The prognostic factors in children undergoing pulmonary metastatectomy

Tuğba Acer[1], İbrahim Karnak[1], Arbay Özden Çiftçi[1], Zuhal Akçören[2], F. Cahit Tanyel[1], Mehmet Emin Şenocak[1]

[1] Department of Pediatric Surgery and [2] Unit of Pediatric Pathology, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey

SUMMARY: Acer T, Karnak İ, Çiftçi AÖ, Akçören Z, Tanyel FC, Şenocak ME. The prognostic factors in children undergoing pulmonary metastatectomy. Turk J Pediatr 2012; 54: 45-51.

A retrospective analysis was performed to determine the prognostic factors affecting survival in children who underwent pulmonary metastatectomy. Seventeen patients who underwent pulmonary metastatectomy between 2000 - 2006 were evaluated retrospectively by means of age, sex, primary diagnosis, time of metastasis appearance, number of nodules found on imaging examinations, type of management, surgical data, and outcome. Video-assisted thoracoscopic surgery (VATS) was used in 11 patients, and all patients underwent thoracotomy consequently. The nodule was composed of tumor cells in 13 (76%) patients and had positive surgical margins in 5 (38%). The time of metastasis appearance, number of metastases and completeness of the nodule excision did not affect survival (p=0.31, p=0.87 and p=0.56, respectively). Nodule size >1 cm was associated with dismal survival (p=0.008).

Time elapsed until the diagnosis of pulmonary metastasis, number of metastases and the completeness of metastatectomy do not have an impact on survival. The only significant prognostic factor is the size of the largest metastatic nodule. The presence of a metastatic nodule >1 cm is associated with a worse outcome in pediatric patients. VATS is an adjunct method to thoracotomy in the surgical management of pulmonary metastasis in children.

***Key words:** pulmonary metastasis, metastatectomy, surgery, child, video-assisted thoracoscopic surgery.*

The lungs are the primary site of metastasis for some tumors in children such as osteosarcoma, Wilms' tumor and soft tissue sarcomas. Systemic chemotherapy usually causes regression of pulmonary metastasis. However, surgery is indicated to determine the nodule histology and for total excision of pulmonary nodules.

When a pulmonary metastatectomy is considered, the surgeon should be sure of the following: the patient must be free of recurrent or residual disease in the primary tumor site or of extrapulmonary metastatic disease; radiological visualization of the pulmonary metastasis has been made; no residual metastases will be left after the operation, and no residual pulmonary insufficiency will occur postoperatively[1-7]. The absence of alternative therapy that is superior to surgery has also been considered as a criterion when deciding surgery in this situation[8-10].

Video-assisted thoracoscopic surgery (VATS) or thoracotomy is used to perform metastatectomy. Some authors prefer VATS because the technique is minimally invasive without a troublesome incision causing postoperative pain, longer hospitalization time and scarring on the incision line[10-20]. Thoracotomy is superior to VATS by ease of detection and excision of deeply located nodules, as it allows palpation of lung tissue[1,7,21-28].

Various prognostic factors have been suggested in adults with pulmonary metastasis. However, these prognostic factors as concerns a pure pediatric patient population that underwent pulmonary metastatectomy have been evaluated previously in only a few reports[29-32]. Therefore, a retrospective analysis was performed to determine the prognostic factors affecting survival in children with pulmonary metastasis who were treated by metastatectomy in a reference center.

Material and Methods

The patients who underwent excision of a pulmonary metastasis between 2000 and 2006 were evaluated retrospectively. The charts of the patients were reviewed for clinical features, radiological examinations and details of surgery. The age and sex, primary diagnosis, time elapsed from admission to development of metastasis, number of nodules found on imaging examinations, type of management, surgical findings and details of surgery, and outcome were noted. Patients who were referred for resection of pulmonary metastasis were evaluated accordingly with our previously published patient selection algorithm[3].

