



Advancing surgical options in esophageal cancer: key findings from the ROMIO randomized clinical trial

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Comment on: ROMIO Study Group. Laparoscopic or open abdominal surgery with thoracotomy for patients with oesophageal cancer: ROMIO randomized clinical trial. *Br J Surg* 2024;111:znae023.

Keywords: ROMIO; randomized clinical trial (RCT); laparoscopy; esophageal cancer

Submitted Oct 25, 2024. Accepted for publication Dec 17, 2024. Published online Jan 20, 2025.

doi: 10.21037/jtd-24-1803

View this article at: <https://dx.doi.org/10.21037/jtd-24-1803>

We thank the editors of the *Journal of Thoracic Disease* for inviting us to provide editorial commentary on a paper by the ROMIO Study Group which was published earlier this year in *British Journal of Surgery* (1). This study is a significant step forward in comparing hybrid minimally invasive esophagectomy (MIE) with traditional open surgery for patients with localized esophageal cancer. As surgical techniques evolve, the question of whether minimally invasive approaches offer meaningful advantages over conventional methods becomes more important. The ROMIO randomized clinical trial (RCT), with over 500 patients, sought to address this by investigating whether a hybrid approach, which involves laparoscopic gastric mobilization combined with thoracotomy, leads to faster recovery and fewer complications compared to open esophagectomy. The results of this trial provide essential guidance for clinicians and contribute to the ongoing discussion in surgical oncology.

Esophageal cancer remains one of the leading causes of cancer-related mortality worldwide, with significant geographical variation in incidence rates. In 2020, over 600,000 new cases of esophageal cancer were diagnosed globally (2). Surgery remains the cornerstone of curative treatment for localized esophageal cancer, and in recent years, advances in surgical techniques have sparked a debate over whether minimally invasive methods can improve patient outcomes. MIE is thought to reduce postoperative pain, and improve recovery times and complication rates

compared to traditional open surgery (3,4). However, the benefits of MIE in terms of long-term survival, recurrence, and quality of life are still under investigation. This study was designed to explore whether a hybrid approach, which includes minimally invasive techniques for the abdominal phase of surgery combined with thoracotomy for the chest phase, could offer a balance between minimizing the physical impacts of surgery and maintaining the effectiveness of traditional surgery (5,6). The findings of this trial are crucial for determining the future direction of surgical practice in treating esophageal cancer. The primary outcome of this study was patient-reported physical function, measured using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) over a 3-month period following surgery (7).

Contrary to expectations, this trial found no significant difference in physical function between patients who underwent hybrid esophagectomy and those who had open surgery. Both groups showed similar recovery trajectories in terms of their physical abilities and quality of life 3 months post-surgery. *Table 1* shows RCTs that compare MIE and open esophagectomy, including our study. We compared laparoscopic versus open abdominal lymph node dissection for esophageal squamous cell carcinoma using propensity score matching (12). A retrospective analysis of 459 patients showed that the laparoscopic group had fewer Clavien-Dindo (CD) grade ≥ 2 complications, lower rates of

Table 1 Randomized control trials (including our study) comparing short-term and long-term outcomes of MIE and open esophagectomy

