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Thoracic cavity-to-cage ratio is a predictor of technical difficulties in minimally invasive esophagectomy

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Abstract

Background

Technical difficulties are occasionally encountered when performing conventional minimally invasive esophagectomy (C-MIE) and robot-assisted MIE (RAMIE) in patients with a narrow thoracic cavity. Thoracic cavity-to-cage ratio (TCCR) is an indicator of thoracic cavity length. We hypothesized that TCCR can be a predictor of technical difficulties in C-MIE and RAMIE.

Methods

We evaluated 340 patients who underwent MIE for esophageal squamous cell carcinoma between April 2010 and March 2021. TCCR was calculated as the diameter of the thoracic cavity to that of the thoracic cage at the brachiocephalic vein, tracheal bifurcation, and inferior right pulmonary vein levels. Moreover, TCCR score, which is an indicator of the whole thoracic cavity length based on TCCR at the three levels, was defined. The thoracic procedure time was considered an indicator of surgical difficulty.

Results

We divided the patients into the C-MIE (n = 295) and RAMIE (n = 45) groups. The patients in each group were divided into two cohorts according to median thoracic procedure time. Based on a multivariate analysis, body mass index (p = 0.0007), clinical N (p = 0.0191), and TCCR score (p = 0.0005) were independent factors for thoracic procedure time in the C-MIE group. Moreover, TCCR at the tracheal bifurcation level (p = 0.0331) was the only independent factor for thoracic procedure time in the RAMIE group.

Conclusions

TCCR could be a predictor of technical difficulties in both C-MIE and RAMIE.

Introduction

Esophageal cancer is the 10th most frequent cancer and is the 6th most common cause of cancer-related deaths. [1] In East Asian countries, esophageal squamous cell carcinoma (ESCC) is the major histologic type. Although radical esophagectomy is a promising treatment option, it is also among the most invasive surgical procedures for esophageal cancer. In 1992, Cuschieri et al. [2] initially showed thoracoscopic esophagectomy as a minimally invasive esophagectomy (MIE). Moreover, the incidence of respiratory complications was significantly lower in thoracoscopic esophagectomy than in open procedure. Biere et al. [3] revealed that conventional MIE (C-MIE) is associated with a lower incidence of pulmonary infection, better short-term quality of life, decreased volume of blood loss, and shorter hospital stays. Parel et al. [4] showed that the long-term oncological outcomes of C-MIE may be similar to those of open esophagectomy. By contrast, C-MIE requires a more skilled technique and longer operative time than open esophagectomy. [3] Previous studies have shown that C-MIE was stabilized after 30–40 procedures. [5-9] Robot-assisted minimally invasive esophagectomy (RAMIE) was first reported in 2003. [10] RAMIE can overcome the technical limitations of C-MIE. Some studies revealed that RAMIE is safe in terms of postoperative complications and oncological outcomes. [7, 11-16] C-MIE and RAMIE for esophageal cancer have been increasingly used worldwide.

However, technical difficulties are occasionally encountered when performing C-MIE or RAMIE in some cases. Moreover, studies about preoperative factors affecting surgical difficulties in MIE, particularly RAMIE, are extremely limited. We hypothesized that thoracic cavity length is associated with technical difficulties in MIE. Thoracic cavity-to-cage ratio (TCCR), which is an indicator of thoracic cavity length, was defined. Therefore, the current study aimed to evaluate whether TCCR is associated with thoracic procedure time in C-MIE and RAMIE.

Materials and methods

Patients and data extraction

In total, 457 patients who underwent esophagectomy for thoracic ESCC between April 2010 and March 2021 at Kobe University were evaluated. Patients with distant metastases, neoadjuvant chemoradiation therapy, salvage surgery, and missing records were excluded. Finally, 340 patients were analyzed. The diagnosis of esophageal cancer was based on biopsy before surgery or treatment with neoadjuvant chemotherapy. All cases were staged according to the 8th version of the TNM staging system for ESCC of the American Joint Committee on Cancer and the Union for International Cancer Control. [17] This study was approved by the institutional review board and ethics committee of Kobe University. Operative and clinical data (age, sex, clinical T [cT], clinical N [cN], thoracic procedure time, and volume of blood loss) were obtained from the medical records of patients. All data were extracted from a registered database.

