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A 20-year retrospective analysis of CT-based pre-operative identification of pulmonary metastases in patients with osteosarcoma: A single-center review☆,☆☆

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ABSTRACT

Purpose: Cooperative studies support complete metastasectomy in osteosarcoma (OS). Pre-operative CT is used to identify and quantify metastases and can facilitate minimally invasive techniques. Here we assess the accuracy of pre-operative CT compared to findings at thoracotomy and its change over time.
Methods: We reviewed OS thoracotomies performed at our institution from 1996 to 2015. The number of metastases identified on pre-operative chest CT was compared to the number of metastases seen on pathology (both metastases with viable cells and non-viable, osteoid-only metastases).
Results: Eighty-eight patients underwent 161 thoracotomies with a median of 14 days (range, 1–85) between CT and surgery, a median of 2 CT-identified lesions (range, 0–15), and a median of 4 resected lesions (range, 1–25). In 56 (34.8%) cases, more metastases were found surgically than were seen on CT, and among these, 34 (21.1%) had a greater number of viable metastases. There was poor overall correlation between CT and pathology findings (Kendall Tau-b = 0.506), regardless of CT slice thickness, decade of thoracotomy, or total number of CT-identified lesions.
Conclusions: CT accuracy in pre-operatively quantifying OS pulmonary metastases has not improved in recent decades. Consequently, we recommend an open technique with direct lung palpation for complete identification and resection of OS pulmonary metastases.
Level of evidence: Level IV, retrospective study with no comparison group.

In recent cooperative group trials, overall survival in osteosarcoma (OS) has been approximately 75% [1]. Unfortunately, survival is drastically lower in patients with relapsed OS [2,3], 75% of whom relapse with metastases in the lungs [4,5]. Over the last four decades, significant progress has been made in the treatment of pulmonary metastases in OS, bringing the overall survival from 0% in 1970 [6] to 17–34% in the most recent published series [7–11]. Prognosis in patients with pulmonary metastases has repeatedly been shown to depend on the extent of treatment-induced necrosis in the lesions, disease-free interval before relapse, the total number of metastases, and unilateral versus bilateral involvement. The single most important prognostic factor, however, is the ability to achieve complete resection of the metastases, with little or no benefit derived from systemic therapy [2,7–20].

Concomitant with the ongoing advances in treatment of pulmonary OS metastases, rapid progress has been made in minimally invasive surgery. Given its benefits with respect to post-operative pain and length of stay, its application to childhood cancer has expanded [21]. Use of minimally invasive techniques in OS metastasectomy, however, has been limited by difficulty visualizing and/or locating the metastases without palpation. Over the last two decades, multiple techniques have been developed to circumvent this problem in metastatic childhood cancers, including OS. Intraoperative thoracoscopic ultrasound, pre-operative tattooing of lesions, and pre-operative wire localization have all been shown to successfully localize pulmonary lesions identified on pre-operative CT and allow resection in the majority of patients [22–25].

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Unfortunately, minimally invasive resection of pulmonary metastases is still inherently limited to the lesions identified on pre-operative CT scan, despite all of the aforementioned technologies.

We previously published a series showing that pre-operative CT scanning underestimated the total number of histologically proven OS metastases in 35% of the thoracotomies performed [26]. In this study we have significantly expanded our series in order to further analyze the overall accuracy of pre-operative CT and the change in that accuracy over the last two decades, given the significant advances in CT imaging. This retrospective study uses data from thoracotomies performed by the Pediatric Surgical Service at Memorial Sloan Kettering Cancer Center over the last 20 years.

1. Patients and methods

1.1. Inclusion criteria

With institutional review board approval, we retrospectively identified and analyzed records of all thoracotomies performed for metastatic OS by the Pediatric Surgical Service at Memorial Sloan Kettering Cancer Center from May 1996 to 2015 (n = 176). As shown in Fig. 1, patients who underwent palliative thoracotomies and those with hilar lymph node, mediastinal, parietal pleura, or chest wall involvement were excluded (n = 8). Thoracotomies with miliary disease (>25 lesions) on pre-operative CT or at operative resection were excluded because of the difficulties posed by confluence of lesions (n = 4). Patients lacking complete pre-operative CT imaging of the lungs were also excluded (n = 3). A total of 161 thoracotomies in 88 patients were included in the analysis.