Trial	Ref.	Author, year	Number of patients	Approach	Outcomes
TIME (Netherlands)	(3)	Biere <i>et al.</i> , 2012	115	MIE (thoracoscopy plus laparoscopy) vs. open esophagectomy	Pulmonary infection within the first 2 weeks: 12% vs. 34%, P=0.005
	(8)	Straatman <i>et al.</i> , 2017			Whole stay in hospital: 11 vs. 14 days, P=0.044 3-year DFS: 40.2% vs. 35.9%, P=0.60 3-year OS: 41.2% vs. 42.9%, P=0.63
MIRO (France)	(4)	Mariette <i>et al.</i> , 2019	207	HMIE (thoracotomy plus laparoscopy) vs. open esophagectomy	Postoperative complication (\geq CD2) within 30 days: 36% vs. 64%, P<0.001
	(9)	Nuytens <i>et al.</i> , 2021			Pulmonary complication: 18% vs. 30% 3-year DFS: 57% vs. 48% 3-year OS: 67% vs. 55% 5-year DFS: 52% vs. 44%, P=0.26 5-year OS: 59% vs. 47%, P=0.09
ROBOT (Netherlands)	(10)	van der Sluis <i>et al.</i> , 2019	112	RAMIE (robot-assisted thoracoscopy plus laparoscopy) vs. open esophagectomy	Pulmonary complication: 32% vs. 58%, P=0.005
	(11)	de Groot <i>et al.</i> , 2020			Cardiac complication: 22% vs. 47% P=0.006 Mean postoperative pain (visual analog scale): 1.86 vs. 2.62, P=0.001 5-year OS: 41% vs. 40%, P=0.83 5-year RFS: 42% vs. 43%, P=0.75
ROMIO (United Kingdom)	(1)	ROMIO Study Group, 2024	533	HMIE (thoracotomy plus laparoscopy) vs. open esophagectomy	Pulmonary infection within 30 days: 32% vs. 34% No difference in cost-effectiveness
Our study (Japan)	(12)	Ofuchi <i>et al.</i> , 2024	459	MIE (laparoscopy) vs. open (laparotomy)	Postoperative complication (\geq CD2): 28.1% vs. 40.3%, P=0.04 Pulmonary complication: 12.9% vs. 22.3%, P=0.039 Surgical site infection: 2.9% vs. 7.9%, P=0.02 3-year OS: 81.2% vs. 69.5%, P=0.12 3-year DFS: 61.1% vs. 58.2%, P=0.54

MIE, minimally invasive esophagectomy; ref., reference; DFS, disease-free survival; OS, overall survival; HMIE, hybrid minimal invasive esophagectomy; CD2, Clavien-Dindo classification grade 2; RAMIE, robot-assisted minimal invasive esophagectomy.

surgical site infections, and more independent postoperative activities of daily living (ADL) compared to the open surgery group, while both groups had similar lymph node harvest rates and no significant difference in overall or relapse-free survival. This result stands in contrast to previous studies, such as our study and the MIRO trial, which suggested that laparoscopic techniques could reduce postoperative complications and improve recovery (13). The postoperative complication rates, including pulmonary infections, anastomotic leaks, and surgical site infections,

were also similar between the two groups, with no clear advantage for the hybrid approach. The finding that hybrid surgery did not significantly reduce recovery time raises important questions about the general assumption that minimally invasive techniques automatically lead to better short-term outcomes. While a hybrid approach minimizes incision to the abdominal region, the thoracotomy for the chest phase may offset some of the potential benefits. It is possible that for certain patients, especially those with higher risk factors, a hybrid technique could still offer

specific benefits; however, this was not demonstrated across the overall patient population in this study.

Complication rates in both groups were closely monitored, with a particular focus on respiratory complications, which are common in esophagectomy due to the proximity of the surgical site to the lungs and diaphragm. The incidence of pulmonary complications, including infections, was approximately 30% in both groups, with no significant difference between the hybrid and open approaches. This is a significant finding because one of the primary goals of minimally invasive surgery is to reduce such complications by reducing the strain of surgery and promoting faster mobilization postoperatively. Anastomotic leaks are a critical concern following esophagectomy, and can lead to severe morbidity and prolonged hospital stays. This study found comparable rates of anastomotic leakage between the two groups, which counters the idea that hybrid techniques provide superior outcomes in terms of surgical complications. This suggests that, while hybrid surgery may be technically less invasive in certain aspects, the thoracic component, which remains open, may still contribute to the overall risk profile seen in traditional open surgery.