Treatment strategy

At our institution, patients, excluding those with clinical T1, N0, M0 status, were treated with cisplatin/5-fluorouracil (CF) neoadjuvant chemotherapy regimen. The CF regimen comprised 800 mg/m^2 of 5-fluorouracil, administered as a continuous 24-h intravenous infusion, and 80 mg/m^2 of intravenous cisplatin on days 1–5. Esophagectomies were performed after two cycles of neoadjuvant chemotherapy. Until

2018, all patients with ESCC underwent C-MIE in prone position. Then, RAMIE was approved by the Japanese insurance system in 2018, and its application was introduced in the same year. Hence, procedures performed between 2010 and 2018 commonly comprised C-MIE. Since 2018, RAMIE has been conducted as much as possible without arbitrary patient selection. In C-MIE, all surgeons had more than 60 cases before this study and were not affected by the impact of surgeon experience. Although the number of RAMIE cases was not large, it is performed by operators who have experienced more than 300 cases of C-MIE.

Surgery

All patients with MIE underwent either C-MIE or RAMIE (da Vinci® Xi Surgical System, Intuitive Surgical, Inc., Sunnyvale, CA) in prone position. Under single-lumen tracheal tube intubation, a blocker was inserted into the right bronchus for one-lung ventilation anesthesia. In C-MIE, the thoracic procedure was performed with five trocars inserted into the intercostal space (ICS). In RAMIE, four 8- or 12-mm ports were inserted into the third, fifth, seventh, and ninth ICSs along the middle axillary line. Meanwhile, an assistant port was inserted into the sixth ICS in the anterior axillary line. Carbon dioxide pneumothorax was accomplished at a pressure of 8 mmHg. The surgical techniques for RAMIE and C-MIE have been published in detail in previous studies. [18-20]

Thoracic cavity-to-cage ratio

We analyzed all presurgical computed tomography (CT) scan images, which were obtained using cervico-thoraco-abdominal CT scan while in supine position.

Moreover, the distance from the dorsal edge of the sternum to the ventral edge of the vertebral body (diameter of the thoracic cavity) and the distance from the ventral edge of the sternum to the tip of the spinous process (diameter of the thoracic cage) at the brachiocephalic vein (BV) (Figure 1A), tracheal bifurcation (TB) (Figure 1B), and inferior right pulmonary vein (IRPV) levels (Figure 1C) on axial CT images. TCCR was calculated as the diameter of the thoracic cavity to that of the thoracic cage at each level. The TCCR cutoff value at each level was determined via a receiver operating characteristic (ROC) analysis. [21, 22]

Subsequently, we defined TCCR score as the total points based on TCCR. Specifically, a TCCR greater than or equal to the cutoff value at one level is assigned with one point. Consequently, the TCCR score comprises four degrees (0, 1, 2, and 3) since it is evaluated at three levels (BV, TB, and IRPV).

The images were analyzed using the Synapse VINCENT image analysis system (Fujifilm Medical, Tokyo, Japan) by a single observer (TA) who was blinded to the clinical information of patients.

Statistical analysis

Univariate and multivariate analyses using the logistic regression model were performed to identify the independent factors of thoracic procedure time. The optimal cutoff values of continuous variables were determined via an ROC analysis if necessary. All analyses were conducted with the JMP 13 software program (SAS Institute, Cary, NC, the USA). Any variable considered significant ($p < 0.05$) in the univariate analysis was a candidate for the multivariate analysis. A p value of < 0.05 was considered statistically significant.

Results

Characteristics of patients

In total, 340 patients from our database were included. Among them, 281 and 59 were men and women, respectively, with a median age of 67 (range: 40–83) years. Moreover, 217 (63.8%) patients received preoperative therapy. The patients were divided into the C-MIE group (n = 295; 86.8%) and the RAMIE group (n = 45; 13.2%). Table 1 shows the characteristics of patients in each group. The median TCCR at the BV, TB, and IRPV levels were 0.4750, 0.5285, and 0.5600 in the C-MIE group, and 0.4712, 0.5197, and 0.5504 in the RAMIE group, respectively. The median thoracic procedure times in the C-MIE and RAMIE groups were 310 (159–600) and 430 (240–540) min. The median volumes of blood loss in the C-MIE and RAMIE groups were 170 (0–2605) and 40 (0–380) mL, respectively.

