



Editorial

Laparoscopic Surgery Alters the Pattern of Recurrence Following Rectal Cancer Surgery: A Conceptual Hypothesis



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Low rectal cancers, anatomically defined as tumors located within 5 cm of the dentate line, represent a biologically and clinically distinct subset of colorectal malignancies. These tumors present specific therapeutic challenges and demonstrate unique patterns of metastatic dissemination compared to mid- and upper rectal cancers. Notably, multiple retrospective and prospective series have consistently demonstrated that low rectal cancers carry approximately double the risk of pulmonary metastases (compared to high rectal cancers) following curative-intent resection, independent of neoadjuvant chemoradiotherapy.^{1,2} This pattern underscores the critical importance of understanding how the surgical approach may influence oncological outcomes beyond traditional endpoints such as disease-free survival (DFS).

The recent laparoscopy-assisted versus open surgery for low rectal cancer (LASRE) trial,³ a multicenter, randomized controlled trial conducted across several institutions in China, contributes high-quality prospective data to this discourse. The trial aimed to establish the non-inferiority of laparoscopic surgery versus open surgery in terms of three-year DFS in patients with low rectal cancer. A total of 1,070 patients were enrolled over 4.5 years, of whom 96% received neoadjuvant chemoradiotherapy, a figure reflective of modern practice in this subgroup. The primary endpoint demonstrated no statistically significant difference in three-year DFS: 81.4% in the laparoscopic group versus 79.8% in the open group ($p = 0.56$). These results corroborate existing literature supporting the oncological adequacy of laparoscopic approaches in rectal cancer resection when performed in appropriately selected patients.

However, a particularly intriguing secondary finding within the LASRE dataset warrants further attention: the significantly lower rate of pulmonary metastases observed in the laparoscopic cohort compared to the open cohort (5% vs 9%, $p = 0.011$). The authors did not indicate whether pulmonary metastasis was a pre-specified secondary endpoint in the trial protocol, and this result is not explored in depth by the trial authors. Furthermore, no adjustment appears to have been made for multiple hypothesis

testing across various recurrence sites. Without formal correction (e.g., Bonferroni or false discovery rate adjustment), the statistical significance of this result may be overstated. Nonetheless, it raises a provocative hypothesis that the surgical approach may influence not only the overall recurrence rate but also the anatomical pattern of metastatic spread.

If overall recurrence rates are indeed similar between the two groups, as reported, the logical inference is that the reduction in pulmonary metastases in the laparoscopic group must be offset by a corresponding, albeit statistically undetectable, redistribution of metastases to alternative sites such as the peritoneum, liver, bone, inguinal nodes, or locoregional tissues. These shifts, particularly if modest and dispersed across multiple sites, may escape detection in trials not powered for such granular analysis.

The biological plausibility of such a phenomenon invites speculation but remains incompletely understood. Several potential mechanisms may account for a reduced incidence of lung metastases in the laparoscopic group. One hypothesis suggests that minimally invasive surgery results in less manipulation and disruption of the primary tumor, thereby decreasing haematogenous dissemination of tumor cells during surgery.⁴ Another possibility is that laparoscopic techniques result in less intraoperative trauma and blood loss, preserving postoperative immune function that is critical for early elimination of circulating tumor cells.⁵ Additionally, CO₂ pneumoperitoneum used in laparoscopy may influence venous return, tumor microenvironment, or local immune surveillance in ways that differentially impact metastatic seeding.⁶ Although these mechanisms have been suggested in studies on non-rectal tumors, they highlight the need for further mechanistic studies, including translational research involving animal models or analysis of perioperative circulating tumor cell dynamics.

It is important to recognize the methodological limitations of the LASRE trial in this context. Although adequately powered to evaluate non-inferiority with respect to DFS, the study was not designed to detect small but clinically meaningful differences in site-specific recurrence patterns. Detecting such differences would require trials of substantially larger size or meta-analyses with homogeneous definitions and data collection. The challenges of conducting large-scale surgical randomized controlled trials are well-documented,⁷ particularly in the context of evolving surgical technologies and practitioner learning curves.

Beyond theoretical plausibility, these findings also have po-

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tential clinical implications. Pulmonary metastases, while serious, may be resectable in a select subset of patients with favorable disease biology. However, other sites of recurrence, such as bone or brain metastases, often preclude curative treatment. Thus, even if the overall recurrence rate remains unchanged, a shift in the distribution of metastatic sites could meaningfully impact long-term survival, quality of life, or eligibility for salvage therapies. From a preventive standpoint, these findings suggest that high-risk patients (e.g., those with advanced T stage, threatened circumferential resection margins, or adverse molecular features) might benefit from minimally invasive surgery as part of a broader strategy to reduce metastatic seeding. Furthermore, closer surveillance of pulmonary function and perioperative optimization of immune competence may represent adjunctive measures to mitigate recurrence risk.

Thus, while the LASRE trial reinforces the oncological safety of laparoscopic resection in low rectal cancer, its unanticipated findings regarding pulmonary metastases merit further investigation. Whether this observation represents a true biological effect or a statistical anomaly remains to be determined. Nonetheless, it raises important questions about how surgical technique may subtly influence tumor behavior and metastatic pathways. Future research must aim to elucidate the underlying mechanisms, validate recurrence patterns in larger datasets, and determine whether these patterns translate into differences in long-term survival or quality of life for patients with low rectal cancer.

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