These findings have profound implications for clinical decision-making in esophageal cancer surgery. Because there were no significant differences in recovery and complication rates, both hybrid and open esophagectomy can be considered safe and effective options for patients with localized esophageal cancer. Surgeons can make their decision based on factors such as patient anatomy, comorbidities, and their own experience with each technique, rather than being driven by concerns that one approach may be vastly superior to the other in terms of outcomes. However, this trial also highlights the need to consider individual patient characteristics when selecting a surgical approach. One important finding was the impact of body mass index (BMI) on recovery outcomes. Patients with a lower BMI appeared to benefit more from hybrid surgery, experiencing faster recovery times compared to those with a higher BMI. This suggests that BMI, along with other factors such as age, pre-existing conditions, and tumor location, should be taken into account when determining the best surgical option for each patient.

In addition to clinical outcomes, cost-effectiveness is an increasingly important consideration in modern healthcare. This study included an economic analysis to determine whether hybrid esophagectomy offers any financial advantages over open surgery. Despite the higher

upfront costs associated with hybrid surgery, which includes specialized equipment and longer operating times, the trial found no significant cost savings at 3 months post-surgery. Hospital stays, re-admissions, and the need for additional interventions were similar between the two groups, indicating that the potential financial benefits of hybrid surgery may be overstated. Given the ongoing financial pressures faced by healthcare systems worldwide, this finding is particularly relevant. Healthcare providers should base their decisions on the clinical outcomes and patient characteristics rather than the assumption of cost savings.

This study has some limitations that must be acknowledged. One of the most significant limitations is its focus on short-term outcomes. While 3-month recovery data provides valuable insights, long-term outcomes such as overall survival, recurrence rates, and quality of life beyond the immediate postoperative period were not fully explored. Given that esophageal cancer is associated with relatively high rates of recurrence and long-term complications, it is essential to understand how different surgical techniques affect patients over the long term. Additionally, robot-assisted surgery (14), which has become widespread in recent years, was also excluded from this study. As a result, the findings may not fully reflect the potential benefits of more advanced minimally invasive approaches. Future research should focus on comparing hybrid surgery including robotic techniques to provide a more comprehensive understanding of the best surgical approach for esophageal cancer. The ROBOT and ROBOT-2 trials, which examined fully MIE using robotic assistance, found that robotic techniques offered significant advantages in terms of reducing postoperative pain and improving recovery times (10,14). While this study did not include robot-assisted surgery, its findings suggest that the hybrid approach may not offer the same level of benefit seen in fully minimally invasive procedures. Future trials that directly compare hybrid, fully minimally invasive, and robotic-assisted techniques are needed to clarify these issues.

This study represents an important milestone in the evolution of esophageal cancer surgery, although it also highlights the need for further research. As robotic-assisted surgery continues to improve, there is potential for the more widespread adoption of fully minimally invasive techniques that could further reduce surgical trauma and improve patient outcomes. Long-term studies examining survival, recurrence, and quality of life will be critical in determining the true value of these approaches.

Additionally, future research should focus on refining patient selection criteria to ensure that each individual receives the surgical technique most suited to their specific needs. Factors such as BMI, age, comorbidities, and tumor stage all play a role in determining the best approach, and more personalized treatment plans could lead to better outcomes.

This study provides valuable insights into the comparative effectiveness of hybrid and open esophagectomy for esophageal cancer. While both techniques are safe and effective, the trial found no significant differences in short-term recovery or complication rates, suggesting that surgeons can base their decisions on individual patient characteristics rather than on the assumption of the superiority of one technique over another. The lack of significant cost savings associated with hybrid surgery further underscores the need to focus on clinical outcomes when making surgical decisions. By refining surgical techniques and personalizing treatment plans, clinicians can improve patient outcomes and ensure that esophageal cancer surgery continues to advance.

Acknowledgments

We would like to thank Editage (<https://www.editage.com/>) for the English language editing.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Journal of Thoracic Disease*. The article has undergone external peer review.

Peer Review File: Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-24-1803/prf>

Funding: None.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-24-1803/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Ofuchi T, Kosumi K, Iwatsuki M. Advancing surgical options in esophageal cancer: key findings from the ROMIO randomized clinical trial. *J Thorac Dis* 2025;17(1):5-9. doi: 10.21037/jtd-24-1803