Technique of Video-Assisted Thoracoscopic Surgery (VATS)

Video-assisted thoracoscopic surgery was performed by applying standard rules. The patient was placed in the decubitus position on the side opposite to the location of the metastasis. Single lung ventilation technique was applied. Thoracoscopy was performed initially. The pleural space and the lung surface were evaluated through two ports: a 5 mm camera port and a 5 mm working port. The location and number of metastatic nodules were noted. The nodule was excised together with surrounding healthy tissue using electrocautery. The surface was checked for bleeding and air leak and controlled by cautery, and then a chest tube was placed. Conversion to the thoracotomy was decided if the metastases could not be visualized on thoracoscopy. The lung surface was inspected and the lung was palpated carefully for nodules. If the nodule was superficial, a wedge resection was performed with surrounding normal-appearing tissue. A segmentectomy or lobectomy was preferred if the nodule was located deeply or the remaining part of the lung lobe could not be expanded after resection, respectively. A chest tube was placed at the end of the thoracotomy.

The data were expressed as mean ± standard deviation (SD). The relations between the number or the size of the metastatic nodule and survival and the relation between the time of appearance of the nodule and survival were analyzed using Student's t test and chi-square test. P values lower than 0.05 were considered to be significant.

Results

Seventeen patients were included. The clinical and surgical data are summarized in Table I and Table II. The male to female ratio was 12/5 and the mean age was 11.9 years (range: 5-17 years). The primary diagnoses were osteosarcoma (n=3), Ewing's sarcoma (n=2), Wilms' tumor (n=2), clear cell sarcoma (n=1), renal cell carcinoma (n=1), mesoblastic nephroma (n=1), primitive neuroectodermal

Table I. Summary of Clinical Data

Case no	Age (year)	Sex	Primary disease	Time interval to metastasis
1	12	M	Wilms' tumor	8 years
2	5	M	Wilms' tumor	1 years
3	5.5	F	Clear cell sarcoma	17 months
4	12	M	Renal cell carcinoma	Present at admission
5	7	F	Mesoblastic nephroma	2 years
6	15	M	Osteosarcoma	7 months
7	13	M	Osteosarcoma	22 months
8	15	F	Osteosarcoma	2 years
9	17	M	Ewing's sarcoma	Present at admission
10	17	M	Ewing's sarcoma	3 years
11	13	M	Hodgkin lymphoma	7 months
12	15	M	Non-Hodgkin lymphoma	5.5 years
13	12	M	Hepatocellular carcinoma	Present at admission
14	7	F	PNET	19 months
15	11	F	PNET	3.5 years
16	10	M	Neurogenic sarcoma	3 months
17	16	M	Rhabdomyosarcoma	5 months

M: Male. F: Female. PNET: Primitive neuroectodermal tumor.

Table II. Radiological, Surgical and Histopathological Characteristics of the Pulmonary Metastasis

Case no	Pulmonary metastasis						Outcome
	Location	No	Size (cm)	Type of excision	Histopathology		
					Diagnosis	Margin	
1	LI	1	3x3.5	TT + wedge res.	Wilms' tumor	+	DOD
2	LS, LI	3	1 / 0.2-0.3	TS / TT + wedge res.	Wilms' tumor	-	FOD
3	RI	1	0.5	TT + wedge res.	No active tumor	-	?
4	RI	4	0.2	TS / TT + wedge res.	RCC	-	FOD
5	LI	1	2x3	TS / TT + lobectomy	Cellular MN	-	DOD
6	RS, M	4	1.2x0.3 / 0.3 / 0.2	TS / TT + wedge res.	Osteosarcoma	+	DOD
7	RS	1	1x0.5	TT + wedge res.	Osteosarcoma	-	FOD
8	RS	1	0.4	TS / TT + wedge res.	Osteosarcoma	-	FOD
9	LI	1	1x0.5	TS / TT + wedge res.	Ewing's sarcoma	-	DOD
10	RI	3	1.5 / 1 / 3	TT + wedge res.	Ewing's sarcoma	+	DOD
11	LS	1	0.5x0.5	TS / TT + wedge res.	Lymphoma	+	FOD
12	RS, RI	8	0.2x0.3	TS + biopsy	No active tumor	-	FOD
13	RI	1	0.4	TS / TT + wedge res.	No active tumor	-	DOD
14	RS	1	1x1	TT + segmentectomy	PNET	-	DOD
15	LI	1	2.5x2	TT + wedge res.	PNET	-	DOD
16	RI	1	1	TT + segmentectomy	No active tumor	-	?
17	LS, LI	3	2x3 / 4	TT + LI lobectomy + LS wedge biopsy	RMS	+	DOD