Factors influencing thoracic procedure time in C-MIE and RAMIE

The patients in each group were divided into two cohorts according to median thoracic procedure time (C-MIE group: 310 min and RAMIE group: 430 min, respectively). Based on the ROC analysis of median thoracic procedure time, the cutoff value of TCCR at the BV, TB, and IRPV levels in the C-MIE group were 0.5079, 0.5248, and 0.5759, and the AUCs were 0.5688, 0.5738, and 0.5618 (p = 0.0299, 0.0720, and 0.2474, respectively). The TCCR cutoff value at the BV, TB, and IRPV levels in the RAMIE group were 0.4517, 0.4980, and 0.5208, and the AUCs were 0.6522, 0.7312, and 0.6522 (p = 0.0635, 0.0047, and 0.0667, respectively).

In the C-MIE group, the univariate analysis showed that body mass index (BMI), cN, and TCCR at the three levels were correlated with thoracic procedure time (Table 2). Moreover, the TCCR score was correlated with thoracic procedure time in the univariate analysis. Moreover, it was used in the multivariate analysis. The multivariate analysis showed that BMI (hazard ratio [HR] = 2.4598; 95% confidence interval [CI]: 1.4583–4.1491; p = 0.0007), cN (HR = 1.7859; 95% CI: 1.0995–2.9006; p = 0.0191), and TCCR score (HR = 2.4580; 95% CI: 1.4807–4.0806; p = 0.0005) were independent factors for thoracic procedure time (Table 3). In the RAMIE group, the univariate analysis revealed that age, BMI, and TCCR at the TB level were correlated with thoracic procedure time (Table 4). The TCCR score did not significantly differ in the univariate analysis. Based on the multivariate analysis, the TCCR at the TB level (HR = 13.3650; 95% CI: 1.4364–124.3527; p = 0.0227) was an independent factor for thoracic procedure time (Table 5).

Discussion

This study showed that a small TCCR was associated with prolonged thoracic procedure time in MIE. Extremely few studies have shown the predictive factors of technical difficulties in C-MIE. Fujiwara et al. [23] showed that clinical T3, a tumor associated factor, was a predictor of surgical difficulties. In our study, cN was correlated with thoracic procedure time. Patients with advanced-stage tumors and lymph node metastases can be difficult to operate due to edema and infiltration in the surrounding tissues. Moreover, BMI was correlated with surgical difficulties, [24] and this result is similar to that of this study. One thing especially worth mentioning is that there was no correlation between BMI and TCCR (data not shown), and both were independent predictors of surgical difficulties. Okamura et al. [25] revealed that the extent of mediastinal adiposity influenced thoracic procedure time and recurrent laryngeal nerve palsy. Moreover, it was more closely correlated with thoracic procedure time compared with BMI. Excessive fat volume could prohibit the accurate identification of vessels, organs, and nerves, leading to prolonged procedure time. Some studies showed the association between technical difficulties and the characteristics of anatomical structures. The sternum-vertebra distance, [23] area of the upper thoracic cage, [6] deep-seated esophagus, [26] and vertebral body projection at the middle thoracic part [27] were the predictive factors of technical difficulties in C-MIE. These predictors may be factors representing the thoracic cavity length. A narrow thoracic cavity inhibits proper tissue retraction for dissecting the esophagus and regional lymph nodes. In this study, when the absolute value of the distance from the dorsal edge of the sternum to the ventral edge of the vertebral body (diameter of the thoracic cavity) was smaller, the thoracic procedure time was shorter (data not shown). This might be attributed to the fact that most short-distance cases had a small physical size, and the range of dissection became smaller. TCCR may be a simple and direct factor that could evaluate the relative thoracic cavity length, regardless of physical size. We considered that each TCCR at the BV, TB, and IRPV levels reflects the upper, middle, and lower thoracic cavity length, respectively. In this study, in the C-MIE group, the TCCRs at all levels were correlated with thoracic procedure time in the univariate analysis. Hence, a comprehensive assessment of the whole thoracic cavity, which can reflect the indexes of all three levels, must be conducted. Therefore, the TCCR score was defined and used as an indicator of the whole thoracic cavity length in the multivariate analysis. In performing C-MIE, the forceps motion is limited, and highly skilled techniques are required for dissecting the esophagus and lymph nodes. Therefore, the comprehensive narrowness comprised the BV (upper mediastinum), TB (middle mediastinum), and IRPV (lower mediastinum) levels might affect thoracic procedure time.

