become the more salient question in the future, rather than additional comparisons between surgical and medical therapies.⁸

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Commentary: Upping our game

Todd L. Demmy, MD

In this issue of the *Journal*, Liu and colleagues¹ report a useful large case series of osteosarcoma patients who underwent resection of their lung metastases. Fewer involved lobar regions (rather than just absolute numbers) and lower alkaline phosphatase levels were nuanced advantages that should be studied by others for replication. Like other thoughtful investigators, the authors recommend a prospective trial to validate their findings.

Is a randomized study the correct next step for a complex diverse disease for which we have new tools for study? Patients receive benefit, suffer harm, or break even from our attempts at local resection, depending on their sarcoma biologies. Aggressive tumors beat surgical therapies, and some experts argue that patients with indolent sarcoma might live just as long without operative interference.²

Most surgeons have seen metastatic disease accelerate after cancer operations because of inflammatory cytokines, stimulation of angiogenesis, or removal of tumor-related

CENTRAL MESSAGE

Concomitant regional therapy and genomic-based patient selection will enhance the oncologic surgical validity of sarcoma pulmonary metastasectomy.

inhibitory factors.^{3,4} However, even when appropriately counseled regarding potentially unfavorable recurrence dynamics, patients face a psychologic imperative to accept surgery rather than watching their disease progress as other options fail. This imperative would likely be a larger barrier to randomized investigations than observed when comparing open operations with minimally invasive operations. Perhaps patients would agree to be randomized between immediate or delayed surgical approaches to test a noninferiority hypothesis. However, would such hypotheses, if proven, provide sufficient evidence to change practice for patients with few other optimistic options?

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FIGURE 1. Pulmonary artery and vein control (*inset*) techniques are simple and well established and could allow surgeons to provide adjuvant lung drug delivery while performing routine operations.⁶

Over the past decade, we have seen our medical colleagues move to a much more personalized approach to thoracic malignancy.⁵ To foster similar surgical relevance for sarcoma metastasectomy, now is the time to “up our game.” To do this, we need to contribute scientific insight on par with other specialties to improve our therapeutic and classification systems.

As surgeons, we routinely control vessels and organ tissues in ways that could empower regional therapies. During resection of measurable tumors, the augmentation of drug delivery or immune recognition of minimal residual disease by reengineering organ perfusion systems and other methods well known to thoracic surgeons is being explored in active clinical trials (Figure 1).^{7,8} We also are adept at airway control, which could be used for selective drug delivery.

Sarcoma metastatic lung tumors contain a wealth of genomic data to help us understand this disease, which is made enigmatic by rarity and its further parsing into numerous grades, histological subtypes, and clonal expansions.⁹ The development of practice guidelines recommending gene sequencing for metastatic sarcomas is a reasonable goal, as is commonly used for stage IV primary lung cancers to guide mutation-focused systemic therapies.¹⁰ Because

cases are uncommon, the ability to tabulate and enroll patients prospectively into an international registry (previously done retrospectively) would be manageable.¹¹

Linking registry clinical outcomes broadly with genomic data is attainable given contemporary technology.¹² We would then have the tools to support the validity of resections and emerging surgical-based adjuvant therapies for these patients. Correlative genomic data should then yield a predictive strategy providing equipoise needed for participants and investigators to accept assortment into surgical and nonoperative options needed for this challenging, understudied disease.

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