than N0 patients but both derive substantial benefit from surgical resection. It is enormously important not to over-emphasize the utility of prognostic factors. Although prognosis is important for comparisons between groups and/or studies, it also is a form of selection bias. Simply selecting the best prognostic patients does not guarantee surgical benefit.

Undoubtedly, prognostic factors are valuable when considering metastasectomy in colorectal cancer patients. It also is clear that surgical benefit may be derived in both good and poor prognostic groups. That is why prospective randomized clinical trials remain critical in determining true surgical benefit in any clinical/surgical situation rather than accepting the mere appearance of good outcomes

based on the selection bias inherent in the sole use of prognostic factors in patient selection.

References

1. Zellweger M, Abdelnour-Berchtold E, Krueger T, Ris HB, Perentes JY, Gonzalez M. Surgical treatment of pulmonary metastasis in colorectal cancer patients: current practice and results. *Crit Rev Oncol Hematol*. 2018;127:105-16.
2. Treasure T, Farewell V, Macbeth F, Monson K, Williams NR, Brew-Graves C, et al. Pulmonary metastasectomy versus continued active monitoring in colorectal cancer (PulMiCC): a multicenter randomized clinical trial. *Trials*. 2019;20:718-31.
3. Afrăsănie VA, Marinca MV, Alexa-Stratulat T, Gaftan B, Păduraru M, Adavidoaiei AM, et al. KRAS, NRAS, BRAF, HER2 and microsatellite instability in metastatic colorectal cancer— practical implications for the clinician. *Radiol Oncol*. 2019;53:265-74.
4. Corsini EM, Mitchell KG, Correa A, Morris VK, Antonoff MB. Effect of primary colorectal cancer tumor location on survival after pulmonary metastasectomy. *J Thorac Cardiovasc Surg*. 2021;162:296-305.

See Article page 296.

Commentary: Molecular biology, location, and survival following pulmonary metastasectomy for colorectal carcinoma

Anna L. McGuire, MD, MSc, FRCSC

In this issue of the *Journal*, Corsini and colleagues¹ explore a truly novel concept in thoracic surgery relating to pulmonary metastasectomy for primary colorectal carcinoma: the independent impact of bowel segment location on patient survival time. Herein we are provided

CENTRAL MESSAGE

Differential survival following pulmonary metastasectomy by colonic primary location may be a useful proxy for molecular etiology.

From the Division of Thoracic Surgery, Department of Surgery, Vancouver General Hospital, University of British Columbia; and Vancouver Coastal Health Research Institute, Vancouver General Hospital, Vancouver, British Columbia, Canada.

Disclosures: Dr McGuire receives in-kind research support from Contextual Genomics, Inc (Vancouver, British Columbia, Canada), and research funding from AstraZeneca Canada for study unrelated to the current submission.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication April 19, 2020; accepted for publication April 20, 2020; available ahead of print May 1, 2020.

Address for reprints: Anna L. McGuire, MD, MSc, FRCSC, Division of Thoracic Surgery, Department of Surgery, Vancouver General Hospital, Vancouver Coastal Health, 2775 Laurel St, Suite 7113, V5Z 1M9, Vancouver, British Columbia, Canada (E-mail: anna.mcguire@vch.ca).

J Thorac Cardiovasc Surg 2021;162:307-8

0022-5223/\$36.00

Copyright © 2020 Published by Elsevier Inc. on behalf of The American Association for Thoracic Surgery

<https://doi.org/10.1016/j.jtcvs.2020.04.075>

a tool that, with ongoing study, could further refine existing prognostic models following pulmonary resection.^{2,3} Particularly relevant in the current evolving era of molecular diagnostics and precision oncology, there is value in synthesizing these data with a purpose to clinically inform risk/benefit discussions with patients regarding multimodal treatment decisions. As thoracic surgical oncologists, we aim to maximize survival as well as quality of life for each patient with pulmonary metastases. We understand that pulmonary metastasectomy is only one component of a multimodal treatment paradigm, including

a growing armamentarium of systemic options for consideration, such as traditional chemotherapy, targeted biologic therapies, and immune therapy.⁴

Interestingly, data from the authors' high-volume tertiary cancer center found that clinical and statistical differences do exist with respect to survival following pulmonary metastasectomy by primary colorectal carcinoma location. In particular, carcinoma located in left-sided bowel segments (splenic flexure to rectosigmoid junction) was associated with prolonged overall survival following pulmonary metastasectomy. This finding remained evident with multivariable sensitivity analysis, above and beyond previously reported prognostic factors (hazard ratio, 0.31; $P = .036$).¹

Although we must be cautious of inherent bias related to unknown confounders that may be present in single-center historical cohort studies, the methods presented here are rigorous and thoughtful. This is evident in the interesting subgroup analysis included by the authors, whereby they estimated a propensity score with a purpose to balance known covariates and directly compare right- and left-sided bowel segment metastasectomy outcomes.

By obviating a relationship with patient mortality, the paper establishes precedent when planning future prospective and multicenter studies to incorporate this parameter. Specifically, an important aspect of future trial design on pulmonary metastasectomy would be to include subgroup assessment by primary bowel segment in planned

analyses, in addition to molecular pathologic assessment. For example, current evidence suggests that patients with metastatic tumors originating on the right side of the colon are unlikely to respond to epidermal growth factor receptor–targeted biologic therapy, whereas data on the response in patients with primary tumors originating in the transverse colon are lacking.⁴ In this way, the biological and molecular basis of the observed association between primary tumor bowel location and overall survival may be further clarified. This novel report is striking for critical insights provided regarding the clinical significance of colonic segment for thoracic surgeons and our patients undergoing pulmonary metastasectomy.

References

1. Corsini EM, Mitchell KG, Correa A, Morris VK, Antonoff MB. Effect of primary colorectal cancer tumor location on survival after pulmonary metastasectomy. *J Thorac Cardiovasc Surg*. 2021;162:296-305.
2. Rena O, Casadio C, Viano F, Cristofori R, Ruffini E, Filosso PL, et al. Pulmonary resection for metastases from colorectal cancer: factors influencing prognosis. Twenty-year experience. *Eur J Cardiothorac Surg*. 2002; 21:906-12.
3. Inoue M, Kotake Y, Nakagawa K, Fujiwara K, Fukuhara K, Yasumitsu T. Surgery for pulmonary metastases from colorectal carcinoma. *Ann Thorac Surg*. 2000;70: 380-3.
4. National Comprehensive Cancer Network (NCCN). Colon Cancer (Version 2. 2020). Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed April 19, 2020.