RAMIE was first reported in 2003. [10] Robotic surgery offers a stable three-dimensional, enlarged view and improves a surgeon's dexterity due to the use of articulated instruments with seven flexible joints. These features can make up for the disadvantages of C-MIE. Upper mediastinum manipulation includes lymph node dissection along the recurrent laryngeal nerve. The dissection of this area is one of the oncologicaly important procedures in radical esophagectomy for esophageal cancer. [28] However, this procedure can cause recurrent laryngeal nerve palsy. Hence, a skilled technique is required. In this study, the TCCR at the BV level (reflecting the upper mediastinum length) was associated with thoracic procedure time in the C-MIE group, but not in the RAMIE group. The superiority of robotic surgery might counteract the impact of the narrow upper mediastinum. Moreover, we previously reported that RAMIE is superior to C-MIE in prone position in decreasing the incidence of left recurrent laryngeal nerve palsy. [16] Based on these facts, RAMIE may be particularly useful for manipulating the upper mediastinum. In the RAMIE group, the multivariate analysis showed that only the TCCR at the TB level (reflecting the middle mediastinum length) was associated with thoracic procedure time. An appropriate surgical field and retraction may be difficult to achieve in the middle mediastinum due to the presence of anatomically firm structures such as the TB and aortic arch even with robotic assistance. To the best of our knowledge, this is the first study that assessed the predictors of technical difficulties in RAMIE.

MIE is one of the most challenging gastroenterological surgeries, and prolonged operative time is correlated with a higher risk of postoperative complications. [29]

Therefore, predicting technical difficulty in MIE is useful for allocating patients to trainees or experienced surgeons. Furthermore, TCCR may be effective when used as a criterion for determining the adaptation of C-MIE and RAMIE.

Our study had several limitations. That is, it was a single-center retrospective study, and the sample size, particularly patients who underwent RAMIE, was relatively small. And, both C-MIE and RAMIE need learning curves for stabilizing the procedure. Since the number of RAMIE cases was rather small, it is possible that the RAMIE surgeon is still in the middle of the learning curve, and it seems necessary to evaluate it again after the training period. Owing to these limitations, the optimal TCCR cutoff value can be modified. Therefore, further multicenter prospective studies with a large sample size should be conducted to confirm the TCCR clinical value at each level among patients with ESCC.

Conclusion

TCCR could be a predictor of technical difficulties in both C-MIE and RAMIE. In C-MIE, thoracic procedure time was affected by the whole thoracic cavity length due to the restricted mobilities of thoracoscopic instruments. By contrast, in RAMIE cases, the joint function could overcome the disadvantages of C-MIE. Consequently, only the TCCR at the TB level, which may be the less flexible field, was found to be a predictor of surgical difficulties. Hence, these results could be useful when determining the adaptation of C-MIE and RAMIE among novice and experienced professionals.

Conflict of interest/Disclosure

The authors have no related conflicts of interest to declare.

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Figure legends

Figure 1

Measurement of thoracic cavity diameter (solid double-headed arrow) and cage (dashed double-headed arrow) at the (A) brachiocephalic vein, (B) tracheal bifurcation, and (C) inferior right pulmonary vein levels

Table 1 Clinicopathological characteristics of the patients.

Factors	**C-MIE group (n = 295)**	**RAMIE group (n = 45)**
Age (years, median, range)	68 (40–83)	66 (45–80)
Sex (male/female)	252/43	29/16
BMI (kg/m^2, median, range)	21.12 (13.60–30.92)	21.49 (15.96–26.17)
Neoadjuvant chemotherapy (+/−)	193/102	24/21
Tumor location (Lt/Mt/Ut)	94/147/54	15/20/10
Maximum tumor diameter (mm, median, range)	34 (0–200)	37 (6–175)
TCCR at the BV level (median, range)	0.4750 (0.3824–0.6502)	0.4712 (0.3862–0.5660)
TCCR at the TB level (median, range)	0.5285 (0.4101–0.7573)	0.5197 (0.4524–0.5873)
TCCR at the IRPV level (median, range)	0.5600 (0.4171–0.8069)	0.5504 (0.4441–0.6038)
Total TCCR score (0/1/2/3)	6/70/67/62	20/14/7/4
cT (≥ 3/< 3)	129/166	17/28
cN (+/−)	153/142	21/24
Thoracic procedure time, min (median, range)	310 (159–600)	430 (240–540)
Volume of blood loss, mL (median, range)	170 (0–2605)	40 (0–380)