LI: Left inferior lobe. LS: Left superior lobe. RS: Right superior lobe. RI: Right inferior lobe. M: Middle lobe. TT: Thoracotomy. TS: Thoracoscopy. WT: Wilms' tumor. RCC: Renal cell carcinoma. MN: Mesoblastic nephroma. PNET: Primitive neuroectodermal tumor. DOD: Died of disease. FOD: Free of disease. Res: Resection.

tumor (PNET) (n=2), lymphoma (n=2), hepatocellular carcinoma (HCC) (n=1), malignant nerve sheath tumor (n=1), and rhabdomyosarcoma (RMS) (n=1). All patients received chemotherapy, and except for two lymphoma patients, underwent surgical excision for control of the primary tumor. Radiotherapy was used in cases with Wilms' tumor (n=1), Ewing's sarcoma (n=2), Hodgkin disease (n=1), PNET (n=1), and RMS (n=1).

Pulmonary metastasis was present at the time of admission in three patients and none of them underwent metastatectomy as an initial mode of treatment. The metastatic nodule appeared within a mean time of 2.27 years (range: 3 months – 8 years) in the remaining 14 cases. No significant relation was found between the appearance time and survival (p=0.31).

The number of nodules detected on computed tomography (CT) did not correlate with the number of nodules found on histopathological examination in 3 patients (17.6%). The CT underestimated the number of nodules. The mean number of metastases was 2.12±1.9 (range: 1 - 8). The number of metastases and survival time did not reveal a statistical significance (p=0.87).

Video-assisted thoracoscopic surgery (VATS) was used in 11 patients. The operation was started with thoracoscopy and then converted to mini-thoracotomy in 9 patients to find all nodules or to excise the nodule completely. One patient with lymphoma underwent only VATS for diffuse nodular involvement. VATS was also used to perform wedge resection in one of the osteosarcoma patients in whom the procedure was converted to thoracotomy.

All patients underwent thoracotomy, in one of them it was a staged thoracotomy. Wedge resection (n=12), segmentectomy (n=2), lobectomy (n=2), and biopsy only (n=1) were performed.

There was a solitary nodule in 11 patients; the numbers of nodules in the remaining patients were as follows: 3 nodules in 3 patients, 4 nodules in 2 patients and 8 nodules in 1 patient. The nodules were located in the superior lobe of the right lung (n=8), middle lobe (n=2), lower lobe of the right lung (n=13), hilum of the right lung (n=1), upper lobe of the left lung (n=4), and lower lobe of the left lung (n=8).

The mean size of the excised metastatic nodules was 1.44±1.24 cm (range: 0.2 – 4 cm). All patients with a metastatic nodule size >1 cm died of disease (6/6); however, only 2 patients with nodule size <1 cm (2/7) died. There was a statistically significant relation between the size of the largest metastatic nodule (>1 cm) and survival ($p=0.008$).

Histopathological examination revealed that the metastasis was composed of tumor cells in 13 patients (13/17), and surgical margins were positive for tumor cells in 5 of them (5/13). No active tumor cells were found in the remaining 4 patients (4/17). Surgical margins were free of tumor in 8 of 13 patients with tumor-positive metastasis, and 4 of them died (50%). Surgical margins were positive for tumor in 5 of 13 patients, and 4 of them died (80%). However, survival rates did not differ with regard to surgical margins ($p=0.56$).

The mean follow-up period was 2 years (range: 1 – 4 years). Six patients are alive (35%), 5 patients are free of disease and 1 patient is under chemotherapy. Nine patients died of disease, of which, 8 had tumor-positive metastasis (89%). The remaining 2 were lost to follow-up.

Regarding the tumor positivity of the metastasis (n=13, 76%), 5 patients (5/13) are alive (4 are free of disease (4/13) and 1 is receiving chemotherapy), and 8 patients (8/13) died. Regarding tumor negativity of the metastasis (n=4, 24%), 1 patient is living, 1 patient died of disease and 2 patients (1 with disease, 1 without disease at the time of last contact) were lost to follow-up.

