



# Minimally invasive esophagectomy with hybrid position can be a promising surgical procedure to achieve radical lymphadenectomy with less postoperative complication

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Esophageal cancer has been a dismal disease because it metastasizes even in the early stage, and it is the 8th leading cause of cancer death worldwide in 2018 (1-3). Multidisciplinary treatment consisting of surgery, chemotherapy, and radiotherapy helped to improve treatment outcomes (4,5). Since 2000, a number of landmark trials have been reported for surgically resectable esophageal cancer and preoperative chemo-/chemoradiotherapy followed by surgery was established as a standard (6-8). More recently, the immune checkpoint inhibitors were reported to be beneficial for metastatic esophageal cancer (9), and it is about to be transferred to neoadjuvant setting (10). Although multidisciplinary treatment is vital, surgical resection has been a mainstay to cure esophageal cancer patients (11).

Esophageal cancer has a widely spread lymphatic route and induces metastasis from the cervix to abdominal field especially in esophageal squamous cell carcinoma (ESCC) (1,2,12). Takeuchi *et al.* validated the sentinel lymph node (LN) mapping in cT1N0 ESCC and confirmed that esophageal cancer located at the middle thoracic esophagus has sentinel LN in cervical and abdominal field at higher than 10% (12-14). Udagawa *et al.* reviewed the distribution of LN metastasis and the efficacy for each LN station (15). To achieve radical lymphadenectomy, three-field LN dissection was reported to improve patient survival and has been conducted as a standard treatment (16-18). On the other hand, esophagectomy is highly invasive and highly morbid. Takeuchi *et al.* found that the operative

morality was 3.4% using the Japanese nationwide registry data. Similarly to other cancer types, the postoperative complication was shown to negatively affect prognosis (19). Furthermore, we previously reported that the postoperative systemic inflammatory response induced by esophagectomy could induce cancer relapse and worsen the prognosis independent of postoperative complications (20). Therefore, establishing safe surgical procedure with less morbidity and mortality has been desirable.

Minimally invasive esophagectomy (MIE) has been introduced in 1992 and has been widespread worldwide (21). Smaller incision and modification of lung mobilization decrease surgical stress. Biere *et al.* conducted a randomized control trial comparing MIE with open esophagectomy and found a significant reduction in pulmonary complication in MIE group (22). The Japanese nationwide registry data was consistent with the result (23). On the other hand, there are few studies comparing the long-term outcome between MIE and open surgery. The current phase III trial, JCOG 1409, will provide the answer to the remaining question (24).

In the current era of MIE, the surgical approach could be a key component that affects the postoperative course. In terms of patient position during thoracic approach, the left lateral or prone position has been widely used. The hybrid position—prone and left lateral decubitus—was developed in 2009 and its utility was reported on 2014 (25). As Kikuchi *et al.* described, upper mediastinal LN dissection with lateral position helps to mobilize the esophagus and bronchus, which could lead safer and radical lymphadenectomy of

nodes along the bilateral recurrent laryngeal nerve. In middle and lower mediastinal LN dissection, prone position is beneficial to keep the mediastinum spacious and eradicate paraesophageal tissue from aorta and contralateral pleura. We recently reported that MIE with hybrid position and extensive LN dissection extended survival in cStage I ESCC in which surgical resection is vital to cure the disease (26). On the other hand, a comparative study with prone and hybrid position is required to prove its superiority to prone position.

In a current study, Kikuchi *et al.* successfully compared prone with hybrid position in MIE. Despite the more advanced-stage disease in hybrid group, MIE with hybrid position demonstrated shorter operation time and was proven to reduce the incidence of postoperative recurrent laryngeal nerve palsy (RLNP), which was reasonable because the operator and assistant can coordinately perform lymphadenectomy in the hybrid position. On the other hand, the diagnosis of trivial RLNP focused on the current report is challenging without routine evaluation using laryngeal scope. Furthermore, the RLNP is occasionally induced by cervical LN dissection in case of three field lymphadenectomy. The validation of current result in the expanded cohort is desirable.

The number of LN retrieved was expected to increase in the hybrid position, whereas there was no difference between groups in the current result. The following points can be given as reasons. First, in the upper mediastinal LN dissection, the cervical approach which was efficiently combined with prone position was equivalent to extensive mediastinal LN dissection by hybrid position. Second, since thoracic duct resection was reported to increase the number of LN retrieved (26,27), there might be the difference in the percentage of patients who underwent TD resection.

As stated in the discussion by Kikuchi *et al.*, to achieve less invasive MIE, robot-assisted MIE (RAMIE) has been introduced. van der Sluis *et al.* conducted a randomized control trial comparing RAMIE with open esophagectomy and found that RAMIE significantly reduced pulmonary complications (28). The same group is currently running subsequent phase III trial comparing MIE with RAMIE.

Again, Kikuchi *et al.* should be commended for successfully suggesting the utility of hybrid position in MIE. This manuscript is highly valuable as a first report that showed the benefit of hybrid position compared with prone position. Along with the establishment of minimally invasive surgery, the safety and efficacy of multidisciplinary treatment has been improved. In Netherlands, SANO

trial has been evaluating the safety of organ preservation approach in those who responded to neoadjuvant chemoradiotherapy, based on the remarkable response rate of neoadjuvant chemoradiotherapy (29-31). Utilizing upgraded biomarker to classify patients (32), organ preservation approach can be safely applied for responders in the near future. We need to establish the ideal treatment that is the least invasive with adequate efficacy, taking into account the advancement of surgical procedure and perioperative treatment.

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