C-MIE, conventional minimally invasive esophagectomy; RAMIE, robot-assisted minimally invasive esophagectomy; BMI, body mass index, TCCR, thoracic cavity-to-cage ratio; BV, brachiocephalic vein; TB, tracheal bifurcation; IRPV, inferior right pulmonary vein; cT, clinical T; cN, clinical N

Table 2 Univariate analysis of the predictive factors of technical difficulties in C-MIE

Factors	**Thoracic procedure time (min)**		**Odds ratio**	**95% CI**	**Univariate analysis (*p* value)**
	≥ 310 (n = 148)	**< 310 (n = 147)**			
Age (years) (≥ 77/< 77)	11/137	16/131	0.6574	0.2942–1.4692	0.3027
Sex (male/female)	131/17	121/26	1.6558	0.8563–3.2017	0.1301
BMI (kg/m^2) (≥ 22.44/< 22.44)	61/87	34/113	2.3303	1.4076–3.8578	**0.0010**
Neoadjuvant chemotherapy (+/−)	102/46	91/56	1.3645	0.8430–2.2088	0.2051
Tumor location					
Lt	43	51	1.000	-	-
Mt	78	69	1.3407	0.7977–2.2534	0.2683
Ut	27	27	1.1860	0.6068–2.3184	0.6178
Maximum tumor diameter (mm) (≥ 38/< 38)	55/84	64/77	0.7878	0.4900–1.2665	0.3243
TCCR at the BV level (< 0.5079/≥ 0.5079)	124/24	104/43	2.1362	1.2162–3.7522	**0.0083**
TCCR at the TB level (< 0.5248/≥ 0.5248)	76/72	56/91	1.7153	1.0792–2.7263	**0.0225**
TCCR at the IRPV level	104/44	81/66	1.9259	1.1924–3.1107	**0.0074**

(< 0.5759/≥ 0.5759)					
Total TCCR score (0, 1/2, 3)	105/43	79/68	2.1019	1.3043–3.4158	**0.0022**
cT (≥ 3/< 3)	71/77	58/89	1.4149	0.8915–2.2457	0.1409
cN (+/−)	86/62	67/80	1.6562	1.0451–2.6247	**0.0311**

C-MIE, conventional minimally invasive esophagectomy; BMI, body mass index; TCCR, thoracic cavity-to-cage ratio; BV, brachiocephalic vein; TB, tracheal bifurcation; IRPV, inferior right pulmonary vein; cT, clinical T; cN, clinical N

Table 3 Multivariate analysis of the predictive factors of technical difficulties in C-MIE

Factors	**Odds ratio**	**95% CI**	***p value***
BMI (kg/m^2) (≥ 22.44/< 22.44)	2.4598	1.4583–4.1491	**0.0007**
Total TCCR score (0, 1/2, 3)	2.4580	1.4807–4.0806	**0.0005**
cN (+/−)	1.7859	1.0995–2.9006	**0.0191**

C-MIE, conventional minimally invasive esophagectomy; BMI, body mass index; TCCR, thoracic cavity-to-cage ratio; cN, clinical N

Table 4 Univariate analysis of the predictive factors of technical difficulties in RAMIE

Factors	**Thoracic procedure time (min)**		**Odds ratio**	**95% CI**	**Univariate analysis (*p* value)**
	≥ 430 (n = 23)	**< 430 (n = 22)**			
Age (years) (≥ 62/< 62)	11/12	17/5	0.2696	0.0742–0.9792	**0.0464**
Sex (male/female)	14/9	15/7	0.7259	0.2128–2.4767	0.6090
BMI (kg/m^2) (≥ 20.22/< 20.22)	12/11	18/4	0.2424	0.0624–0.9423	**0.0323**
Neoadjuvant chemotherapy (+/−)	13/10	11/11	1.3	0.4019–4.2050	0.6614
Tumor location					
Lt	7	8			-
Mt	9	11	0.9351	0.2440–3.5836	0.9220
Ut	7	3	2.6667	0.4917–14.4610	0.2555
Maximum tumor diameter (mm) (≥ 20/< 20)	20/2	16/5	3.1250	0.5341–18.2857	0.1858
TCCR at the BV level (< 0.4517/≥ 0.4517)	10/13	4/18	3.4615	0.8872–13.5058	0.0738
TCCR at the TB level (< 0.4980/≥ 0.4980)	10/13	1/21	16.1538	1.8465–141.3212	**0.0119**
TCCR at the IRPV level (< 0.5208/≥ 0.5208)	9/14	3/19	4.0714	0.9289–17.8462	0.0626

