Commentary: Expanding the legacy of unusual malignancy research

Todd L. Demmy, MD

From the Department of Thoracic Surgery, Roswell Park Cancer Institute, Buffalo, NY; and Department of Surgery, University at Buffalo, Buffalo, NY.

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Address for reprints: Todd L. Demmy, MD, Department of Thoracic Surgery, Roswell Park Cancer Institute, Elm and Carlton streets, Buffalo, NY 14263 (E-mail: todd.demmy@roswellpark.org).

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In this issue of the *Journal*, Choe and colleagues¹ describe their important ongoing research on unusual pleural dissemination presentations of thymic tumors. Among this group's earlier published works is a useful decision-making article on managing pleural relapses.² The excellent outcomes (no operative mortality and good relative long-term survival) for this stage IV disease has been replicated and recently reported by others.^{3,4} Metachronous dissemination after thymectomy (Figure 1) presents at similar rates but tends to have better survival.⁴ In general, this is an exciting time for surgeons, because local therapies for thymoma and even oligometastatic lung cancer are showing promising survivals.^{5,6}

Tempering this enthusiasm is the knowledge that within these modest series are patients with diverse tumor biologies, ages, and comorbidities, all of which have to be considered when offering aggressive therapies. Intuitively, an otherwise healthy patient with relatively indolent, disseminated pleural thymoma is a good surgical candidate. Alternatively, more case comorbidity or tumor virulence reduces the survival benefits provided by local therapies.

Experience in weighing these options is challenged by infrequent patient presentation. For instance, 32 collaborating Japanese institutions took almost 20 years to aggregate 136 cases and observed better survivals with fewer pleural nodules (<10).⁷ What Choe and colleagues¹ have accomplished is therefore remarkable, and there is now sufficient institutional case density there for other research, such as a study to optimize chemotherapy and immunotherapy according to phenotypic and genomic data.

Figure 2 in the article of Choe and colleagues¹ is an excellent attempt to document the long-term experiences of each patient to benefit future investigators. Extrapolation from this figure suggests an important opportunity that investigators need to address. Specifically, to support surgical intervention, we need a long-term effort to amass similar indolent disease data from a broad network. Relying on a

Alternative (metachronous) pleural dissemination of thymoma.

Central Message

The study of unusual tumors may be ideal to re-engineer cancer database systems because of the lack of practical research alternatives and the modest resources (low volume) needed to test new designs.

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single center limits exploration of hypotheses conceived by others and also constrains high-volume centers from validating their observations in larger data sets.

FIGURE 1. Coronal computed tomographic image of patient with right-sided pleural dissemination after a previous thymoma resection.

Unfortunately, traditional randomized clinical trials are impractical for unusual diseases because of relatively rapid changes in understanding of tumor biologies and evolutions in therapies for local control. This issue is being addressed, however, by building into modern clinical protocols “adaptive” designs that take such changes into account proactively. This practice could enable a useful “generational” thymoma protocol.^{8,9}

Until then, reengineering existing cancer databases to behave more flexibly and dynamically link supplemental fields could effectuate rare disease study. This is an attractive option, because these infrastructures already exist to capture ongoing events (such as disease recurrence and death), and resources should not be strained by camping on additional low-volume pilots of data entry. Similar concepts have been described in recent articles and could also bind emerging precision genomic data needed to pick optimal future local and systemic therapies.¹⁰⁻¹³ With such a development, instead of providing analog figures, thought leaders like Choe and colleagues¹ will be able to publish their data fields and ontologies to allow others to enhance their efforts by distributed computing. In this way, their legacy will be preserved and further enhanced by ongoing cooperative research.

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