

What is an appropriate strategy of conversion surgery for cT4b thoracic esophageal cancer?

Esophageal cancer, in which the tumor and/or metastatic lymph node has invaded adjacent structures such as the aorta, the trachea, the bronchus, the pulmonary vein, the pulmonary artery, or the vertebral body, is defined as cT4b.¹ Because cT4b esophageal cancer is unresectable, definitive chemoradiotherapy (CRT) or chemotherapy has been recommended for the treatment of cT4b esophageal cancer.² When cT4b esophageal cancer markedly responds to induction therapy, such as CRT or chemotherapy, T4 invasion to adjacent organs can be relieved and conversion surgery can become an additional treatment option. Reportedly, an R0 resection is an independent prognostic factor in patients with cT4b esophageal cancer who have undergone conversion surgery.³

Because the accurate diagnosis of tumor resectability has not yet been completely established, an R0 resection can be confirmed during or after surgery. A useful preoperative diagnostic method is necessary to consider the potential effectiveness of each conversion surgery. Moreover, there are unclear practical matters regarding whether a lymphadenectomy is necessary and what extent of a lymphadenectomy is appropriate. In this issue of the *Annals of Gastroenterological Surgery*, Ohkura et al have reported a clinically important article entitled, "Advantageous factors of R0 curative conversion esophagectomy and the optimal extent of lymphadenectomy after induction therapy for cT4b thoracic esophageal cancer."⁴

They analyzed 151 patients with cT4b thoracic esophageal cancer divided into two groups: a conversion surgery group (n = 54) and a non-surgical treatment group (n = 97). The survival rate of the R0 curative resection subgroup in the conversion surgery group was comparable to the survival rate of the clinical complete response (cCR) subgroup in the non-surgical treatment group. This finding is consistent with that of a previous report.³ This raises the question: is conversion surgery actually necessary for patients with resectable esophageal cancer who exhibit a cCR in response to induction therapy? Ohkura et al previously reported that the recurrence-free survival and the disease-specific survival were significantly better in esophageal cancer patients who underwent an esophagectomy than in patients who received nonsurgical treatment, but that the overall survival (OS) did not differ significantly between the two groups because of a higher risk of late effects (e.g. respiratory complications)

among patients who achieved a cCR after neoadjuvant therapy.⁵ The intensive care of late effects may reduce the incidence of deaths from causes other than recurrence and may eventually improve the OS.

"Watch and wait" is a novel management strategy in patients with rectal cancer who exhibit a cCR after neoadjuvant CRT. This strategy offers the advantage of organ preservation, but the risk of recurrence remains a disadvantage. The success of the watch and wait strategy reportedly depends on the initial tumor stage.⁶ This strategy might also be worth considering as a new strategy for limited patients with cT4b esophageal cancer who exhibit a cCR in response to induction CRT once accurate methods for diagnosing cCR have been established.

It is usually difficult to determine the possibility of R0 resection preoperatively using currently available diagnostic imaging methods in patients with cT4b esophageal cancer who exhibit a clinical response to induction treatment. Ohkura et al reported that advantageous factors for a R0 curative resection were T4b tumor invasion at the primary site, compared with lymph node metastasis, and a time to conversion surgery from the start of induction therapy within 4 months. The survival rate of patients with cT4b tumor invasion at the primary site was higher than that of patients with invasion from metastatic lymph nodes. They explained this outcome as follows: the high malignant potential of tumors with treatment resistance may lead to a non-curative resection, since the rate of poorly differentiated tumor was significantly higher among patients with T4b invasion at a metastatic lymph node than those with invasion at the primary tumor. Poorly differentiated tumors are likely to have a higher risk of invasion and strong treatment resistance. The survival rate of patients who underwent conversion surgery within 4 months from the start of induction therapy was higher than that of patients who underwent conversion surgery later than 4 months. They explained this factor as follows: because a 3-month interval from the start of induction therapy and surgery is minimal, "time to conversion surgery from start of induction therapy within 4 months" means that the tumor showed a good response to the treatment and that an R0 curative resection was highly achievable.

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As for the optimal extent of lymph node dissection in conversion esophagectomy, most esophageal surgeons perform a primary tumor resection without lymph node dissection or with the dissection of only lymph nodes suspected of containing a metastasis to avoid perioperative complications, because conversion esophagectomy was associated with relatively higher perioperative mortality (0%-21%) and morbidity (29%-87%).⁷ Ohkura et al reported that the survival rate of patients who underwent a D2/3 lymphadenectomy was significantly higher than that of patients who underwent a D0/1 lymphadenectomy. Furthermore, 57% of patients who underwent prophylactic lymph node dissection had histopathologically confirmed viable cancer cells within the dissected regional lymph nodes. Among these patients, 36% of patients had regional lymph node metastases that had produced neither enlargement nor suspicious findings before induction therapy and before conversion surgery. The importance of the authors' interpretation of these findings—that except for cases of apparent non-curative resection, a standard radical lymph node dissection including prophylactic dissection should be attempted while taking adequate care to prevent postoperative complications—should not be overlooked.

To obtain better results from conversion surgery for patients with cT4b thoracic esophageal cancer, (a) the likelihood of an R0 curative resection, (b) the absence of lymph node invasion, (c) a time to conversion surgery from the start of induction therapy within 4 months, and (d) the inclusion of a prophylactic D2-3 lymphadenectomy, if possible, should be taken into consideration.

DISCLOSURE

Conflicts of Interest: The author declares no conflicts of interest for this article.

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REFERENCES

1. Japan Esophageal Society. Japanese classification of esophageal cancer, 11th edition: part I. *Esophagus*. 2017;14:1-36.
2. Kitagawa Y, Uno T, Oyama T, Kato K, Kato H, Kawakubo H, et al. Esophageal cancer practice guidelines 2017 edited by the Japan Esophageal Society: part 1. *Esophagus*. 2019;16:1-24.
3. Miyata H, Sugimura K, Motoori M, Omori T, Yamamoto K, Yanagimoto Y, et al. Clinical implications of conversion surgery after induction therapy for T4b thoracic esophageal squamous cell carcinoma. *Ann Surg Oncol*. 2019;26:4737-43.
4. Ohkura Y, Ueno M, Udagawa H. Advantageous factors of R0 curative conversion esophagectomy and the optimal extent of lymphadenectomy after induction therapy for cT4b thoracic esophageal cancer. *Ann Gastroenterol Surg*. <https://doi.org/10.1002/ags3.12416>
5. Ohkura Y, Shindoh J, Ueno M, Iizuka T, Udagawa H. Comparison of outcome of esophagectomy versus nonsurgical treatment for resectable esophageal cancer with clinical complete response to neoadjuvant therapy. *Ann Surg Oncol*. 2018;25:2428-33.
6. Marijnen CA. Organ preservation in rectal cancer: have all questions been answered? *Lancet Oncol*. 2015;16:e13-22.
7. Makino T, Yamasaki M, Tanaka K, Miyazaki Y, Takahashi T, Kurokawa Y, et al. Treatment and clinical outcome of clinical T4 esophageal cancer: a systematic review. *Ann Gastroenterol Surg*. 2018;3:169-80.

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