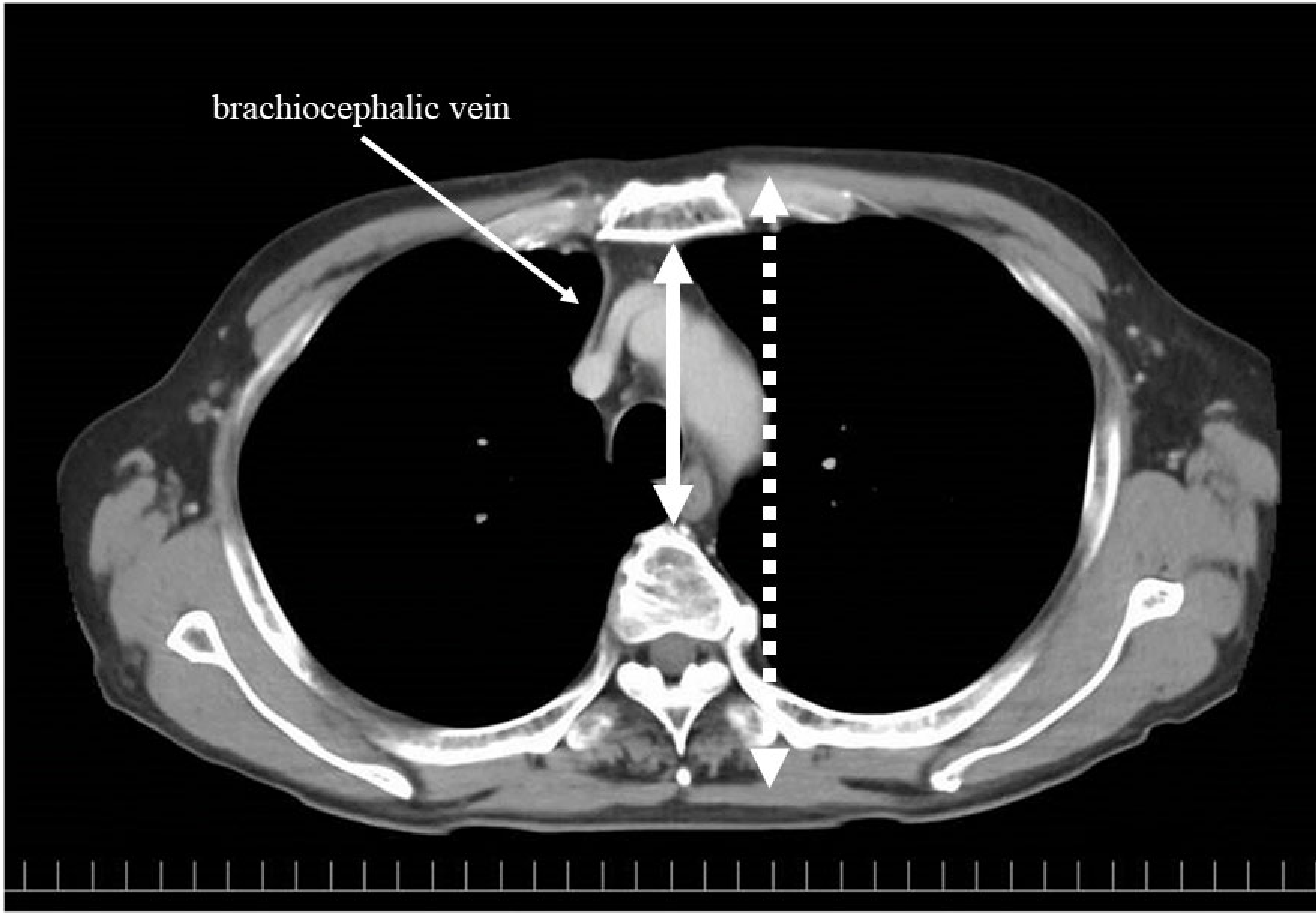
Total TCCR score (0, 1/2, 3)	7/16	3/19	2.7708	0.6138–12.5073	0.1851
cT (≥ 3/< 3)	11/12	6/16	2.4444	0.7040–8.4882	0.1593
cN (+/−)	13/10	8/14	2.275	0.6869–7.5351	0.1785

