they found no significant difference in survival with early or late pulmonary vein ligation.

The possibility of improving long-term survival by changing our surgical techniques is intriguing, but larger, randomized validation studies with clear documentation of the surgical approach, measurement of peripheral circulating tumor cells, and sufficient follow-up are needed to determine whether catching escaping circulating tumor cells will increase disease-free and overall survival.

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Commentary: A surgical shotgun?

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CENTRAL MESSAGE

Early ligation of the pulmonary vein may present a simple means toward reducing the shed of circulating tumor cells during lobectomy.

It has been hypothesized in patients and shown in preclinical studies that local treatment of cancer, whether surgery or radiation therapy, can lead to mechanical disruption of the tumor, shedding of tumor cells, suppression of antitumor immunity, and enhancement of the metastatic process.[1,2] Specific to lung cancer, previous studies have shown increases in pulmonary venous and peripheral blood circulating tumor cells (CTCs) following surgery, raising the question of whether ligating the pulmonary vein and cessation of effluent flow early during lobectomy might reduce shedding of CTCs. One notable study even suggested that late division of the pulmonary vein was associated with decreased overall and progression-free survival.[3] While an intriguing combination of randomized trial along with retrospective propensity-matched data, the methodology of that study has been questioned regarding measurement of CTCs and study design.[4]

In the current issue of the *Journal*, Duan and colleagues[5] provide more prospective evidence of the potential for surgical "shotgunning" of tumor cells into the blood, showing that CTCs in the postoperative pulmonary vein stump were 9-fold greater than at the beginning of the case. The number of CTCs was significantly greater in the stumps of patients

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who had early rather than late ligation of the pulmonary vein, suggesting that CTCs had disseminated into the circulation in the late ligation group where venous drainage was preserved. In this paper and in the field as a whole, one can quibble with methodology of CTC detection, with statistical tests, and with causality of metastasis. Isn't it time to instead ask ourselves, "why wouldn't tumor manipulation cause tumor cells to shed and present a substrate for future metastases?" If we disrupted a tumor into the pleural space, we would certainly worry about subsequent pleural metastasis. So why shouldn't we concern ourselves with intralobar disruption, particularly for those larger tumors where lymphovascular invasion is already present?

Yet many surgeons do not ligate the pulmonary vein as the first step in their operation, a seemingly simple method to decrease the possibility of CTC dissemination. This may be particularly true in the conduct of robotic-assisted operations, in which the vein is often divided as the last step.[6,7] With increasing adoption of minimally invasive techniques including thoracoscopic and robotic-assisted resections, lung retraction and manipulation also may represent an interesting area of investigation. As alluded to by the authors, tumor shedding may vary with different techniques of lung handling. We operate to not only to remove the cancer, but also to afford patients with improved survival. If basic intraoperative techniques may potentiate this, there is little downside to their incorporation.

As molecular techniques improve to identify viable CTCs with metastatic potential, we should launch adequately powered studies to investigate CTC shedding during surgery and the implications on recurrence-free survival. Until then, at least click the safety on the surgical shotgun and ligate the pulmonary vein early in the course of lobectomy. It is an easy precaution to take.

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