage was performed with a single 28F chest tube. At the completion of the procedure and after connection of the chest tube to a waterseal, the surgeon asked the patient to breathe deeply

TABLE 1. Characteristics of the study groups

	Awake group		Control group		Mann–Whitney intergroup <i>P</i> value
Sex (male/female)	8/6		10/4		.69
Age (y)	55	49-67	60	50-62	.83
Histology (colorectal/other)	4/10		5/9		1.0
Disease-free interval	19	12-26	23.5	12-35	.45
Site of the lesion (upper lobe/other lobe)	5/9		7/7		.70
Size of the lesion (mm)	15	10-17	9	5-25	.32

while keeping the thoracoports closed with gauze to allow complete lung reexpansion before closure of the chest.

All patients in the control group were extubated in the operating room.

Statistical Analysis

Group descriptive statistics are presented as median and interquartile range (25th percentile to 75th percentile) or as mean $\pm$ standard deviation as appropriate. Between-group comparisons of continuous variables were performed with the nonparametric Mann–Whitney test, and the frequencies were compared by using the 2-tailed Fisher exact test. Survival was calculated by the Kaplan–Meier method, and between-group comparison was performed with the log-rank test. All calculations were made with the Statistica computer software package (StatSoft Inc, Tulsa, Okla).

Results

During the study period, of 16 patients who were eligible for the procedure and were offered this option, 14 preferred to undergo awake lung metastasectomy and 2 preferred the transxiphoid approach.

The study groups were well matched in terms of age, sex, histology of primary tumor, disease-free interval, and characteristics of the lung lesions (Table 1).

All patients were asymptomatic. Perioperative and postoperative results in the study groups are illustrated in Tables 2 and 3. In particular, intergroup comparisons demonstrated a significant difference in anesthesia time, operative time, and global in-operating room time, which were significantly shorter in the awake group.

In the awake group technical feasibility was judged excellent in 10 instances and good or satisfactory in 2 instances each, despite the unexpected finding of unexpected pleural adhesions in 2 patients. No patient required conversion to general anesthesia and 1-lung ventilation. In the same group, perioperative comfort was judged as good by 12 patients and as acceptable by 1 patient, as indicated by the anesthesia satisfaction score. One patient had a panic attack during the procedure, which was resolved by increased sedation while maintaining spontaneous breathing. At the end of the procedure

TABLE 2. Perioperative data in the study groups

	Awake group (N = 14)		Control group (N = 14)		Mann-Whitney intergroup P value
Anesthesia time (min)	10.5	8-13	37.5	36-40	<.0001
Surgery time (min)	25.5	23-33	48.5	40-55	<.0001
Weaning time (min)	—	—	16	12-20	—
Global operating room time (min)	62.5	55-70	147.5	136-166	<.0001
Anesthesia satisfaction score	4	3-4	—	—	—
Technical feasibility score	4	3-4	—	—	—
Intraoperative heart rate	82.5	80-86	78	72-80	.02
Intraoperative arterial pressure (mm Hg)	109	104-112	108	106-110	.9
Intraoperative PO_2/FIO_2	203	190-213	219	196-244	.1
Intraoperative $Paco_2$ (mm Hg)	46	45-48	39	38-40	<.0001
24-h postoperative PAO_2/FIO_2	364	251-404	237	217-390	.07
24-h postoperative $Paco_2$ (mm Hg)	40	38-41	41	38-45	.3
24-hour VAS	2.5	2-3	3	2-4	.4
Mortality (N)	0		0		—
Morbidity (N)	1		2		.5
Hospital stay (d)	2.5	2-3	4	3-5	.005

VAS, Visual Analogue Scale; PO_2/FIO_2 , ratio of arterial oxygen tension to fraction of inspired oxygen; $Paco_2$, arterial carbon dioxide tension.

ture, $PACO_2$ was significantly higher in the awake group, although arterial oxygenation remained satisfactory throughout the procedure.

In the awake group 18 nodules were palpated and resected (4 patients had resection of 2 nodules), of which 14 had been predicted by CT. Of these, 15 nodules contained metastasis at histologic examination. Eight metastases were located in the upper lobes (6 right and 2 left), 5 metastases were located in the lower lobes (2 right and 3 left), and 2 metastases were located in the middle lobe. The mean diameter of the histology-proven metastatic nodules was 15 ± 7 mm. Three nodules proved non-neoplastic (1 an-thracotic lymph node, 2 granulomas). The mean diameter of benign nodules was 8 ± 5 mm. There was no difference between the awake group and the control group in the number of resected modules (1.29 ± 0.5 vs 1.21 ± 0.4 , $P = .7$).