Discussion

Pulmonary metastasis is usually encountered in the adult patient population, and thus most of the knowledge on this subject has been derived from adult series. The adult series contain a limited number of pediatric cases. A brief review of the medical literature provided only a few articles concerning the prognostic factors in a pure pediatric patient group that underwent pulmonary metastatectomy[29-32].

Various prognostic factors have been suggested in adults with pulmonary metastasis, such as number of nodules[2,17,20,33,34], size of nodule[2,17], uni- or bilaterality[33], number of involved lung lobes[10,35], time to development of metastasis and timing of surgery[36,37], histology of the primary tumor[2], completeness of excision[5,9,33,36], age of patient[17,34], need for conversion to open surgery[17], recurrence at the primary tumor site[9], and necessity for repeated thoracotomies[2,9,34]. It is really impossible to derive a common conclusion from these reports because some of them also contain pediatric patients[5,33,34], and some of them have been composed of at least two groups of patients with different primary pathologies[2,9,16-18,20,28,36-39].

Although of limited number, the pure pediatric reports have suggested prognostic factors are similar, as: number of nodules[29-32], uni- or bilaterality[29-31], increase in nodule size[30], time to development of metastasis and timing of surgery[31], nodal involvement[31], completeness of excision[29,31], age of patient[29], and type of primary tumor[29]. Additionally, most contain at least two groups of patients with different primary pathologies[3,15,29-31].

The present report is based on the results of pediatric pulmonary metastatectomy patients with various primary pathologies, such as Wilms' tumor, clear cell sarcoma, renal cell carcinoma, mesoblastic nephroma, osteosarcoma, Ewing's sarcoma, PNET, lymphoma, HCC, malignant nerve sheath tumor, and RMS. This report suggests no prognostic effect of time of metastasis appearance, number of metastases or completeness of the excision. However, nodule size >1 cm was found prognostic and associated with dismal outcome.

Various reports have suggested that increased numbers of nodules affect prognosis adver sely[2,5,6,24,25,31,32], while others mention no relation between survival and the number of nodules[4,7,9,23,26,29,35,39] as encountered in our report. Interestingly, two patients who underwent metastatectomy for 8 and 4 nodules, respectively, are still alive and free of disease.

Many authors concluded that a longer disease-free interval (DFI) has a positive impact on su rvival[4,6,9,23,24,26,29,31,32]; however, some contrary findings have been reported by others[7,25,35,39]. We considered the patients whose pulmonary nodules were seen after the diagnosis of malignancy and determined that DFI was not a prognostic factor. The limited number of patients and different types of primary pathologies may explain this finding.

The size of the metastatic nodules may influence survival[2,25], while some reports were unable to determine such an influence[24,26,29]. We showed that there was a relation between the size of the metastatic nodule and survival. The size of the nodule, which is the only factor we found to be correlated with survival, may reflect the short doubling time, which is the indicator of the malignant character of the tumor[2]. On the other hand, it should be kept in mind that the series were composed of many different malignancies, which have different biological behavior and various survival rates.

Computed tomography (CT) of the chest is a frequently used imaging method when determining the size and numbers of the metastatic nodules. However, it is known that CT may not show all of the pulmonary nodules. CT may overlook pulmonary nodules especially those <0.5 cm. It has been reported that 25% of cases have more nodules palpated during thoracotomy than are shown on chest CT[27]. Similar conclusions have been reached in other reports[3,11,15,18,21,22,31]. It should be kept in mind that the type of CT is of utmost importance. Spiral CT has a higher accuracy in defining pulmonary nodules[10,20]. CT underestimated the number of pulmonary nodules in 17.6% of patients in the present series.

Complete excision of the metastases has been suggested as a significant prognostic factor in many reports[4-6,9,23,25,29,31,32,40]. Although completeness of excision did not reach a statistically significant importance in the present series, the surgeon always faces the impression of a demand to resect the metastasis completely. Therefore, the surgeon should plan surgery to resect all metastases with free surgical margins.