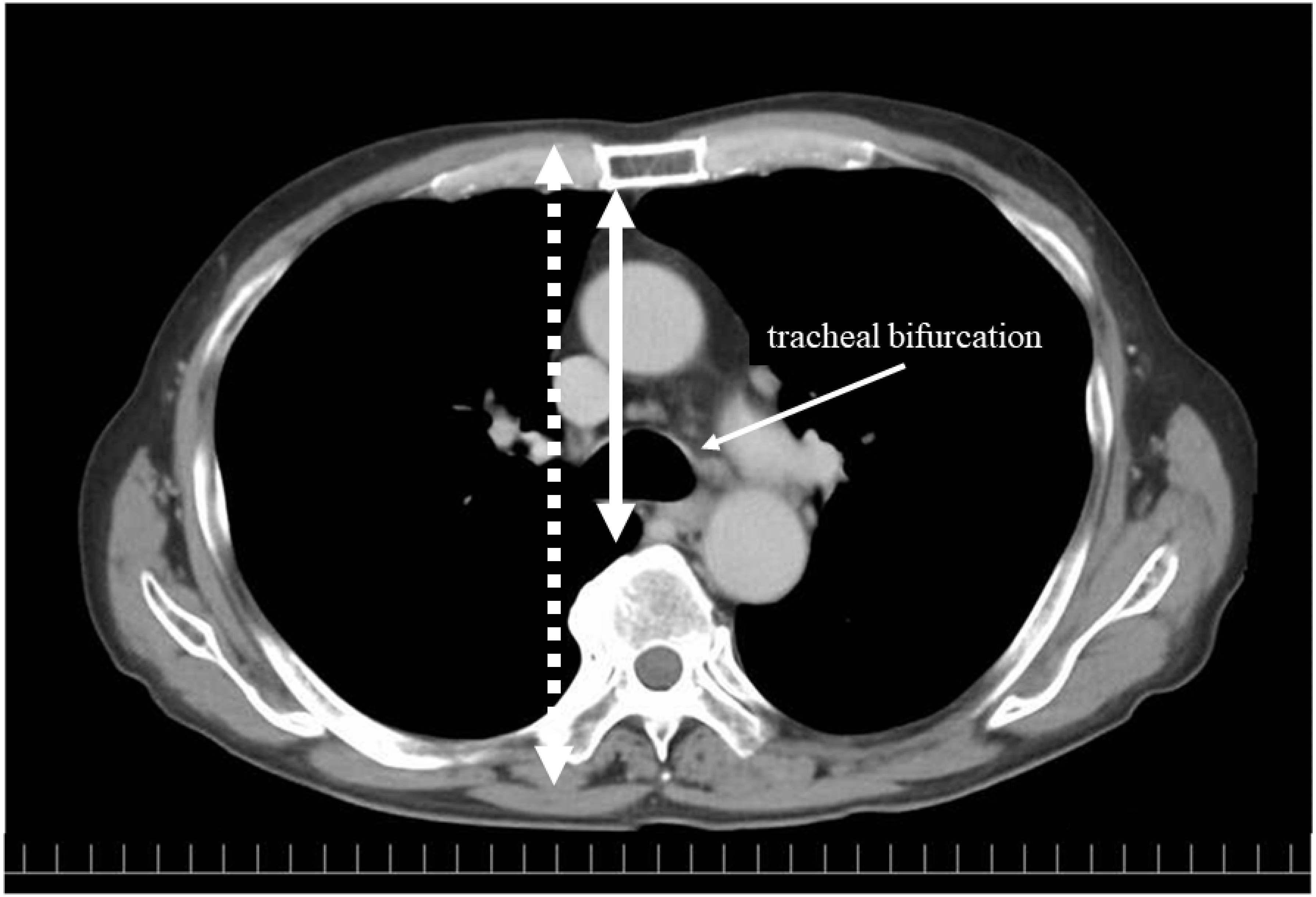
RAMIE, robot-assisted minimally invasive esophagectomy; BMI, body mass index; TCCR, thoracic cavity-to-cage ratio; BV, brachiocephalic vein; TB, tracheal bifurcation; IRPV, inferior right pulmonary vein; cT, clinical T; cN, clinical N