On postoperative day 1, there were no differences in $PACO_2$, PAO_2 , and Visual Analogue Scale, whereas PAO_2/FIO_2 was higher in the awake group, although the difference was not statistically significant.

There was no mortality and major morbidity in the study groups.

The median hospital stay was shorter in the awake group than in the control group, with 7 patients versus 1 patient with a hospital stay of 2 days or less, respectively. In the awake group, a hospital stay longer than 3 days was necessary because of excessive pleural drainage or persistent air leak in 1 patient each; in the control group it was necessary because of pneumonia in 1 patient, excessive pleural drainage in 4 patients, and persistent air leak in 2 patients.

During follow-up, pulmonary metastases developed in 2 patients in the awake group; 9 months after the operation,

contralateral lung metastases developed in 1 patient with skin melanoma; 18 months after the initial operation, a central ipsilateral lung lesion associated with diffuse pleural metastases developed in 1 patient with breast cancer; and 8 months after pulmonary metastasectomy, multiple metastases developed in 1 patient with testicular tumor. One patient had pelvic recurrence 15 months after lung metastasectomy and 35 months after an anterior resection for a rectal carcinoma. There was no difference between groups in the number of lung recurrences (2 vs 3, $P = .66$) and actuarial survival (Figure 2).

Discussion

In 2001 we started an investigational clinical program of awake lung surgery for benign lung nodules.¹⁰ We then considered it a logical extension of the initial indication to offer this option to a limited cohort of patients with solitary peripheral pulmonary metastasis who preferred to undergo an awake thoracoscopic lung resection once informed about the pros and cons of the different surgical approaches.

In this study, awake VATS resection of solitary pulmonary metastases was easily and safely accomplished under TEA in all patients. These results corroborate the data of previous studies¹⁰⁻¹⁴ and contradict the accepted assumption that thoracoscopic lung surgery requires general anesthesia and 1-lung ventilation. Furthermore, awake pulmonary metastasectomy was easily accepted and well tolerated by the patients, as confirmed by the high anesthesia satisfaction score in this group.

The rapidity of the procedure together with the significantly reduced global operating-room time improved patients' turnover in the operating room and offered the dou-

TABLE 3. Individual patients' characteristics and outcome

Group	Age (y)	Sex	Primary tumor	Site*	Size* (mm)	Surgery time	Hospital stay (d)	Recurrence status	Survival status
Control group	50	M	Colorectal	LLL	10	50	3	Lungs	Dead
	60	M	Melanoma	RUL	10	35	3	Multiple	Dead
	35	M	Testis	RUL	25	50	5	Multiple	Alive
	65	M	Colorectal	ML	5	40	6	Liver	Dead
	59	M	Kidney	RLL	5	55	4	Lungs	Alive
	52	M	Colorectal	RUL	5	34	3	No	Alive
	77	F	Breast	LUL	5	49	9	No	Alive
	60	M	Kidney	RLL	23	55	2	No	Alive
	50	F	Breast	LUL	5	48	4	No	Alive
	60	M	Colorectal	RUL	27	45	4	No	Alive
	46	M	Testis	LLL	30	40	3	Contralateral lung	Alive
	70	F	Uterus	RLL	5	60	3	Multiple	Dead
	61	F	Colon	LLL	30	64	4	No	Alive
	62	M	Lung	RUL	8	48	5	Brain	Dead
Awake group	46	M	Osteosarcoma	LUL	5	30	3	No	Alive
	55	F	Melanoma	RLL	25	26	2	Contralateral lung	Dead
	36	F	Osteosarcoma	RLL	14+9	33	2	No	Alive
	68	M	Rectal	ML	20	24	3	Pelvic	Alive
	67	M	Colon	LUL	12	48	3	No	Alive
	52	M	Thymoma	LUL	16	25	3	No	Alive
	78	F	Lung	RLL	9	36	4	Multiple	Dead
	60	M	Colon	LLL	17	20	2	No	Alive
	49	F	Breast	RUL	10	25	1	Ipsilateral lung	Alive
	64	M	Larynx	RUL	15	26	2	No	Alive
	35	M	Testis	ML	15	40	2	Multiple	Dead
	71	F	Rectal	LLL	26	22	5	No	Alive
	51	F	Kidney	LLL	10	20	2	No	Alive
	56	M	Kidney	RLL	15	23	3	No	Alive

RUL, Right upper lobe; ML, middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe. *Characteristics of histologically proven metastases.

ble advantage of less risk for the patient and less cost for the institution.