The type of the primary tumor may affect the management of pulmonary metastasis. The pulmonary involvement or metastasis of lymphoma, Wilms' tumor, HCC, and Ewing's sarcoma may be managed initially with chemotherapy and/or radiotherapy instead of primary pulmonary surgery[41]. Surgical excision is decided if pulmonary metastases do not disappear after chemotherapy and/or radiotherapy. On the other hand, initial total excision of all tumoral foci may be crucial for better survival rates in patients with osteosarcoma and soft tissue sarcoma[2,4,8,14,21,25,35].

The pediatric surgeon should be familiar with the usage of VATS and thoracotomy techniques for the diagnosis and treatment of pulmonary nodules. VATS has some advantages like limited surgical trauma with a consequent reduction in postoperative morbidity and pain, more rapid postoperative recovery, decreased length of hospital stay, lower medical costs, earlier resumption of work[38], and cosmetic benefits. However, VATS does not allow tactile examination of the lung tissue and is usually useful for detection of superficially located lesions. Since the nodule may be overlooked even on CT, a deeply seated lesion cannot be diagnosed when only VATS is used. Some marking or pointing out procedures such as CT-guided transthoracic needle placement[10,13,14,19], injection of radioactive material to the nodules followed by use of tracer during VATS[12], injection of blue dye to the pleural surface of the nodule[10,12,14], and use of tactile probe during VATS[11,14,16] were recommended for proper localization and complete excision of the nodules. Additionally, a new technique has been recommended as palpation of both lungs through a transxiphoid incision during excision of the pulmonary nodules by VATS[18]. In contrast, most authors think that direct palpation of lung tissue is essential to not overlook associated nodules, and thoracotomy has been recommended[4,12].

In our series, in 9 cases, it was thought that exploration would not be sufficient during VATS and the procedure was converted to mini-thoracotomy to evaluate the lung tissue manually. Significant rates of conversion from VATS to thoracotomy have been reported previously for the same reason[12-15,17,19-21].

Although this kind of approach has a scientific basis since more nodules have been found when the VATS procedure was converted to thoracotomy[20,28], the consequent effect on survival should also be considered. Some recent studies concluded that there was no difference between thoracotomy and VATS based on patient survival[11,38]. They concluded that the nodules missed by CT, and which could not be seen during VATS, were too small to influence prognosis, and thus, their excision by thoracotomy did not alter the outcome[13,38]. This explanation seems logical; however, they selected patients with single peripheral nodule for VATS[16,19,38]. These selection criteria may also reflect the good outcome of the patients.

The criteria for choosing VATS or thoracotomy have been defined recently in a pediatric group of patients according to the number and localization of the metastatic nodules[15]. VATS has been recommended in children having <3 nodules and peripherally located nodules. The other cases have been considered to be suitable for thoracotomy[15].

We used VATS as an adjunct method to open surgery in this series. VATS was performed initially to overview the pleural cavity and lung surfaces and then proceeded to preferably limited open surgery for complete evaluation of all lung tissue by manual examination.

Repeated thoracotomies were required in 25.8% of patients when they presented with recurrence[7], and recurrent thoracotomies do not have an adverse prognostic effect[2,5-7,25]. Second thoracotomies were used in three patients presenting with recurrence in our series. It seems rational to perform repeat thoracotomies in patients who meet the surgical criteria for pulmonary metastatectomy[3].

Time elapsed until the diagnosis of pulmonary metastasis, number of metastases and the completeness of metastatectomy do not have an impact on survival. The only significant prognostic factor is the size of the largest metastatic nodule. The presence of a metastatic nodule >1 cm is associated with worse outcome in pediatric patients. VATS is an adjunct method to open surgery in the management of pulmonary metastasis in children. The pediatric surgeon should be familiar with the VATS technique as well as open thoracotomy.