1.2. Operative procedures

At our institution, we perform staged bilateral thoracotomies when metastatic OS is suspected on pre-operative CT-imaging. Our practice is to proceed with a contralateral thoracotomy if the patient is found to have OS metastases on the initial side of the lesion excision, whether or not there is evidence of contralateral disease on CT [27]. We normally perform the contralateral thoracotomy within 2–4 weeks or after WBC and platelet recovery from intervening chemotherapy, if necessary. In this series, vertical transaxillary thoracotomy (n = 12) and posterolateral muscle-sparing thoracotomy (n = 149) were used. After mobilization, a systematic whole-lung palpation technique was employed by each operating surgeon to identify and systematically remove all palpable lesions, regardless of size or intraoperative pathology. The lung was palpated 2–3 times by all participating surgeons after the last palpable lesion was removed to confirm complete resection of metastases.

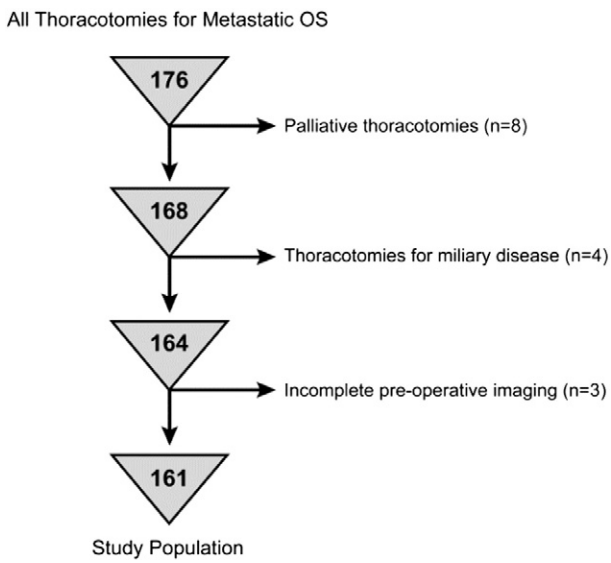

Fig. 1. Flow chart showing reasons for patient exclusion.

1.3. Radiology review

CT scans used in this study had a maximum slice thickness of 5 mm. If 1.25-mm thickness reconstructions were available, they were used for enumeration of lesions and their use was recorded for comparison. If maximum intensity projection sequences were available, they were used in conjunction with standard projection, and a consensus count was obtained prior to our data analyses. Scans were reviewed by either two pediatric radiologists or one pediatric radiologist and one pediatric surgeon. When developing the consensus counts, reviewers were blinded to the initial CT-scan reading, all comparison scans, and the outcome of each thoracotomy. Lack of specific anatomic labeling of resected specimens prevented lesion-for-lesion comparison of CT attributes to pathology, so any CT identifying an equal or greater number of lesions than the number of metastases resected at thoracotomy was considered a predictive pre-operative CT. Overestimation, while increasing the number of resections, was assumed to have no effect on oncologic outcome.

1.4. Pathologic analysis

Pathologic evaluation of all resected lung specimens was performed by standard light microscopy. If a wedge contained multiple individual lesions, each was counted in the pathologic total. Confluent lesions and lesions that required excision of additional margin to achieve complete resection were counted as a single lesion. The degree of necrosis was evaluated in each metastatic lesion and a percent viability was estimated [28]. Metastases were considered viable if any obviously viable OS cells were identified. Bony osteoid metastases devoid of viable cells were counted as non-viable metastases. Non-metastatic lesions resected were also characterized and tallied.

1.5. Statistical analysis

Non-normal distributions of CT lesions, resected lesions, and pathologically confirmed metastases are described using the median, range, and quartiles of each distribution. Age, number of CT lesions, size of the lesions on pathology, and intervals between CT and thoracotomy were compared across subgroups using the Wilcoxon signed rank test. Kendall Tau-b correlation coefficients were calculated to describe the correlation between the number of CT-identified lesions and the total number of metastases on pathology. All statistical analyses were performed using R software (version 3.1.1 2014; R Project for Statistical Computing, Vienna, Austria; www.r-project.org).

2. Results

As described in Table 1, 49 patients (56%) were male and 39 (44%) were female. The median number of thoracotomies per patient was 2 (range 1–5). Median age at thoracotomy for the whole cohort was 16 years (range 6–29). The age of patients with predictive CTs (median 17 y, range 6–29) and patients with CTs underestimating viable metastases (median 15 y, range 10–23) were similarly distributed (p = 0.38). However, patients with CTs underestimating total metastases were younger (median 14.5 y, range 8–29) than patients with predictive CTs (p = 0.005). These differing variables are presented in whisker-and-box plots in Fig. 2. Sex and race were similarly distributed within each group.

There were 498 lesions identified on pre-operative CTs (median 2 per CT, range 0–15), and for 20% of these CTs, thin-cut reconstructions were available for comparison. The number of lesions on CT did not