After VATS metastasectomy, arterial oxygenation worsened during the first postoperative day in both study groups, but this impairment was greater in the general anesthesia group than in the awake group. We hypothesize that operating under epidural anesthesia with spontaneous breathing avoided the related adverse effects of general anesthesia and single-lung ventilation, including barotrauma, atelectrauma, and volutrauma,¹⁵ resulting in a more physiologic postoperative lung reexpansion and a faster recovery. Yet, avoidance of general anesthesia allowed immediate resumption of many daily life activities, including drinking, eating, and walking, which eventually was reflected by a short hospitalization (50% of the patients were discharged within the second postoperative day).

Among the differences with general anesthesia surgery, an important one relates to the patient's active participation with the surgical procedure. Psychologic inferences of this novel policy still need to be elucidated, although we hypothesize that it might help reassure the patient about the

real effectiveness and limited physiologic impact of the surgical procedure.

After a preliminary discussion with our oncologists, it emerged that an ethical dilemma was to ensure a careful full lung palpation as we routinely perform with the transxiphoid approach, which we consider essential to enable discovery of incidental radiologically occult lesions. For this reason we modified the standard digital-instrumental palpation method to allow bimanual-like lung tissue palpation during awake VATS without the need for inserting 1 hand inside the chest.

In our series, nodules as small as 5 mm were identified with this method, and the low rate of ipsilateral lung recurrence might suggest that it was as effective as bimanual palpation in detecting all palpable lesions. Furthermore, despite the use of helical CT scan, which is currently the most accurate tool in detecting metastases, direct lung palpation allowed us to discover some radiologically undetected lesions in our selected cohort, a finding that is in line with the data of previous studies.^{5,6,8}

Awake lung surgery under TEA is being increasingly reported and has been used for the treatment of secondary

Figure 2. Kaplan–Meier actuarial survival curves of the study groups. Censored patients at 12, 24, and 36 months in the awake and control groups were 10 versus 14, 6 versus 13, and 1 versus 12 patients, respectively.

pneumothorax in high-risk patients with emphysema¹³ and after lung transplantation,¹⁴ for resection of pulmonary nodules,¹⁰ and for lung volume reduction surgery.¹¹ Nonetheless, TEA also has potential complications, which include epidural hematoma, spinal cord injury, and phrenic nerve palsy caused by an inadvertently high anesthetic level, which, however, never occurred in this series.

Limitations and Criticism

The main limitations of this study are its retrospective nature, small cohort, and comparison with an historical cohort undergoing a slightly different surgical approach. Criticisms might be also raised against the pathophysiologic effects of awake lung surgery. In fact, an open pneumothorax could induce a mediastinal movement with compression of the dependent lung and functional compromise. In addition, the difference in pleural pressure could create a re-breathing effect eventually resulting in hypercapnia. However, in the awake group we found a trivial increase in PACO_2 , and satisfactory oxygenation was easily maintained throughout the procedure by ventimask. We hypothesize that the nearly complete lung collapse created through an open pneumothorax minimized this effect. Furthermore, it is likely that in an awake patient, the maintained diaphragmatic motion decreases the detrimental effect of the abdominal pressure, which leads the paralyzed diaphragm to compress the dependent lung during general anesthesia.

Further concerns relate to the patient participation in operating room conversations or the risk of perioperative panic attacks. Nonetheless, we found that reassuring the patient during the procedure, explaining to him or her step by step what is being performed, and showing the ongoing procedure in the operating video improved the “perioperative wellness” and expectations of patients with cancer. A panic attack occurred in only 1 patient and was easily managed by moderately increasing the deepness of sedation while maintaining spontaneous breathing. As long as the physiologic impact of awake VATS metastasectomy is definitively elucidated, we believe it is better to use this approach for unilateral procedures that require a staged bilateral approach for bilateral lung metastasectomy.

Conclusions

In this study, awake VATS resection of solitary pulmonary metastases was easily and safely performed. Despite the limited cohort and retrospective nature of this study, we suggest that this surgical modality may evolve to offer potential advantages in comparison with conventional VATS resection performed under general anesthesia and 1-lung ventilation, particularly in regard to operating room time and hospital stay. We believe that further investigation is warranted to confirm our preliminary findings and to help identify optimal indications for this novel surgical option.

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