REFERENCES

1. Rehders A, Hosch SB, Scheunemann P, Stoecklein NH, Knoefel WT, Peiper M. Benefit of surgical treatment of lung metastasis in soft tissue sarcoma. Arch Surg 2007; 142: 70-75.
2. Weiser MR, Downey RJ, Leung DH, Brennan MF. Repeat resection of pulmonary metastases in patients with soft-tissue sarcoma. J Am Coll Surg 2000; 191: 184-190.
3. Karnak I, Şenocak ME, Kutluk T, Tanyel FC, Büyükpamukçu N. Pulmonary metastases in children: an analysis of surgical spectrum. Eur J Pediatr Surg 2002; 12: 151-158.
4. Billingsley KG, Burt ME, Jara E, et al. Pulmonary metastases from soft tissue sarcoma: analysis of patterns of disease and postmetastasis survival. Ann Surg 1999; 229: 602-612.
5. Pfannschmidt J, Klode J, Muley T, Hoffmann H, Dienemann H. Pulmonary resection for metastatic osteosarcoma: a retrospective analysis of 21 patients. Thorac Cardiovasc Surg 2006; 54: 120-123.
6. Sternberg DI, Sonett JR. Surgical therapy of lung metastases. Semin Oncol 2007; 34: 186-196.
7. Antunes M, Bernando J, Salete M, Prieto D, Eugénio L, Tavares P. Excision of pulmonary metastases of osteogenic sarcoma of the limbs. Eur J Cardiothorac Surg 1999; 15: 592-596.
8. Greelish JP, Friedberg JS. Secondary pulmonary malignancy. Surg Clin North Am 2000; 80: 633-657.
9. Verazin GT, Warneke JA, Driscoll DL, Karakousis C, Petrelli NJ, Takita H. Resection of lung metastases from soft-tissue sarcomas. A multivariate analysis. Arch Surg 1992; 127: 1407-1411.
10. Dowling RD, Landreneau RJ, Miller DL. Video-assisted thoracoscopic surgery for resection of lung metastases. Chest 1998; 113: 2S-5S.
11. Nakajima J, Takamoto S, Tanaka M, Takeuchi E, Murakawa T, Fukami T. Thoracoscopic surgery and conventional open thoracotomy in metastatic lung cancer. Surg Endosc 2001; 15: 849-853.
12. Burdine J, Joyce LD, Plunkett MB, Inampudi S, Kaye MG, Dunn DH. Feasibility and value of video-assisted thoracoscopic surgery wedge excision of small pulmonary nodules in patients with malignancy. Chest 2002; 122: 1467-1470.
13. Smith TJ, Rothenberg SS, Brooks M, et al. Thoracoscopic surgery in childhood cancer. J Pediatr Hematol Oncol 2002; 24: 429-435.
14. Lin JC, Wiechmann RJ, Szwerc MF, et al. Diagnostic and therapeutic video-assisted thoracic surgery resection of pulmonary metastases. Surgery 1999; 126: 636-641.
15. Guye E, Lardy H, Piolat C, et al. Thoracoscopy and solid tumors in children: a multicenter study. J Laparoendosc Adv Surg Tech A 2007; 17: 825-829.
16. Mack MJ, Hazelrigg SR, Landreneau RJ, Acuff TE. Thoracoscopy for the diagnosis of the indeterminate solitary pulmonary nodule. Ann Thorac Surg 1993; 56: 825-832.

17. Cardillo G, Regal M, Sera F, et al. Videothoracoscopic management of the solitary pulmonary nodule: a single-institution study on 429 cancer patients. Ann Thorac Surg 2003; 75: 1607-1611.

18. Mineo TC, Ambrogi V, Paci M, Lavicoli N, Pompeo E, Nofroni I. Transxiphoid bilateral palpation in video-assisted thoracoscopic lung metastasectomy. Arch Surg 2001; 136: 783-788.

19. Schwarz RE, Posner MC, Ferson PF, Keenan RJ, Landreneau RJ. Thoracoscopic techniques for the management of intrathoracic metastases. Surg Endosc 1998; 12: 842-845.

20. Mutsaerts EL, Zoetmulder FA, Meijer S, Baas P, Hart AA, Rutgers EJ. Outcome of thoracoscopic pulmonary metastasectomy evaluated by confirmatory thoracotomy. Ann Thorac Surg 2001; 72: 230-233.

21. Castagnetti M, Delarue A, Gentet JC. Optimizing the surgical management of lung nodules in children with osteosarcoma: thoracoscopy for biopsies, thoracotomy for resections. Surg Endosc 2004; 18: 1668-1671.

22. 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.

23. Van Geel AN, Pastorino U, Jauch KW, et al. Surgical treatment of lung metastases: the European organization for research and treatment of cancer - soft tissue and bone sarcoma group study of 255 patients. Cancer 1996; 77: 675-682.