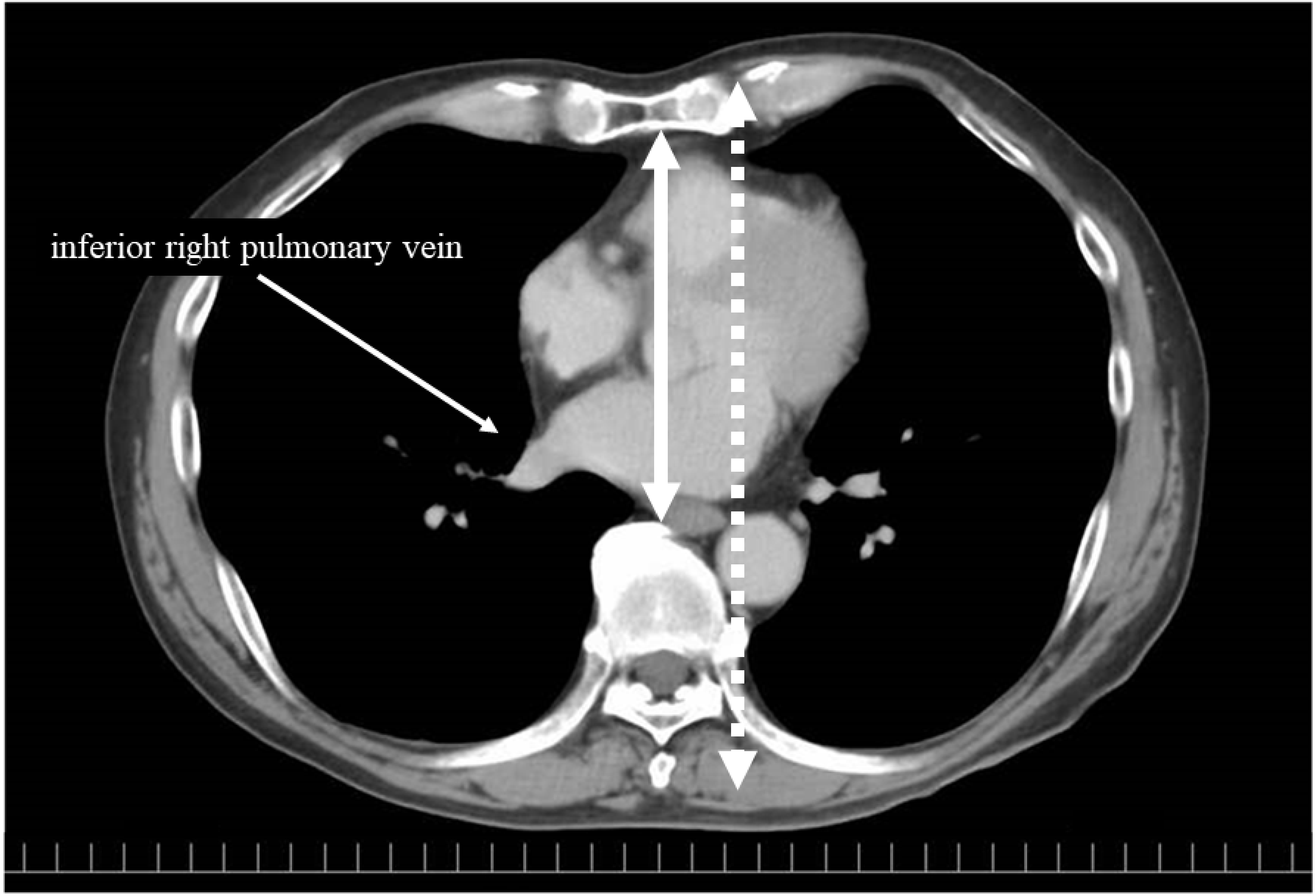
Table 5 Multivariate analysis of the predictive factors of technical difficulties in RAMIE

Factors	**Odds ratio**	**95% CI**	***p value***
Age (years) (≥ 62/< 62)	0.3610	0.0828–1.5738	0.1750
BMI (kg/m^2) (≥ 20.22/< 20.22)	0.2815	0.0615–1.2889	0.1025
TCCR at the TB level (< 0.4980/≥ 0.4980)	13.3650	1.4364–124.3527	**0.0227**

RAMIE, robot-assisted minimally invasive esophagectomy; BMI, body mass index; TCCR, thoracic cavity-to-cage ratio; TB, tracheal bifurcation


brachiocephalic vein


tracheal bifurcation


inferior right pulmonary vein