24. Belal A, Salah E, Hajjar W, et al. Pulmonary metastatectomy for soft tissue sarcomas: Is it valuable? J Cardiovasc Surg 2001; 42: 835-840.

25. Suzuki M, Iwata T, Ando S, et al. Predictors of long-term survival with pulmonary metastasectomy for osteosarcomas and soft tissue sarcomas. J Cardiovasc Surg 2006; 47: 603-608.

26. Harting MT, Blakely ML, Jaffe N, et al. Long-term survival after aggressive resection of pulmonary metastases among children and adolescents with osteosarcoma. J Pediatr Surg 2006; 41: 194-199.

27. McCormack PM, Ginsberg KB, Bains MS, et al. Accuracy of lung imaging in metastases with implications for the role of thoracoscopy. Ann Thorac Surg 1993; 56: 863-865.

28. McCormack PM, Bains MS, Begg CB, et al. Role of video-assisted thoracic surgery in the treatment of pulmonary metastases: result of a prospective trial. Ann Thorac Surg 1996; 62: 213-216.

29. Temeck BK, Wexler LH, Steinberg SM, McClure LL, Horowitz MA, Pass HI. Metastasectomy for sarcomatous pediatric histologies: results and prognostic factors. Ann Thorac Surg 1995; 59: 1385-1389.

30. Absalon MJ, McCarville MB, Liu T, Santana VM, Daw NC, Navid F. Pulmonary nodules discovered during the initial evaluation of pediatric patients with bone and soft-tissue sarcoma. Pediatr Blood Cancer 2008; 50: 1147-1153.

31. Burk CD, Belasco JB, O'Neill JA Jr, Lange B. Pulmonary metastases and bone sarcomas. Surgical removal of lesions appearing after adjuvant chemotherapy. Clin Orthop Relat Res 1991; 262: 88-92.

32. Mialou V, Philip T, Kalifa C, et al. Metastatic osteosarcoma at diagnosis: prognostic factors and long-term outcome. The French pediatric experience. Cancer 2005; 104: 1100-1109.

33. Bacci G, Rocca M, Salone MC, et al. High grade osteosarcoma of the extremities with lung metastases at presentation: treatment with neoadjuvant chemotherapy and simultaneous resection of primary and metastatic lesions. J Surg Oncol 2008; 98: 415-420.

34. Wu PK, Chen WM, Chen CF, Lee OK, Haung CK, Chen TH. Primary osteogenic sarcoma with pulmonary metastasis: clinical results and prognostic factors in 91 patients. Jpn J Clin Oncol 2009; 39: 514-522.

35. Carter SR, Grimer RJ, Sneath RS, Matthews HR. Results of thoracotomy in osteogenic sarcoma with pulmonary metastases. Thorax 1991; 46: 727-731.

36. Smith R, Pak Y, Kraybill W, Kane JM 3rd. Factors associated with actual long-term survival following soft tissue sarcoma pulmonary metastasectomy. Eur J Surg Oncol 2009; 35: 356-361.

37. Tanaka Y, Maniwa Y, Nishio W, Yoshimura M, Okita Y. The optimal timing to resect pulmonary metastasis. Eur J Cardiothorac Surg 2008; 33: 1135-1138.

38. Mutsaerts EL, Zoetmulder FA, Meijer S, Baas P, Hart AA, Rutgers EJ. 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.

39. Flye MW, Woltering G, Rosenberg SA. Aggressive pulmonary resection for metastatic osteogenic and soft tissue sarcomas. Ann Thorac Surg 1984; 37: 123-127.

40. Matsunaga T, Sasaki F, Ohira M, et al.; Japanese Study Group for Pediatric Liver Tumor. Analysis of treatment outcome for children with recurrent or metastatic hepatoblastoma. Pediatr Surg Int 2003; 19: 142-146.

41. Ehrlich PF, Hamilton TE, Grundy P, Ritchey M, Haase G, Shamberger RC. National Wilms' Tumor Study Group (National Wilms' Tumor Study 5). The value of surgery in directing therapy for patients with Wilms' tumor with pulmonary disease. A report from the National Wilms' Tumor Study Group (National Wilms' Tumor Study 5). J Pediatr Surg 2006; 41: 162-167.